Body Mass Index Recovery after Lung Transplant for Cystic Fibrosis

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Abstract

Rationale: Many lung transplant recipients with cystic fibrosis (CF) have low preoperative body mass index (BMI); however, post-transplant BMI recovery is not well understood.

Objectives: To evaluate BMI recovery (≥ 18.5 kg/m^2) among CF lung transplant recipients with low preoperative BMI and to investigate the association of survival with BMI recovery.

Methods: The United Network for Organ Sharing and CF Foundation patient registries (June 2005–December 2016) were used to identify CF lung transplant recipients. Among recipients surviving ≥ 1 year, Cox modeling compared post-transplant 1-year conditional survival between recipients with low (<17 and 17–18.49 kg/m^2) versus normal preoperative BMI, stratified by BMI recovery.

Results: Of 1,977 CF lung transplant recipients, 272 (14%) and 449 (23%) had a preoperative BMI of <17 and 17–18.49 kg/m^2, respectively. For subgroups with a BMI of <17 and 17–18.49 kg/m^2, 29% versus 49%, respectively, of those alive at 1 year recovered their BMI. Among recipients with low preoperative BMI, adjusted post-transplant 1-year conditional survival was worse than that in those with preoperative BMI ≥ 18.5 kg/m^2; however, BMI recovery mitigated this. Preoperative BMI < 17 kg/m^2 had an adjusted hazard ratio of 1.29 (95% confidence interval [CI], 0.92–1.81) with BMI recovery versus 1.57 (95% CI, 1.09–2.25) without recovery, and preoperative BMI 17–18.49 kg/m^2 had an adjusted hazard ratio of 1.28 (95% CI, 1.02–1.61) with BMI recovery versus 1.72 (95% CI, 1.14–2.59) without recovery.

Conclusions: Patients with lower preoperative BMI were less likely to achieve BMI recovery within 1 year. However, for those who did, BMI recovery within 1 year after transplant was associated with longer survival.

Keywords: BMI; underweight; survival; forced expiratory volume in 1 second; lung function

Cystic fibrosis (CF) is an autosomal recessive disease that develops from mutations in the CFTR (cystic fibrosis transmembrane conductance regulator) gene (1). Although pulmonary complications are the primary driver of mortality, extrapulmonary manifestations, including malnutrition, are closely linked to morbidity and mortality (2). Promising therapeutics (e.g., CFTR modulators) can slow the decline in lung function and improve nutritional outcomes (3, 4), but lung transplant (LTx) continues to be required for many individuals with CF who experience progressive respiratory failure despite optimal medical management (5). Selecting candidates for LTx takes into account lung disease severity, as well as nutritional status and other medical comorbidities that correlate with post-transplant outcomes (6, 7).

Poor nutritional status as measured by body mass index (BMI) is an independent risk factor for pretransplant death in advanced cystic fibrosis lung disease (ACFLD), and low BMI is an indication for early referral to an LTx center (6, 8, 9). Underweight status has been shown to be common in ACFLD, with one study demonstrating BMI < 18.5 kg/m^2 in 42% of CF transplant recipients (10). The mechanism of weight loss and malnutrition in ACFLD is multifactorial, driven by significant energy expenditure (increased work of breathing from ACFLD and repeated respiratory infections), gut inflammation and pancreatic insufficiency resulting in malabsorption, and poor appetite (11, 12). Although several studies describe the impact of preoperative malnutrition on pre- and post-transplant outcomes in CF (13–18), there are limited data about the effects of post-transplant nutritional status on patient outcomes.

The aim of this study was to evaluate the proportion of CF LTx recipients with low preoperative BMI who recover BMI ($\geqslant 18.5$ kg/m^2) after transplant and to determine whether post-transplant BMI recovery is associated with improved survival. Given that impaired nutrition is in part related to ACFLD, we hypothesized that a majority of malnourished individuals with CF who undergo LTx would have a normal BMI ($\geqslant 18.5$ kg/m^2) within 1 year of LTx. Furthermore, we hypothesized that those with low preoperative BMI who did not reach a normal BMI by 1 year would have worse post-transplant 1-year conditional survival and lung function recovery than individuals who achieved a normal BMI. Some of the results of this study have been previously reported in the form of an abstract (19).

Methods

Population
This retrospective cohort study included individuals with CF in the United States who had their first single-organ LTx between June 1, 2005, and December 31, 2015; participants were included if they initially underwent transplant during the study period even if they subsequently underwent repeat transplant, with follow-up time starting at the first transplant. United Network for Organ Sharing (UNOS) registry data were provided by the Organ Procurement and Transplantation Network (OPTN) and merged with data from the Cystic Fibrosis Foundation Patient Registry (CFFPR). CFFPR encounter-level data and UNOS thoracic data were available through December 31, 2016 (to allow at least 1 yr of post-transplant follow-up). Details of the linkage between UNOS and CFFPR records have been described previously (20). Recipients were excluded if they were < 18 years old at transplant.

Data
Recipient characteristics at the time of LTx were obtained from the combined UNOS CFFPR dataset (*see* the METHODS section of the online supplement). Patient BMI was documented by UNOS at the time of LTx. BMI categorization was based on the World Health Organization international classification of adult underweight status (BMI < 17 kg/m^2, moderate to severe underweight; BMI 17–18.49 kg/m^2, mild underweight; and BMI $\geqslant 18.5$ kg/m^2, normal) (21). BMI recovery was defined as documentation of BMI $\geqslant 18.5$ kg/m^2 and was recorded on the date of the first post-transplant CFFPR encounter with BMI $\geqslant 18.5$ kg/m^2. BMI recovery could be documented within 1 year ($\leqslant 365$ d), 2 years ($\leqslant 730$ d), or ever during available follow-up.

Statistical Analysis
Descriptive statistics were used to compare the population of patients with and without post-transplant BMI data in CFFPR. We used a chi-square test to compare the proportion of recipients with lung function recovery (proportion with forced expiratory volume in 1 s [FEV_1] $> 80\%$ of predicted or forced vital capacity $> 80\%$ of predicted within 1 yr after LTx) among those with low preoperative BMI (< 17 and 17–18.49 kg/m^2) with that in a reference group with preoperative BMI $\geqslant 18.5$ kg/m^2.

We used multivariable Cox modeling to assess 1-year conditional survival among patients with low preoperative BMI, stratified by BMI recovery within 1 year (yes/no/unavailable), using preoperative BMI $\geqslant 18.5$ kg/m^2 as the reference group. For those undergoing a repeat LTx, survival time included time after retransplant. We identified a minimal set of covariates *a priori* as potential confounders of the relationship between preoperative low BMI and post-transplant survival, including CF genotype, age at LTx, insurance status at LTx (private/Medicaid/other), lung allocation score (LAS) at LTx, transplant hospitalization length of stay $\geqslant 28$ days, any documented insulin use by 1 year post-transplant, and maximum FEV_1 percent predicted by 1 year after LTx based on prior literature and clinical experience (22–24). All Cox models were stratified by LTx center, allowing center-specific baseline hazards and variable practices related to LTx in patients with CF with low BMI (25, 26). Sensitivity analyses repeated the Cox model for the subset of transplant centers that had post-transplant CFFPR encounter data within 1 year of LTx for at least 70% of CF recipients.

Tests of nonzero slope from regression of scaled Schoenfeld residuals on time found no evidence that the proportional hazards assumption was violated. All analyses were performed using Stata version 16 (StataCorp) with a two-sided significance value of 0.05. This study was approved by the University of Washington Institutional Review Board (7923).

Results

Recipient Characteristics at LTx
Our cohort included 1,977 adult recipients of single-organ first LTx (Figure 1). Of these, 1,256 (63%) had BMI $\geqslant 18.5$ kg/m^2, 449 (23%) had BMI 17–18.49 kg/m^2, and 272 (14%) had BMI < 17 kg/m^2 preoperatively. Recipients with preoperative BMI < 17 kg/m^2 were more often women and younger and had higher LASs (Table 1). Characteristics of the recipients who did not have CFFPR
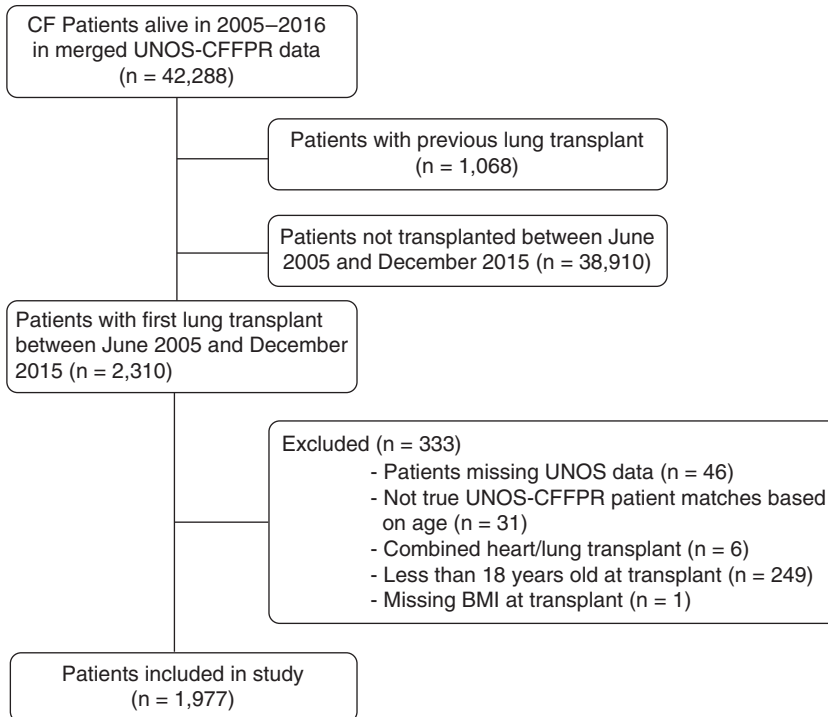
Figure 1. Consolidated Standards of Reporting Trials diagram. BMI = body mass index; CF = cystic fibrosis; CFFPR = Cystic Fibrosis Foundation Patient Registry; UNOS = United Network for Organ Sharing.

encounters with BMI recorded in the first year after LTx are available in Table E1 in the online supplement.

Post-transplant BMI Recovery

Sixty-five percent of recipients had at least one CFFPR encounter with BMI data recorded within 1 year after LTx (67% for preoperative BMI $\geqslant 18.5$ kg/m^2, 64% for BMI 17–18.49 kg/m^2, and 57% for BMI < 17 kg/m^2). Among recipients with low preoperative BMI who had BMI data available within 1 year after transplant, 49% of those with preoperative BMI 17–18.49 kg/m^2 recovered to BMI $\geqslant 18.5$ kg/m^2 compared with 29% of those with preoperative BMI < 17 kg/m^2. By 2 years after transplant, BMI recovery occurred for 48% of those with preoperative BMI 17–18.49 kg/m^2 versus 37% of those with preoperative BMI < 17 kg/m^2 (Table 2). The median BMI change (difference between BMI at transplant and highest recorded BMI within the first year after transplant) was 1.7 kg/m^2 (interquartile range [IQR], 0.3–3.3) for those who had a normal BMI ($\geqslant 18.5$ kg/m^2) at transplant compared with 2.2 kg/m^2 (IQR, 1.0–3.7) for those with BMI 17–18.49 kg/m^2 at transplant and 2.7 kg/m^2 (IQR, 1.4–4.4) for those with BMI < 17 kg/m^2 at transplant.

Table 1. Recipient characteristics at time of lung transplant

	Subgroups Defined by BMI at Transplant			
	$\geqslant$18.5 kg/m^2 (*n = 1,256*)	17–18.49 kg/m^2 (*n = 449*)	<17 kg/m^2 (*n = 272*)	All (*N = 1,977*)
Male sex, *n* (%)	715 (57)	226 (50)	118 (43)	1,059 (54)
Age, yr, median (IQR)	31 (26–39)	27 (23–33)	25 (22–30)	29 (24–37)
Race, *n* (%)				
White	1,236 (98)	438 (98)	267 (98)	1,942 (98)
African American	14 (1)	9 (2)	—*	25 (1)
Hispanic	46 (4)	17 (4)	6 (2)	69 (3)
Other	9 (1)	6 (1)	5 (2)	20 (1)
Private insurance, *n* (%)	732 (58)	253 (56)	163 (60)	1,148 (58)
CF mutation class, *n* (%)				
1–3, high risk	888 (71)	313 (70)	195 (72)	1,397 (71)
4–5, low risk	79 (6)	11 (2)	11 (4)	101 (5)
Not yet classified	141 (11)	58 (13)	39 (14)	238 (12)
Other	148 (12)	67 (15)	27 (10)	242 (12)
Pancreatic insufficiency, *n* (%)	1,233 (99)	446 (100)	268 (99)	1,948 (99)
Height, cm, mean (SD)	167 (9)	166 (9)	166 (8)	167 (9)
Weight, kg, median (IQR)	58 (52–66)	49 (45–53)	44 (41–48)	54 (48–61)
BMI, kg/m^2, median (IQR)	21 (19–22)	18 (17–18)	16 (16–17)	19 (18–21)
Functional status, *n* (%)				
Unknown	11 (1)	10 (2)	—*	24 (1)
10%: Moribund, fatal processes progressing rapidly	57 (5)	18 (4)	13 (5)	88 (4)
	168 (13)	51 (11)	54 (20)	273 (14)

(*Continued*)

Table 1. (*Continued*)

	Subgroups Defined by BMI at Transplant			
	≥18.5 kg/m² (*n = 1,256*)	17–18.49 kg/m² (*n = 449*)	<17 kg/m² (*n = 272*)	All (*N = 1,977*)
20%: Very sick, hospitalization necessary: active treatment necessary				
30%: Severely disabled: hospitalization is indicated, death not imminent	84 (7)	25 (6)	24 (9)	133 (7)
40%: Disabled: requires special care and assistance	207 (16)	90 (20)	49 (18)	346 (17)
50%: Requires considerable assistance and frequent medical care	185 (15)	62 (14)	43 (16)	290 (15)
60%: Requires occasional assistance but is able to care for needs	224 (18)	76 (17)	29 (11)	330 (17)
70%: Cares for self: unable to carry on normal activity or active work	178 (14)	71 (16)	31 (11)	280 (14)
80%: Normal activity with effort: some symptoms of disease	99 (8)	32 (7)	15 (6)	146 (7)
90%: Able to carry on normal activity: minor symptoms of disease	31 (2)	10 (2)	7 (3)	48 (2)
100%: Normal, no complaints, no evidence of disease	12 (1)	4 (1)	—*	20 (1)
Diabetes status, *n* (%)				
None documented	344 (28)	117 (26)	89 (33)	550 (28)
Impaired glucose tolerance	110 (9)	43 (10)	18 (7)	172 (9)
Diabetes	794 (64)	289 (64)	165 (61)	1,248 (63)
Insulin status, *n* (%)				
No CFRD treatment	362 (29)	134 (30)	89 (33)	585 (30)
Dietary change or oral hypoglycemic agents	49 (4)	20 (4)	12 (4)	81 (4)
Intermittent insulin (e.g., with illness, steroids)	50 (4)	22 (5)	15 (6)	88 (4)
Chronic insulin	787 (63)	273 (61)	156 (57)	1,216 (62)
HbA1c, %, median (IQR)	6.3 (5.7–7.1)	6.3 (5.8–6.9)	6.2 (5.7–7.3)	6.3 (5.7–7.0)
Lung allocation score, median (IQR)	40 (37–48)	42 (38–50)	45 (39–68)	41 (37–50)
FEV₁ percent predicted, median (IQR)	22 (18–27)	21 (18–25)	20 (17–25)	21 (18–26)
Length of stay from treatment to discharge, d, median (IQR)	17 (12–26)	16 (13–24)	18 (14–29)	17 (12–26)

Definition of abbreviations: BMI = body mass index; CF = cystic fibrosis; CFRD = cystic fibrosis–related diabetes; FEV_1 = forced expiratory volume in 1 second; HbA1c = hemoglobin A1c; IQR = interquartile range; SD = standard deviation.
*Values < 5 were suppressed to avoid identification of individuals within the cohort.

Posttransplant Graft Failure and Lung Function Recovery

Within 2 years after transplant, only 0–2% of recipients with a preoperative BMI of ≥18.5 kg/m² and 17–18.49 kg/m² received a repeat transplant during the study period, whereas 9% of recipients with preoperative BMI < 17 kg/m² underwent retransplant, none of whom had reached BMI ≥ 18.5 kg/m² (Table 3). Low preoperative BMI recipients who achieved normal BMI within 1 year after LTx had a similar proportion with lung function recovery compared with the group with normal preoperative BMI, whereas those who did not achieve normal BMI within 1 year were less likely to have recovered lung function (Table 3). Among recipients with low BMI at the time of transplant (<18.5 kg/m²), 26% had an episode of acute rejection within the first year, whereas 61% had no documented episode of rejection (14% were missing data about acute rejection). For LTx recipients who did not recover BMI by 1 year after LTx, 31% had an episode of acute rejection compared with 28% among those who did recover BMI.

Posttransplant Survival

By 1 year after transplant, 10%, 14%, and 12% of recipients with a preoperative BMI of ≥18.5 kg/m², 17–18.49 kg/m², and <17 kg/m², respectively, had died (Table 2). Among recipients who survived at least 1 year after LTx, those with preoperative BMI ≥ 18.5 kg/m² had median survival time of 10.4 years (95% confidence interval [CI], 9.5–12.2).

Among recipients with preoperative BMI 17–18.49 kg/m² who survived at least 1 year after LTx, 1-year conditional survival time was 9.2 years (95% CI, 7.9–10.5), and
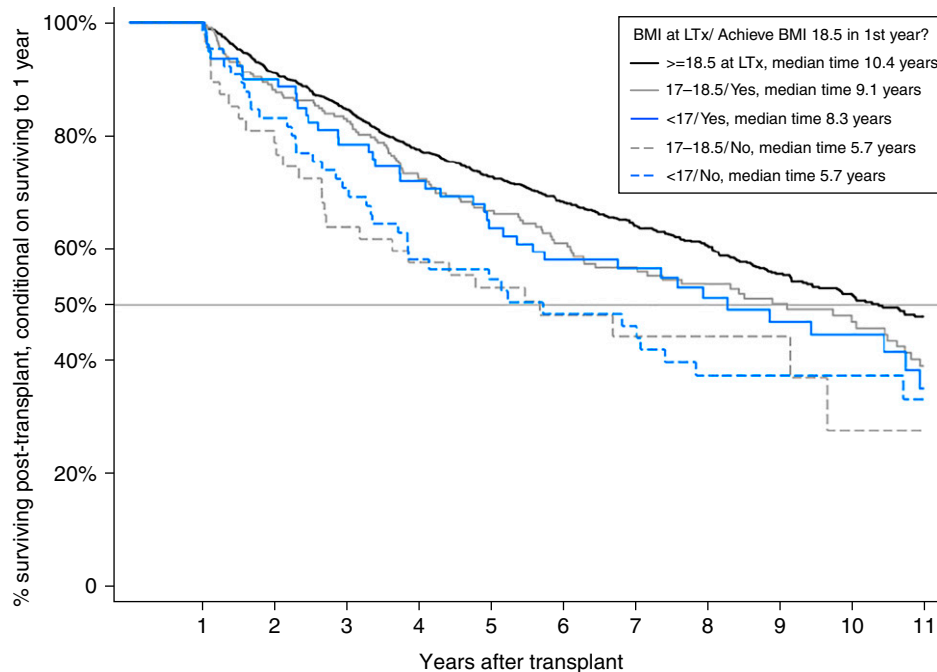
Figure 2. Kaplan-Meier survival curves for subgroups defined by body mass index (BMI) at lung transplant (LTx) and within 1 year after transplant.

the 5-year survival proportion was 0.67 (Table E2). When 1-year conditional survival was stratified by the presence or absence of BMI recovery within 1 year after transplant, among those with preoperative BMI 17–18.49 kg/m^2, the median survival was 9.1 years (95% CI, 6.3–10.7) versus 5.7 years (95% CI, 2.7–9.7), respectively (Figure 2).

When recipients with preoperative BMI 17–18.49 kg/m^2 were compared with those with preoperative BMI $\geq$ 18.5 kg/m^2, the adjusted hazard ratio (HR) for death conditional on surviving to 1 year was 1.28 (95% CI, 1.02–1.61) for those who achieved BMI $\geq$ 18.5 kg/m^2 within 1 year and 1.72 (95% CI, 1.41–2.59) for those who did not (Table 4). Among those with preoperative BMI <17 kg/m^2, there was a higher risk of death for recipients, regardless of BMI recovery, but BMI recovery attenuated the risk (HR, 1.29 [95% CI, 0.92–1.81] versus 1.57 [95% CI, 1.09–2.25], respectively) (Table 4).

Results of a sensitivity analysis omitting centers with post-transplant encounter data for <70% of recipients within 1 year after LTx were comparable to the primary results, but none reached statistical significance (Table 4). For LTx recipients who did not have BMI data available by 1 year, the adjusted HR showed a lower risk of death than that for recipients with BMI $\geq$ 18.5 kg/m^2 (Table 4).

Discussion

In this large cohort of patients with CF undergoing LTx in the United States, we found that less than half of those who underwent LTx with a low preoperative BMI were able to achieve a normal BMI by 1 year after transplant. Furthermore, at 2 years after transplant, there remained 56% of this cohort who had not yet achieved a normal BMI ($\geq$18.5 kg/m^2). Strikingly, after adjustment for markers of disease severity at transplant and of early postoperative recovery, failure to recover BMI by 1 year was associated with poorer long-term survival and worsened post-transplant lung function recovery. Causal inference from observational data is limited, and early postoperative events (e.g., primary graft dysfunction, acute cellular rejection requiring hospitalization, serious infections) could explain the lack of BMI recovery and the worsened long-term outcomes, but these findings identify a potentially modifiable post-transplant condition (persistent low BMI) and its association with poorer lung function and survival.

Low preoperative BMI has been associated with worse post-transplant survival among patients with a variety of underlying lung conditions (18). However, underweight patients with CF have been shown to have a higher risk of death without

LTx, highlighting the importance of low preoperative BMI as a marker of "transplant need" (10, 27, 28). In addition, recent research has found that LTx recipients with CF who have low preoperative BMI have post-transplant survival that is comparable to that of other common transplant cohorts (25). For our cohort, low preoperative BMI was associated with worse 1-year survival, but this risk varied on the basis of post-transplant BMI recovery. Existing studies suggest that weight gain after transplant may be associated with post-transplant survival (29), but only a small, single-center study by Levine and colleagues specifically looked at BMI recovery after LTx for CF (30). Our results would support this assertion, placing emphasis on the importance of nutrition in the post-transplant period. In a recent consensus statement about the post-transplant care of LTx recipients with CF, the CF Foundation recommended "ongoing consultation with a dietitian with CF expertise, to receive individualized nutritional therapy to achieve an established BMI or weight-for-length goal" (31). However, there are no specific, standardized nutritional guidelines or recommendations to aid in recovering BMI after LTx.

In addition to a potential relationship between BMI recovery and survival in the post-transplant period, improvements in nutritional status are also likely linked to

Table 2. Recipient outcomes by 1 and 2 years after lung transplant

	Preoperative BMI ≥ 18.5 kg/m² (n = 1,256)		Preoperative BMI 17–18.49 kg/m² (n = 449)		Preoperative BMI <17 kg/m²	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
By 1 yr after transplant						
Alive at 1 yr	1,131	90% (88–92)	388	86% (83–89)	240	88% (84–92)
Alive, achieved BMI ≥18.5 kg/m²	—	—	218	49% (44–53)	80	29% (24–35)
Alive, did not achieve BMI ≥18.5 kg/m²	329	26% (24–29)	47	10% (8–14)	65	24% (19–29)
Alive but no BMI data	125	10% (8,12)	123	27% (23–32)	95	35% (30–41)
Died by 1 yr			61	14% (11–17)	32	12% (8–16)
Died before achieving BMI ≥ 18.5 kg/m²	—	—	10	2% (1–4)	5	2% (1–4)
Died after achieving BMI ≥ 18.5 kg/m²	—	—	11	2% (1–4)	4	1% (1–4)
Died but no BMI data	91	7% (6–9)	40	9% (7–12)	23	8% (6–12)
By 2 yr after transplant						
Alive at 2 yr	1,031	82% (80–84)	342	76% (72–80)	212	78% (73–82)
Alive, achieved BMI ≥ 18.5 kg/m²	—	—	217	48% (44–53)	100	37% (31–43)
Alive, did not achieve BMI ≥ 18.5 kg/m²	224	18% (16–20)	28	6% (4–9)	44	16% (12–21)
Alive but no BMI data	225	18% (16–20)	97	22% (18–26)	68	25% (20–30)
Died by 2 yr			107	24% (20–28)	60	22% (18–27)
Died before achieving BMI ≥ 18.5 kg/m²	—	—	19	4% (3–7)	17	6% (4–10)
Died after achieving BMI ≥ 18.5 kg/m²	—	—	37	8% (6–11)	12	4% (3–8)
Died but no BMI data	119	9% (8–11)	51	11% (9–15)	31	11% (8–16)

Definition of abbreviations: BMI = body mass index; CI = confidence interval.

lung function recovery (22). Poor lung function recovery early post-transplant, recently coined as "baseline lung allograft dysfunction," is associated with post-transplant survival (32). An association between BMI and post-transplant lung function in LTx recipients with CF was suggested in a single-center study of 50 LTx recipients with CF in Israel, where the trend in FEV_1 mirrored the trend in BMI over the first 2 years after LTx, but no statistical testing was performed (30). Our results show that low-BMI LTx recipients with CF who recovered BMI had lung function recovery ($FEV_1 > 80\%$ and forced vital capacity > 80% of predicted) similar to that in those who started with a BMI ≥ 18.5 kg/m². Although lung function recovery is significantly associated with BMI recovery in LTx recipients with CF in our data, causal inference is limited. These findings support the importance of monitoring post-transplant BMI and supporting nutritional recovery after LTx. Even though pretransplant nutritional outcomes are improving with CFTR modulators, and even though there will likely be fewer individuals with malnutrition at the time of transplant, we hypothesize that the link between malnutrition and post-transplant lung function is likely to hold true in the era of highly effective modulators.

The present study has an important strength: It used a merged dataset with records from the CFFPR and the UNOS/OPTN registry, which yielded novel data about longitudinal BMI and lung function recovery for LTx recipients with CF in the United States. The present study also has limitations. First, national registry data do not take into account transplant center–specific policies, varying BMI requirements for LTx candidacy, or post-transplant care. Transplant centers that accept candidates with very low BMI may be different in meaningful ways from ones that do not. Analyses were stratified by transplant center, but residual confounding may remain. Second, missing data are informative for this cohort because recipients who did not have BMI data in the CFFPR appeared to have the extremes of health—either death within 1 year of LTx or a much lower risk of death overall. We postulate that low-BMI LTx recipients without post-transplant CFFPR BMI data who survive beyond 1 year have lower medical complexity or CF complications, which may lead them to remain away from their CF center for post-

Table 3. Retransplant, BMI, and lung function after lung transplant for recipients with BMI data within 1 year after transplant

	Preoperative BMI ≥ 18.5 kg/m² (n = 836)	Preoperative BMI 17–18.5 kg/m²: Achieved BMI ≥ 18.5 kg/m² within 1 yr after LTx?		Preoperative BMI < 17 kg/m²: Achieved BMI ≥ 18.5 kg/m² within 1 yr after LTx?	
		Yes (n = 229)	No (n = 57)	Yes (n = 84)	No (n = 70)
Retransplant, n (%)					
Within 1 yr after LTx	4 (0)	0 (0)	0 (0)	0 (0)	4 (6)
Within 2 yr after LTx	12 (1)	4 (2)	0 (0)	0 (0)	6 (9)
First BMI after LTx, kg/m², median (IQR; range)	21.1 (IQR, 19.5–22.9; range, 14.8–32.5)	18.7 (IQR, 17.9–19.9; range, 14.6–26.1)	17.3 (IQR: 16.4–18.1; range, 13.0–18.4)	18.4 (IQR, 16.9–19.3; range, 14.6–23.9)	16.2 (IQR, 15.2–17.0; range, 12.8–18.4)
Months from LTx to first BMI, median (IQR; range)	2 (IQR, 1–4; range, 0–12)	1 (IQR, 1–4; range, 0–12)	2 (IQR, 1–5; range, 0–12)	2	3 (IQR, 1–5; range, 0–12)
Months from LTx to first lung function measurement, median (IQR; range)	2 (IQR, 1–5; range, 0–64)	2 (IQR, 1–4; range, 0–53)	2 (IQR, 1–5; range, 0–12)	2	3 (IQR, 1–7; range, 1–35)
Lung function: FEV₁% and FVC%					
Any recorded value within 1 yr after LTx, n (%)	791 (95)	212 (93)	55 (96)	82 (98)	62 (89)
Any recorded value within 2 yr after LTx, n (%)	805 (96)	214 (93)	55 (96)	84 (100)	62 (89)
Number of FEV₁% measurements within 1 yr, median (IQR; range)	4 (IQR, 2–7; range, 0–21)	4 (IQR, 2–8; range, 0–18)	2 (IQR, 1–4; range, 0–19)	4 (IQR, 3–7; range, 0–16)	3 (IQR, 1–5; range, 0–18)
First FEV₁% after LTx, median (IQR; range)	68 (IQR, 54–82; range, 11–128)	61 (IQR, 48–78; range, 21–128)	58 (IQR, 45–65; range, 29–97)	66 (IQR, 49–78; range, 28–105)	59 (IQR, 46–70; range, 22–101)
Maximum FEV₁% in 1 yr after LTx, median (IQR; range)	82 (IQR, 69–95; range, 17–146)	82 (IQR, 70–93; range, 33–134)	65 (IQR, 54–76; range, 29–102)	79 (IQR, 70–89; range, 31–119)	71 (IQR, 58–86; range, 22–103)
Minimum post-LTx FEV₁% within 1 yr, median (IQR; range)	65 (IQR, 49–78; range, 10–128)	58 (IQR, 43–74; range, 21–121)	54 (IQR, 44–65; range, 16–91)	59 (IQR, 41–73; range, 21–99)	57 (IQR, 43–69; range, 21–101)
Any FEV₁% > 80 within 1 yr after LTx, n (%)	435 (55)	115 (54); P = 0.85*	9 (16); P < 0.01*	36 (44); P = 0.06*	19 (31); P < 0.01*
First FVC% after LTx, median (IQR; range)	66 (IQR, 52–78; range, 21–123)	58 (IQR, 46–73; range, 26–111)	55 (IQR, 46–65; range, 29–85)	63 (IQR, 50–74; range, 26–112)	57 (IQR, 45–71; range, 22–111)
Maximum FVC% in 1 yr after LTx, median (IQR; range)	79 (IQR, 69–91; range, 24–133)	78 (IQR, 67–88; range, 27–118)	62 (IQR, 51–71; range, 31–97)	77 (IQR, 71–88; range, 41–112)	68 (IQR, 59–81; range, 22–111)
Minimum post-LTx FVC% within 1 yr, median (IQR; range)	64 (IQR, 50–75; range, 19–123)	56 (IQR, 45–70; range, 26–111)	55 (IQR, 44–64; range, 27–83)	62 (IQR, 48–71; range, 26–95)	55 (IQR, 45–65; range, 20–101)
Any FVC% > 80 within 1 yr after LTx, n (%)	382 (48)	95 (45); P = 0.37*	9 (16); P < 0.01*	35 (43); P = 0.33*	17 (27); P < 0.01*

Definition of abbreviations: BMI = body mass index; FEV₁ = forced expiratory volume in 1 second; FVC = forced vital capacity; IQR = interquartile range; LTx = lung transplant.
*P values from chi-square test comparing proportion with reference group with BMI ≥ 18.5 kg/m² at LTx.

Table 4. Adjusted* Cox modeling results for death, contingent on surviving to 1 year after LTx (reference group, BMI ≥ 18.5 kg/m² at LTx)

Centers	HR	95% CI	P Value
Including all centers, n = 1,733 with 783 deaths			
17–18.49 kg/m² at LTx, BMI ≥ 18.5 kg/m² within 1 yr	1.28	(1.02–1.61)	0.03
17–18.49 kg/m² at LTx, no BMI ≥ 18.5 kg/m² in 1 yr	1.72	(1.14–2.59)	0.01
17–18.49 kg/m² at LTx, no BMI data in 1 yr	0.62	(0.44–0.86)	<0.01
<17 kg/m² at LTx, BMI ≥ 18.5 kg/m² within 1yr	1.29	(0.92–1.81)	0.14
<17 kg/m² at LTx, no BMI ≥ 18.5 kg/m² in 1 yr	1.57	(1.09–2.25)	0.02
<17 kg/m² at LTx, no BMI data in 1 yr	0.93	(0.66–1.31)	0.69
Sensitivity analysis omitting centers with post-transplant encounter data for <70% of recipients within 1 yr after LTx, n = 956 with 433 deaths			
17–18.49 kg/m² at LTx, BMI ≥ 18.5 kg/m² within 1 yr	1.15	(0.88–1.52)	0.31
17–18.49 kg/m² at LTx, no BMI ≥ 18.5 kg/m² in 1 yr	1.68	(0.92–3.06)	0.09
17–18.49 kg/m² at LTx, no BMI data in 1 yr	0.44	(0.21–0.93)	0.03
<17 kg/m² at LTx, BMI ≥ 18.5 kg/m² within 1 yr	1.28	(0.85–1.91)	0.23
<17 kg/m² at LTx, no BMI ≥ 18.5 kg/m² in 1 yr	1.48	(0.94–2.32)	0.09
<17 kg/m² at LTx, no BMI data in 1 yr	1.10	(0.65–1.87)	0.72

Definition of abbreviations: BMI = body mass index; CI = confidence interval; HR = hazard ratio; LTx = lung transplant; N/A = not applicable.
*Covariates include genotype (1–3, 4–5, N/A, other), age at transplant, insurance status at transplant (private, Medicaid, other), lung allocation score at transplant, transplant length of stay ≥ 28 d, any documented insulin use by 1 year after LTx, and maximum recorded forced expiratory value in 1 second percentage during first year after LTx. Models stratified by LTx center.

transplant care. Because of the potential for bias in the cohort of LTx recipients who returned to a CF center and have data in the CFFPR, sensitivity analyses were limited to transplant centers with high rates of capture of post-transplant data (>70% of recipients with CFFPR data). These sensitivity analyses showed similar results, although they had less power to show statistical significance with smaller numbers of events in the low-BMI subgroups. Third, in this study, BMI was used as a surrogate for nutritional status because the UNOS and CFF registries do not collect other variables that could more accurately reflect body composition and overall nutritional health. Finally, postoperative complications such as primary graft dysfunction, acute cellular rejection (large percentage missing), and infection are not reliably captured in the available registries and thus could bias the results. Analyses were adjusted for immediate postoperative hospitalization length of stay and LAS at the time of transplant to account for early postoperative complications, but other events that were not included in the analyses may explain poor recovery of both BMI and lung function for some recipients.

In conclusion, we present the largest study to describe post-transplant BMI recovery for LTx recipients with CF and examine the association between BMI recovery and survival of LTx recipients with CF. Optimal post-transplant management is evolving, and this study highlights the important role of an interdisciplinary shared model of post-transplant CF care that includes ongoing CF-specific nutritional education and interventions, because less than half of underweight recipients were alive with a normal BMI by 1 year after transplant. Having low preoperative BMI is a risk factor for poor outcome after LTx, but this study underscores the importance of attention to BMI recovery post-transplant. Future research should investigate whether approaches to augment weight gain after transplant improve outcomes, particularly among recipients with very low BMI at the time of transplant. ∎

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