OPEN

Evaluation of Malnutrition Risk in Lung Transplant Candidates Using the Nutritional Risk Index

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Background. Malnutrition in lung transplant (LTx) candidates is an important risk factor for adverse outcomes. We sought to evaluate the Nutritional Risk Index (NRI) in LTx candidates, a validated measure of malnutrition risk in chronic disease. We aimed to characterize malnutrition risk using NRI, evaluate change in body weight between nutritional risk groups, and assess association of malnutrition risk with pretransplant and posttransplant outcomes. **Methods.** Retrospective, single-center cohort study of LTx candidates (2014–2015) evaluated by a dietitian before listing. Nutritional parameters, weight change pretransplant and posttransplant, and clinical outcomes were abstracted up to 1-year posttransplant. NRI was calculated as follows: $(1.519 \times \text{albumin}) + (41.7 \times \text{current weight/ideal weight})$ with high malnutrition risk defined as the lowest quartile of NRI for cystic fibrosis (CF) and non-CF patients. **Results.** The cohort comprises 247 LTx candidates (57% male; median age 59 y; non-CF 88%). Non-CF candidates had a greater mean NRI compared with CF patients (109 ± 11 versus 95 ± 12; $P < 0.0001$). 86% with high malnutrition risk maintained/gained weight (≥5%) pretransplant. In 196 LTx recipients, malnutrition risk was not associated with hospital stay, discharge disposition, or 1-year mortality. The median percent weight gain for LTx recipients in the first year was 10.5% (4.0–20.1), with high malnutrition risk recipients having comparable or greater weight gain to the low-risk group (mean difference for non CF: 6.8%; $P = 0.02$ and CF: –3.8%; $P = 0.65$). **Conclusions.** Malnutrition risk assessed with NRI was not prognostic of posttransplant outcomes in this retrospective cohort. LTx candidates with high malnutrition risk were able to maintain their weight pretransplant and demonstrated considerable weight gain in the first-year posttransplant.

(*Transplantation Direct* 2020;6: e574; doi: 10.1097/TXD.0000000000001028. Published online 23 June, 2020.)

INTRODUCTION

Lung transplantation is a life-saving procedure for those with end-stage lung disease that is increasingly offered to older candidates.[1] Lung transplant (LTx) candidates are at higher risk of malnutrition given risk factors such as older age and disease severity, predisposing them to a negative balance of energy, protein, and other essential nutrients.[2,3] Malnutrition is known to be an important contributing risk factor associated with adverse outcomes in chronic disease and can have negative consequences on protein/

Received 23 April 2020. Revision received 13 May 2020.

Accepted 14 May 2020.

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Dmitry Rozenberg receives research support from the Sandra Faire and Ivan Fecan Professorship in Rehabilitation Medicine.

The authors declare no conflicts of interest.

This work was in part presented at the American Thoracic Society Meeting in 2019 (Dallas, TX). Chohan K, et al. Am J Resp Crit Care, May 2019, A5721.

K.C., J.P., S.D., R.V., L.W., L.G.S., B.S., and D.R. made substantial contributions to the conception and design of the work. K.C. wrote the first draft of the article. J.P., S.D., R.V., L.W., L.G.S., B.S., and D.R. revised the article for important intellectual content. All authors made substantial contributions to the analysis or interpretation of data. All authors approved the article and agreed to be accountable for all aspects of the work ensuring that questions related to the accuracy or integrity of the work are appropriately investigated and resolved.

Supplemental digital content (SDC) is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.transplantjournal.com).

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ISSN: 2373-8731

DOI: 10.1097/TXD.0000000000001028

energy balance, physical function, and clinical outcomes.[4-6] Thus, identifying potentially modifiable risk factors such as malnutrition may help offset some of the morbidity and mortality associated with lung transplantation.[7,8]

In lung transplantation, nutritional status has often been evaluated with surrogate markers such as body mass index (BMI), serum albumin, and total protein, which have been associated with increased morbidity and mortality posttransplantation.[9-11] A large retrospective study of 453 patients found that patients with low serum albumin or total protein had worse survival and increased risk of postoperative infections.[9] These findings were supported by a recent systematic review that showed that LTx candidates with a BMI < 18.5 kg/m^2 had a higher risk of posttransplant mortality when compared with those with a normal BMI.[10] Although these variables cannot attribute malnutrition risk, they highlight that compromised nutritional status can result in adverse outcomes in LTx patients with possible mechanisms including impairments in immune response, respiratory muscle function, and protein-energy imbalance.[2,12]

Several nutritional tools for malnutrition screening and diagnosis have been published, such as the Mini-Nutritional Assessment,[13] Malnutrition Screening Tool (MST),[14] and Subjective Global Assessment.[15] These nutritional tools often require integration of physical examination or patient-reported findings such as appetite and unintentional weight loss. Currently, there are no standardized malnutrition screening instruments used in LTx candidates. An ideal tool would identify those at risk of malnutrition, thus creating an opportunity to improve nutritional status. A screening tool not previously applied in chronic lung disease is the Nutritional Risk Index (NRI). The NRI is a simple tool that incorporates albumin, weight, and ideal body weight (BW) ratios, values that can be ascertained solely from medical records. The NRI has the potential to stratify nutritional risk based on an individual's score.[16] NRI has been shown to be a strong prognostic marker in congestive heart failure (CHF) patients,[17] those with left ventricular assist devices (LVAD),[18] and those undergoing gastrectomy.[16] The combination of both anthropometric and biochemical parameters (ie, albumin) allows for a more holistic evaluation of nutritional state through indirect evaluation of systemic inflammation, renal and liver function, and caloric intake, several factors known to effect albumin levels.[19-21] Thus, NRI may be a novel marker of malnutrition risk that may help with prognosticating outcomes pretransplant and posttransplant.

Nutritional intervention during the pretransplant period in LTx candidates has been evaluated in a limited number of studies, mainly in chronic obstructive pulmonary disease patients. Førli et al[22] demonstrated that underweight LTx candidates who received an energy-rich diet as inpatients had a significant weight gain (median of 1.2 kg) compared with those receiving standard diet during a mean hospital stay of 12 days. In LTx candidates receiving nutritional counseling as outpatients, there was a significant gain in weight and self-reported well-being.[23] In a study of 36 LTx candidates with cystic fibrosis (CF), nutritional supplementation resulted in limited change in BMI or fat-free mass despite evaluation every 3–4 months by a dietitian pretransplant.[24] However, it remains unclear whether LTx candidates at higher risk of malnutrition who receive nutritional care pretransplant have greater weight gain than candidates at lower risk of malnutrition. Furthermore, the clinical implications of malnutrition may be quite different in CF patients due to malabsorption, CF-related diabetes, and pancreatic insufficiency,[25,26] but CF has often been studied independently in transplant nutritional studies.[24,27] Thus, the main purpose of this study was to test whether the application of NRI as a screening tool for malnutrition may help identify LTx candidates who may benefit from additional nutritional support and potentially help with prognostication of transplant outcomes.

The main aims of the current study were to (1) characterize malnutrition risk using the NRI in non-CF and CF LTx candidates, (2) assess any differences in nutritional recommendations and weight change across malnutrition risk groups pretransplant, and (3) evaluate the association of malnutrition risk with pretransplant intensive care unit (ICU) admission, delisting/waitlist mortality, and early posttransplant outcomes, such as BW, functional recovery, and 1-year mortality. We hypothesized that NRI scores would be significantly lower in patients with CF compared with other indications for transplantation. Most LTx candidates with high malnutrition risk will be able to meet nutritional recommendations aimed at attenuating pretransplant weight loss. High malnutrition risk will be associated with increased pretransplant and posttransplant morbidity and mortality.

MATERIALS AND METHODS

Study Design and Participants

This was a retrospective cohort study of 247 consecutive adult LTx candidates (≥18 y) listed for their first transplant at the University Health Network (January, 2014–December, 2015). We excluded patients who did not have a nutritional assessment at our center or albumin measurement within 6 months of listing (Figure 1). Only LTx candidates who had a nutritional assessment within 6 months of transplant listing were included in the analysis evaluating any differences in nutritional recommendations and weight change across malnutrition risk groups pretransplant, as per aim 2 (Figure 1). Patient's demographic and clinical characteristics along with posttransplant outcomes were abstracted using electronic chart review and the Toronto Lung Transplant Database. The study was approved by the University Health Network Research Ethics Board (18-5443).

Nutritional Risk Index

The NRI was calculated using patient's serum albumin, weight, and anthropometric data with the following equation: (1.519 × serum albumin) + (41.7 × present weight/ideal BW [kg]), originally developed in surgical patients,[28] but applied in CHF,[17,29] LVAD,[18] and oncologic populations.[30] Ideal BW was calculated utilizing the devine formula.[31] CF and non-CF diagnostic groups were analyzed separately, given the different pathophysiology and potentially severity of malnutrition risk underlying these 2 groups.[25] Given no established cutoffs for NRI in LTx, we defined the lowest quartile (Q1) to represent high malnutrition risk compared with low malnutrition risk (Q2–Q4) stratified for non-CF and CF patients. NRI was calculated closest to the time of LTx assessment to parallel nutritional assessments. Correlation and agreement between NRI and another MST were applied retrospectively from chart review in this LTx cohort. The MST incorporates degree of recent weight loss and poor appetite with a total score (0–5), with MST score ≥ 2 characterized as being at risk of malnutrition.[14]

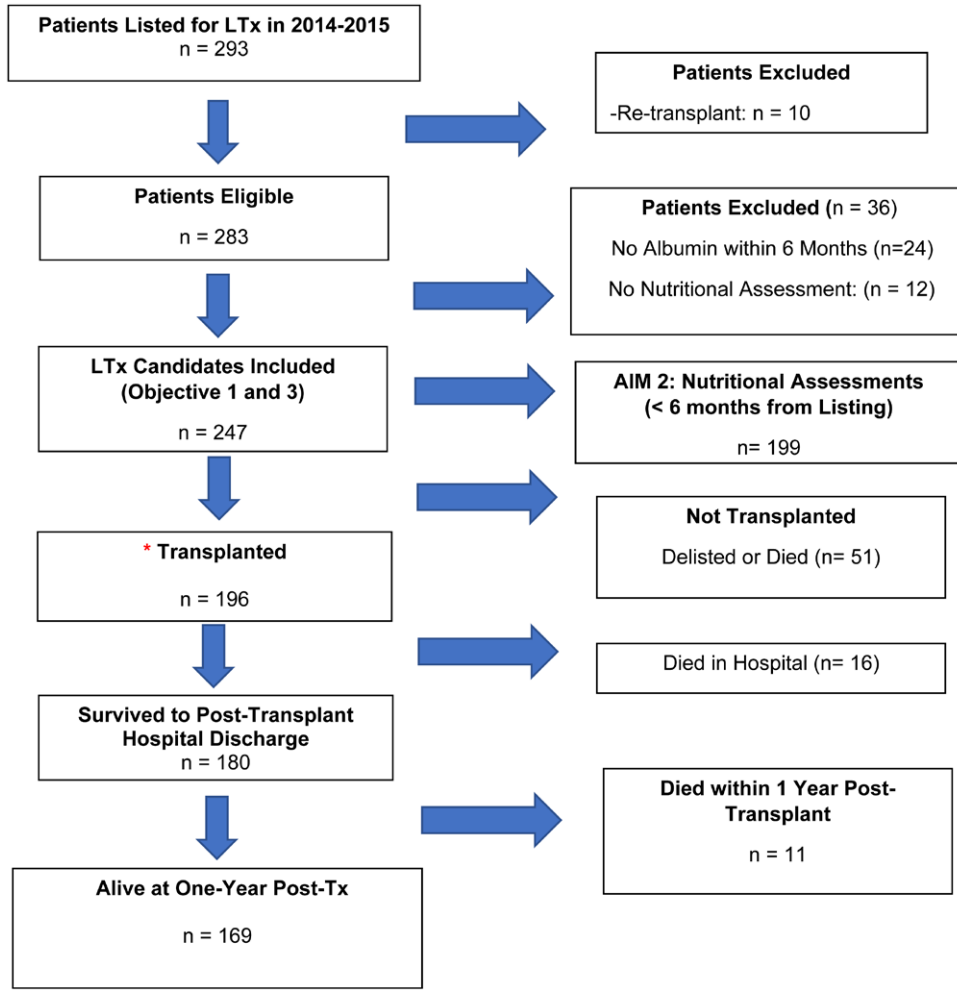

FIGURE 1. Flow diagram of study participants. *Of the 196 patients transplanted, 159/196 (81%) had initial nutritional assessment < 6 mo from listing. LTx, lung transplant; Tx, transplantation.

Nutritional Assessment

LTx candidates generally undergo a comprehensive nutritional assessment by a registered dietitian at our center. From the nutritional assessment, we abstracted candidates' weight change and whether it was unintentional in the 1-year preceding the assessment. Conditions such as gastroesophageal reflux disease and gastrointestinal dysmotility were abstracted from medical records. For CF patients, we captured the presence of CF-related diabetes, liver disease, or pancreatic insufficiency.

The specific nutrition-related goals for each patient, such as weight gain, maintenance, or loss, were recorded, along with 2 intermediate categories of maintenance-gain or maintenance-loss based on the nutritional consultation. The use of oral nutritional supplementation (ONS) or enteral tube feeding in addition to ongoing food-based caloric supplementation was recorded. Dietitians assessed a candidate's weight, BMI, daily dietary habits, and estimated total caloric requirements without using any malnutrition screening instruments.

Individualized nutritional recommendations were made by the dietitians after both objective and patient-reported clinical assessments. Application of available disease-specific guidelines,[32-34] Canada's Food Guide recommendations,[35] and the plate model (half a plate of vegetables, quarter of protein, and quarter of starch or grain) were utilized. In addition, consistent use of strategies to optimize caloric and protein intake were also provided with educational reading material.[36] A 5% change in BW in the pretransplant period after a nutritional consultation was considered significant, as previously described in chronic disease.[37,38] Dietitians typically followed LTx candidates every 2–3 months or more frequently as needed pretransplant. After LTx, nutrition care was individualized according to the needs of each patient, with not all patients being seen. At hospital discharge post LTx, patients were provided with educational material on healthy eating to support recovery and manage potential posttransplant comorbidities (ie, excess weight gain, diabetes).[39] LTx recipients had ongoing access to a dietitian, in person or by phone, over the first-year posttransplant. Furthermore, after completion of a formal supervised exercise training program pretransplant and posttransplant (3 mo),[40] LTx recipients received brief physical activity counseling from a physical therapist at the time of their 6-minute follow-up assessments (3, 6, 9, and 12 mo).

Bodyweight was abstracted from charts in the pretransplant period (assessment, listing, 6 and 12 wks, and every 3 mo) and posttransplant at 3, 6, and 12 months. Weight was evaluated in our program using a calibrated electronic scale during clinic visits.

Patient Characteristics

Clinical characteristics such as age, sex, transplant indication, anthropometric measurements (weight, height, BMI), transplant listing urgency, and 6-minute walk distance (6MWD and percent predicted)[41] were abstracted from electronic medical records and the Toronto Lung Transplant Database. Listing urgency status was based on subjective categorization into status 1, status 2, or rapidly deteriorating, shown to be associated with the Lung Allocation Score.[42] Bone metabolism was classified as osteoporotic, osteopenic, and normal from chart abstraction based on Canadian osteoporosis practice guidelines.[43]

Clinical Outcomes

The composite of pretransplant medical delisting or death was ascertained with delisting representing a contraindication to transplant. We abstracted whether patients were admitted to the ICU pretransplant for respiratory failure or sepsis. Posttransplant outcomes included ICU and hospital length of stay, discharge disposition (inpatient rehabilitation versus discharge home), the change in exercise capacity using 6MWD from pretransplant values and mortality in the first year. We also evaluated posttransplant weight at 3, 6, and 12 months compared with the last available assessment pretransplant. At our center, patients participate in a rehabilitation program (aerobic and strength training) for the pretransplant period and 3 months posttransplant, as previously described.[40]

Statistical Analysis

Analysis was performed using Graph-Pad Prism (version 7.0) and R (version 3.32). We described continuous and categorical variables using mean ± SD, median (interquartile range [IQR]), frequencies (n), and percentages where applicable. Data distribution was evaluated visually and with the use of Kolmogorov-Smirnov and Pearson omnibus normality tests. Analysis for non-CF and CF patients were performed separately. The difference in malnutrition groups was evaluated using descriptive statistics, t-tests, and chi-squared tests. High malnutrition risk was defined as the lowest quartile of NRI for non-CF and CF patients. Pearson and Spearman correlations were used to assess the relationship of the NRI with albumin, BMI, BW, and MST pretransplant. We used t-tests to evaluate the change in weight between the high malnutrition risk and low-risk groups in the pretransplant and posttransplant period. Multivariable linear and logistic regression models were used to evaluate the associations between malnutrition risk and pretransplant and posttransplant outcomes, adjusting for age, sex, and diagnosis. We also tested the models using NRI as a continuous parameter. A P value of <0.05 was considered statistically significant for all analyses.

RESULTS

Study Population

The study included 247 LTx candidates as outlined in Figure 1. 57% were male, and the median age was 59 years (IQR, 47–64). The most common indications for transplant were interstitial lung disease (n = 139; 56%), chronic obstructive pulmonary disease (n = 50; 20%), and CF (n = 29; 12%). Mean BMI was 24.8 ± 5.0 kg/m^2 with 30 (12%) categorized as underweight (BMI < 18.5 kg/m^2). Of the 196 LTx patients transplanted, all underwent initial nutritional assessments, but 159 (81%) had nutritional assessments within 6 months of transplant listing. The 36 LTx candidates excluded from the study were not different than the study population with respect to baseline NRI, demographics, diagnosis, 6MWD, but had a higher listing urgency (Table S1, SDC, http://links.lww.com/TXD/A260).

Non-CF LTx candidates had significantly higher NRI (109 ± 11) than those with CF (95 ± 12; P < 0.0001), Figure S1 (SDC, http://links.lww.com/TXD/A260). The distribution of NRI scores is shown in Figure 2, defining high malnutrition risk for non-CF (NRI ≤ 102.6) and CF (NRI ≤ 87.5) based on the lowest quartile for each group.

Non-CF LTx candidates at high malnutrition risk were more likely to be underweight (BMI < 18.5 kg/m^2; n = 17/55 [31%] versus n = 2/163 [1%]; P < 0.0001), have a lower 6MWD (m) (269 ± 114 versus 316 ± 105; P = 0.01), and higher prevalence of osteoporosis (15/43 [35%] versus 25/132 [19%]; P = 0.02) than those at low risk, Table 1. No difference between those at high and low risk of malnutrition was observed with respect to age, non-CF diagnosis, or Canadian transplant listing urgency. For LTx candidates with CF, those categorized as high malnutrition risk had a higher transplant listing urgency (rapidly deteriorating: n = 3/8 [38%] versus n = 0/21 [0%]; P = 0.01), but no differences in age, BMI, or 6MWD were observed (Table 1). The NRI in all patients demonstrated moderate-strong correlations (r value ranges, 0.59–0.82) with BMI, albumin, and BW at LTx assessment, Figure S2A–C (SDC, http://links.lww.com/TXD/A260). The NRI showed a weak correlation with MST as a continuous measure (r = –0.39; P < 0.0001; Figure S2D, SDC, http://links.lww.com/TXD/A260) and fair agreement (Kappa: 0.29; 95% confidence interval [CI], 0.15-0.43) as a categorical MST ≥ 2.

Nutritional Recommendations and Change in Body Weight Pretransplant

LTx candidates (n = 199) were evaluated by a dietitian within 6 months of transplant listing with 56 (28%) characterized as having high malnutrition risk. Non-CF LTx candidates at high risk compared with those at low risk were more likely to have self-reported unintentional weight loss in the preceding 12 months (32/49 [65%] versus 29/126 [23%];

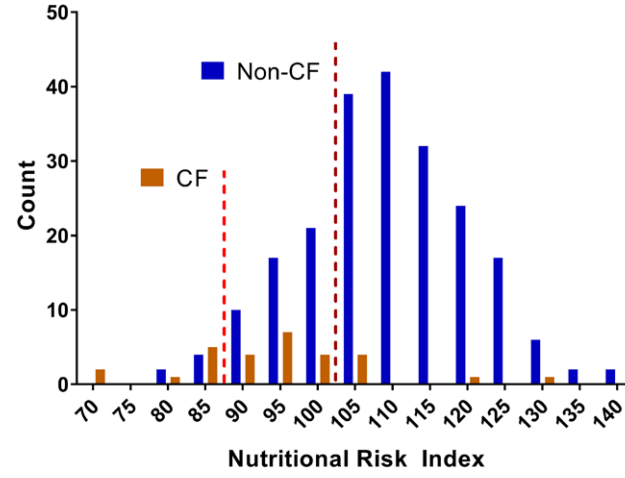

FIGURE 2. Distribution of nutritional risk index scores for non-CF and CF lung transplant candidates. Red vertical dashed line represents lowest quartile for nutrition risk index for non-CF and CF patients. CF, cystic fibrosis.

TABLE 1.

Baseline characteristics based on malnutrition risk

	Non-CF			CF		
Parameter	High malnutrition risk (Q1) n = 55	Low risk (Q2–Q4) n = 163	*P*	High malnutrition risk (Q1) n = 8	Low risk (Q2–Q4) n = 21	*P*
Median age, Y	58 (51–65)	61 (55–65)	0.29	25 (21–40)	34 (28–41)	0.07
Male sex	32 (58%)	97 (60%)	0.86	3 (38%)	10 (48%)	0.62
BMI (kg/m^2)	20.1 ± 2.4	27.2 ± 4.0	<0.0001	18.6 ± 1.9	20.7 ± 4.3	0.19
BMI categories						
Underweight (BMI < 18.5 kg/m^2)	17 (31%)	2 (1%)	<0.0001	4 (50%)	7 (33%)	0.74
Normal (18.5–24.9 kg/m^2)	37 (67%)	49 (30%)		4 (50%)	12 (57%)	
Overweight (25–29.9 kg/m^2)	1 (2%)	67 (41%)		0 (0%)	1 (5%)	
Obese (≥30 kg/m^2)	0 (0%)	45 (28%)		0 (0%)	1 (5%)	
Diagnosis						
Interstitial lung disease	32 (58%)	107 (66%)	0.47	NA	NA	NA
COPD	16 (29%)	34 (21%)				
Pulmonary arterial hypertension	2 (4%)	11 (6.5%)				
Other	5 (9%)	11 (6.5%)				
Albumin (g/L)	37 ± 5	41 ± 3	<0.0001	30 ± 6	39 ± 3	<0.0001
GERD	18 (33%)	50 (31%)	0.78	2 (25%)	1 (5%)	0.11
Gastrointestinal dysmotility	3 (5%)	2 (1%)	0.07	1 (13%)	2 (10%)	0.81
Osteoporosis	15/43 (35%)	25/132 (19%)	0.02	2/8 (25%)	2/19 (10%)	0.62
Osteopenia	21/43 (49%)	58/132 (44%)		3/8 (37.5%)	8/19 (42%)	
Normal bone density	7/43 (16%)	49/132 (37%)		3/8 (37.5%)	9/19 (47%)	
6-min walk distance (n = 54, 160); (n = 6, 20)	269 ± 114	316 ± 105	0.01	472 ± 91	387 ± 108	0.11
6-min walk distance % (n = 54; 160); (n = 6; 20)	40 ± 17	47 ± 16	0.004	64 ± 16	54 ± 14	0.14
Canadian transplant listing status						
Status 1	21 (38%)	63 (39%)	0.65	1 (12.5%)	11 (52%)	0.01
Status 2	25 (45%)	81 (50%)		4 (50%)	10 (48%)	
Status 3	9 (16%)	19 (12%)		3 (38%)	0	

Data are presented as mean ± SD, median with IQR (25%–75%), or proportions (%).
BMI, body mass index; CF, cystic fibrosis; COPD, chronic obstructive pulmonary disease; GERD, gastroesophageal reflux disease; IQR, interquartile range; NA, not applicable.

P < 0.0001) and more likely to use ONS (23/49 [47%] versus 10/123 [8%]; *P* < 0.0001) at the time of initial nutritional assessment, Table 2. Gastric tube feeding was undertaken by 6 (3%) LTx candidates, with 5 of these being CF patients, Table 2. ONS use was higher in CF patients with high malnutrition risk than those with low risk at the time of nutritional assessment, Table 2. There were no differences observed in pancreatic function, CF-related liver disease, or diabetes in CF patients with high malnutrition risk compared with those with low risk, Table 2.

As in Figure 3A for non-CF LTx candidates, weight gain (9/49 [18%] versus 2/125 [2%]) or gain/maintenance (26/49 [53%] versus 8/125 [6%]; *P* < 0.0001) was more commonly recommended in those with high malnutrition risk than those with low risk. Similarly, non-CF candidates with high malnutrition risk were more likely to be recommended ONS (n = 35/49 [71%] versus n = 20/123 [16%]; *P* < 0.0001) after the initial nutritional assessment, Table 2. The majority of non-CF LTx candidates with high malnutrition risk compared with those with low risk had gained (≥5%; n = 11/46 [24%] versus n = 4/115 [3%]) or maintained their weight (n = 28/46 [61%] versus n = 82/115 [71.5%]); *P* = 0.0002 after the nutritional assessment, Table 2. For the CF patients (Figure 3B), there was no significant percent change in BW after nutritional assessment with 2/19 (11%) losing ≥5% weight (Table 2).

Malnutrition Risk and Pretransplant Clinical Outcomes

A total of 28 patients were admitted to the ICU pretransplant for respiratory failure or sepsis, and 51 patients were delisted or died pretransplant, with non-CF patients comprising 23/28 (82%) and 45/51 (88%), respectively. In the non-CF cohort, no association was observed between high malnutrition risk and pretransplant ICU admission (odds ratio [OR], 2.2; 95% CI, 0.8-5.7; *P* = 0.13) or delisting/mortality (OR, 0.96; 95% CI, 0.4-2.1; *P* = 0.92), adjusted for age, sex, and diagnosis. Similarly, no crude association was observed in high malnutrition risk CF patients and respiratory failure (OR, 2.0; 95% CI, 0.3-15.0; *P* = 0.50) or pretransplant delisting/mortality (OR, 2.2; 95% CI, 0.2-22.3; *P* = 0.51).

Association Between Malnutrition Risk and Posttransplant Hospital Outcomes

A total of 196 patients were transplanted, with 16 recipients dying in hospital posttransplant (Figure 1). There were no differences in NRI in those surviving the hospital admission and those dying (108 ± 12 versus 105 ± 14; *P* = 0.47). For the 180 LTx recipients surviving the hospital transplant admission, the median ICU, hospital stay, and discharge disposition are summarized for non-CF and CF patients in Table 3, with no differences in early posttransplant outcomes observed. This analysis was also repeated for non-CF (Table S2, SDC, http://links.lww.

TABLE 2.

Pretransplant body weight and nutritional supplemental use

Parameter	Non-CF High malnutrition risk (Q1) n = 49	Non-CF Low risk (Q2–Q4) n = 126	Non-CF P	CF High malnutrition risk (Q1) n = 7	CF Low risk (Q2–Q4) n = 17	CF P
Preceding nutritional assessment						
Weight loss (unintentional)	32 (65%)	29 (23%)	<0.0001	2 (29%)	3 (17.5%)	0.45
Weight loss (intentional)	1 (2%)	20 (16%)		0%	0%	
Stable weight	15 (31%)	61 (48%)		4 (57%)	12 (70.5%)	
Weight gain (unintentional)	0%	14 (11%)		0%	1 (6%)	
Weight gain (intentional)	1 (2%)	1 (1%)		0%	1 (6%)	
Not available	0%	1 (1%)		1 (14%)	0	
Nutritional supplemental use for all candidates	**Non-CF High malnutrition risk (Q1) n = 49**	**Non-CF Low risk (Q2–Q4) n = 126**	**Non-CF P**	**CF High malnutrition risk (Q1) n = 7**	**CF Low risk (Q2–Q4) n = 17**	**CF P**
Oral nutritional supplement use at assessment	23/49 (47%)	10/123 (8%)	<0.0001	5/5 (100%)	7/15 (47%)	0.035
Oral nutritional supplement use recommended after assessment	35/49 (71%)	20/123 (16%)	<0.0001	5/5 (100%)	10/15 (67%)	0.14
Gastric tube feeding	0%	1/123 (1%)	1.0	4/5 (80%)	1/15 (7%)	0.001
CF-related characteristics						
Pancreatic insufficiency	NA	NA	NA	6 (86%)	15 (88%)	0.87
CF-related liver disease				1 (14%)	0%	0.11
CF-related diabetes				3 (43%)	9 (53%)	0.65
Changes in pretransplant body weight	**Non-CF High malnutrition risk (Q1) n = 49**	**Non-CF Low risk (Q2–Q4) n = 126**	**Non-CF P**	**CF High malnutrition risk (Q1) n = 7**	**CF Low risk (Q2–Q4) n = 17**	**CF P**
LTx assessment to transplant or delisting/death						
Time (median d)	246 (103–392)	197 (116–344)	0.67	67 (7–175)	181 (71–239)	0.13
Body weight (% median change) non-CF (n = 46; 115); CF (n = 4; 15)	0.3 (–4.1 to 4.0)	–2.3 (–5.7 to 0)	0.001	3.1 (–2.0 to 7.2)	0 (–2.8 to 0.9)	0.43
Change in body weight % after nutritional assessment	**Non-CF High malnutrition risk (Q1) n = 49**	**Non-CF Low risk (Q2–Q4) n = 126**	**Non-CF P**	**CF High malnutrition risk (Q1) n = 7**	**CF Low risk (Q2–Q4) n = 17**	**CF P**
Loss ≥5%	7/46 (15%)	29/115 (25%)	0.0002	0/4 (0%)	2/15 (13.5%)	0.67
Maintained (<±5%)	28/46 (61%)	82/115 (71.5%)		3/4 (75%)	11/15 (73%)	
Gain ≥5%	11/46 (24%)	4/115 (3.5%)		1/4 (25%)	2/15 (13.5)	
Unable to assess[a]	3/49 (6%)	11/126 (9%)		3/7 (43%)	2/17 (12%)	
Proportion achieving nutritional weight recommendations (gain, maintain, or lose)	32/46 (70%)	68/115 (59%)	0.22	3/4 (75%)	9/15 (60%)	0.58

Data are presented as mean ± SD, median with IQR (25%–75%), or proportions (%).
[a]Unable to assess change due to only 1-time point available.
CF, cystic fibrosis; LTx, lung transplant; NA, not applicable.

com/TXD/A260) and CF recipients (Table S3, SDC, http://links.lww.com/TXD/A260) using NRI as a continuous parameter with no association with early posttransplant outcomes.

Association Between Malnutrition Risk and Posttransplant Weight Change

Non-CF LTx recipients had a significant weight gain over the first-year posttransplant from pretransplant BW with a median change of 9.7% (3.5–19.5), as shown in Figure 4A and Table 4. By 12 months posttransplant, non-CF patients with high malnutrition risk had a median gain of 14.7% IQR (5.7–29.8) compared with those at low risk 8.9% IQR (2.2–16.6); $P = 0.008$, Table 4. Those with high malnutrition risk compared with low risk had a greater gain in weight at 3, 6, and 12 months, independent of age, sex, and diagnosis, Table 4. For CF patients, there was a median weight gain of 17.2% IQR (5.4–31.8) in the first-year posttransplant with no significant difference in weight change observed between the 2 malnutrition risk groups, Table 4.

There was heterogeneity in the pretransplant and posttransplant weight change between malnutrition risk groups highlighted in Figure S3 (SDC, http://links.lww.com/TXD/A260). The change in weight from pretransplant values in the first-year posttransplant was significantly greater in those underweight (BMI < 18.5 kg/m^2) pretransplant compared with those with a normal BMI adjusted for age, sex, and diagnosis, Table S4, SDC, http://links.lww.com/TXD/A260.

Association of Malnutrition Risk and Exercise Capacity Posttransplant

At 3 months posttransplant, the 6MWD was 435 ± 101 m (n = 155), which represents an increase of 138 ± 124 m from

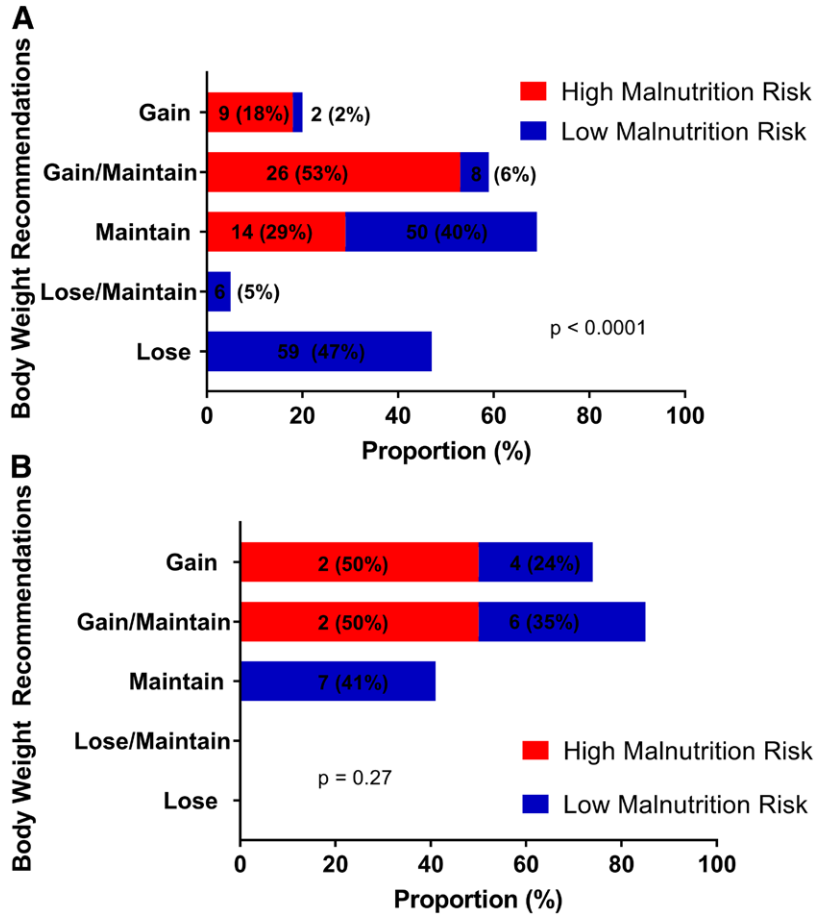

FIGURE 3. Nutritional body weight recommendations after initial nutritional assessment for noncystic fibrosis patients (A) and cystic fibrosis (B). Noncystic fibrosis patients: recommendations available for high malnutrition risk (n = 49) and low risk (n = 125). Cystic fibrosis patients: recommendations available for high malnutrition risk (n = 4) and low risk (n = 17).

pretransplant for the entire cohort. There was a plateau by 3 months posttransplant with no further increase in 6MWD at 6 and 12 months posttransplant 442 ± 118 m ($P = 0.58$; n = 145) and 444 ± 122 m ($P = 0.52$; n = 140), respectively. For non-CF recipients (Figure 4B), high malnutrition risk was associated with a greater improvement in 6MWD at 3 months and 12 months posttransplant compared with pretransplant, independent of age, sex, and diagnosis (Table 4). For CF recipients, no significant mean difference between malnutrition risk groups in 6MWD change from pretransplant values was observed at 3, 6, and 12 months posttransplant, adjusted for sex Table 4.

Association of Malnutrition Risk and Posttransplant Mortality

The 1-year mortality for this cohort of LTx recipients was 14% (n = 27/196), with all deaths occurring in non-CF recipients. In non-CF recipients, there was no association between 1-year mortality and high malnutrition risk defined using the lowest NRI quartile (OR, 1.27; 95% CI, 0.47-3.4; $P = 0.63$) or as continuous NRI measure (OR, 0.71; 95% CI, 0.47-1.05 per 10 points; $P = 0.08$), adjusted for age, sex, and diagnosis in separate models.

DISCUSSION

Most LTx candidates with high malnutrition risk were able to maintain or gain weight pretransplant with access to nutritional care. LTx recipients at high malnutrition risk had comparable or greater improvement in their exercise capacity than those at low risk in the first-year posttransplant. No differences between pretransplant or posttransplant outcomes were observed in non-CF and CF LTx recipients, highlighting that NRI was not prognostic of posttransplant outcomes in our population.

Non-CF LTx candidates had significantly higher NRI values than CF patients demonstrating the inherent differences in malnutrition risk for CF patients. Patients with CF present a unique set of risk factors for malnutrition due to malabsorption, CF-related liver disease, and pancreatic insufficiency.[25] Given the potential differences in malnutrition risk in the CF cohort, we did not utilize the previously applied NRI cutoffs for malnutrition risk of 100 or less in CHF or LVAD patients.[17,29] In fact, applying this cutoff would mean that about 3-quarters of our CF and one-fifth of the non-CF cohort would be characterized as being at risk of malnutrition. The NRI distribution for the non-CF cohort is more representative of advanced CHF populations that had 34% characterized as having moderate-severe malnutrition risk.[29] Thus, future studies evaluating the NRI in chronic lung disease will need to consider these differences between CF and non-CF populations.

In our LTx program, registered dietitians provide nutritional care and individualized recommendations for each patient to optimize their nutritional status pretransplant

TABLE 3.

Posttransplant outcomes based on malnutrition risk in those surviving to hospital discharge

Parameter	Diagnostic group	Total cohort (n = 180)	High malnutrition risk (Q1) (n = 47)	Low risk (Q2–Q4) (n = 133)	P	High malnutrition risk vs low risk Median difference in d (95% CI)[a]	P
D of mechanical ventilation	Non-CF (n = 151)	2 (1–5)	2 (1–4)	2 (1–5)	0.69	1.0 (–0.08 to 1.0)	0.13
	CF (n = 23)	1 (1–3)	2 (1–8)	1 (1–2)	0.15	1.0 (–0.3 to 4.4)	0.67
ICU d	Non-CF (n = 157)	4 (2–15)	4 (2–15)	4 (2–14)	0.77	0.59 (–0.90 to 3.4)	0.59
	CF (n = 23)	3 (2–6)	4 (2–10)	3 (1–4)	0.33	1.0 (–1.2 to 8.6)	0.69
Hospital stay (d)	Non-CF (n = 157)	25 (17–47)	31 (18–48)	23 (16–47)	0.12	8.87 (–1.03 to 12.8)	0.07
	CF (n = 23)	20 (18–36)	29 (18–46)	19.5 (17–29)	0.25	9.2 (–7.9 to 28.7)	0.33
Discharge disposition		Total cohort (n = 180)	High malnutrition risk (Q1) (n = 47)	No risk (Q2–Q4) (n = 133)	P	High malnutrition risk vs low risk OR (95% CI)	P
Discharge to inpatient rehab vs home	Non-CF (n = 157)	28/157 (18%)	9/40 (23%)	19/117 (16%)	0.37	1.76 (0.69–4.50)	0.24
	CF (n = 23)	1/23 (4%)	1/7 (14%)	0/16 (0 %)	0.12	–	

Data presented as median with IQR (25%–75%), proportions (%), and median difference (95% CI).
[a]Multivariable models: non-CF cohort: adjusted for age, sex, and diagnosis.
CF cohort: adjusted for age and sex.
CF, cystic fibrosis; CI, confidence intervals; ICU, intensive care unit; IQR, interquartile range; OR, odds ratio.

based on the patient's underlying diagnosis, age, and comorbidities. To our knowledge, there are no standardized guidelines to combat malnutrition in chronic lung disease, but general recommendations aim to offset weight loss through nutritional recommendations with the goal of preventing any further weight loss.[44-46] We observed that 86% of LTx candidates were able to maintain or gain weight (≥5%) during the pretransplant period with nutritional counseling, but the change in weight on average was minimal as in other studies.[24] Given that nutritional counseling is standard of care at our center, we are unable to evaluate the degree of weight loss that may have ensued without nutritional care. However, it is important to highlight that about one-half of the patients with high malnutrition risk reported weight loss in the preceding 1-year before nutritional assessment. It is possible that improvements in nutritional intake may have had an effect on stabilization of BW.

LTx candidates with high malnutrition risk had comparable or greater gain in their BW and exercise capacity within the first-year posttransplant compared with the group at low risk. Weight gain observed within our cohort is comparable to other studies within the first-year posttransplant (median about 10%) and was more pronounced in CF patients and those who had a BMI < 18.5 kg/m^2, as previously described.[24,47,48] Similarly, the improvement in exercise capacity was comparable or greater for CF and non-CF patients deemed to have high malnutrition risk compared with those at low risk, highlighting the exercise capacity benefits derived with transplantation. The improvement in weight and exercise capacity with transplantation is informative when planning nutritional care and rehabilitation strategies in the posttransplant period, given unifying factors such as alleviation of ventilatory limitations, decreased respiratory energy requirements, and increased physical activity levels.[49,50]

We hypothesized that those at high malnutrition risk would have increased morbidity and mortality pretransplant and posttransplant. This is based on the assumption that those with high malnutrition risk may have decreased physiological reserve and may have a more difficult time combating stressors such as respiratory failure, infection, or surgical stress.[51-53] However, we did not observe any significant differences in pretransplant delisting/mortality, posttransplant hospital outcomes, or 1-year mortality between the nutritional states. One possibility for this lack of association is our intermediate sample size, given the wide confidence intervals observed for several outcomes, such as pretransplant delisting/mortality and posttransplant hospital stay. Second, NRI provides an estimate of malnutrition risk[54] but does not capture an actual diagnosis of malnutrition, which may have been more prognostic.

A fair agreement was observed between NRI and MST in our LTx cohort with respect to malnutrition risk. This may be due to several factors such as the subjectivity of MST given its reliance on self-reported data on weight loss and appetite, retrospective scoring of MST from charts, and absence of validation of these instruments in LTx candidates. It is important to highlight that several nutritional screening instruments have been used in chronic disease including the Malnutrition Universal Screening Tool, Mini-Nutritional Assessment, and NRI,[55] but the performance characteristics of these screening tools are disease specific and can be variable based on the clinical setting.[55-57] We feel that the NRI or other malnutrition screening instruments can potentially help in the ambulatory setting if they are paired with a nutritional assessment to identify candidates at high risk of malnutrition prompting further evaluation and nutritional support. Thus, future work should aim to evaluate the performance characteristics of nutritional screening instruments in LTx candidates relative to other

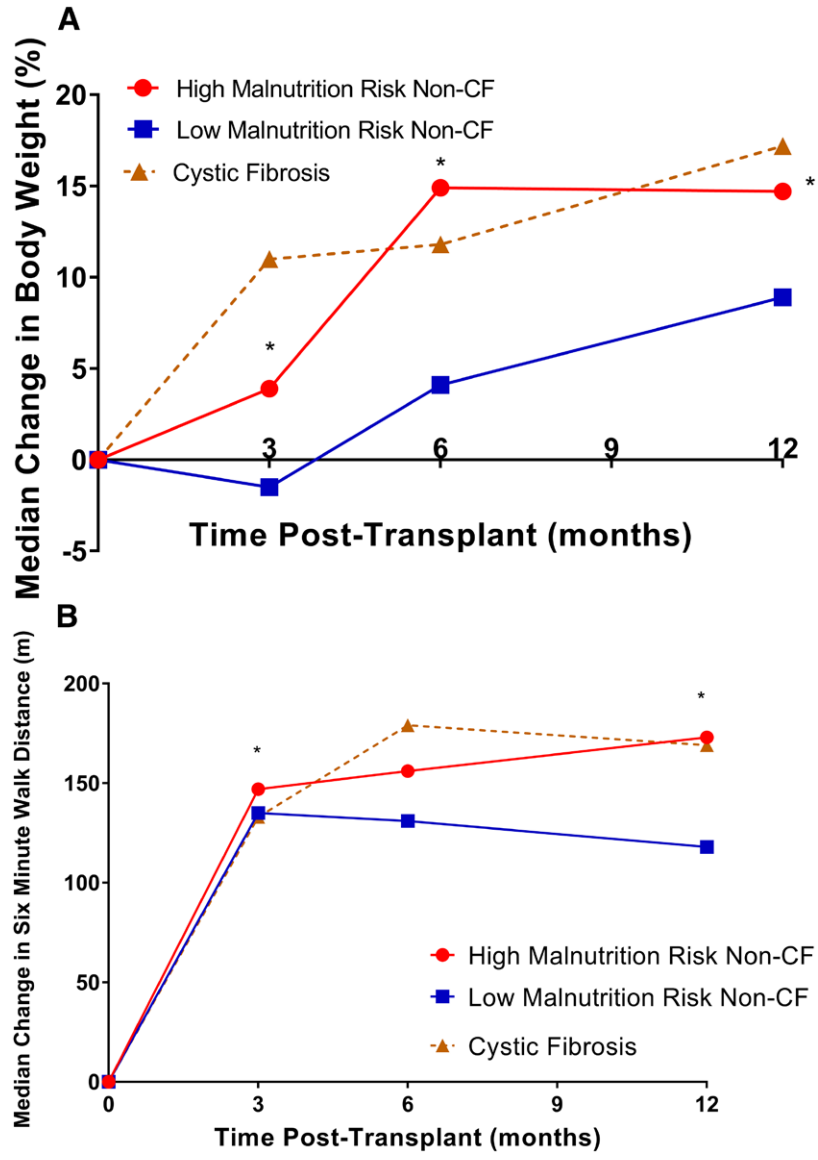

FIGURE 4. Median percent change in body weight (A) and exercise capacity (B) in the first-y post lung transplantation. Results presented as median values with interquartile ranges (not shown). *Represents significant mean difference between high malnutrition risk vs low-risk group in non-CF patients adjusted for age, sex, and diagnosis. CF group is displayed for reference with no adjusted comparison performed within CF group (high malnutrition risk vs low risk) given small sample size. CF, cystic fibrosis.

nutritional tools (ie, Subjective Global Assessment) that can help establish a diagnosis of malnutrition.

There are several limitations that need to be highlighted. First, our study design was retrospective, and thus we are unable to attribute any effects from the standard nutritional care at our center. Second, NRI has not been validated within a lung disease or transplant cohort; thus, we were unable to utilize previously established cutoffs applied in other populations such as CHF or LVAD patients.[17,29] Given the lack of an established cutoff, we assessed outcomes using both distribution methods (lowest quartile) and NRI as a continuous parameter with no differences observed. It is important to highlight that NRI was calculated using standardized equations applied in the literature utilizing an accepted ideal BW formula.[31] Given there is no universal calculation of ideal BW, there is some literature suggesting that utilization of ideal BW ranges may be an emerging concept to explore in future studies,[58] allowing calculation of an estimated NRI range for each individual. Furthermore, NRI was assessed at 1-time point only as albumin is usually collected at the time of LTx assessment or listing at our center and not posttransplant. Thus, we are unable to evaluate whether malnutrition risk changes during the pretransplant or posttransplant period or to what extent lung disease severity may have on the NRI given the cross-sectional assessment. Finally, there was significant improvement in weight posttransplant across all LTx recipients. However, we are unable to attribute this weight gain to muscle mass or adiposity, but previous investigations have demonstrated significant improvements in muscle mass posttransplant.[59,60] Future investigations evaluating malnutrition risk can apply computed tomography measures of visceral or subcutaneous adiposity,[61,62] which may help with assessment of nutritional status. It is also important to highlight that all LTx candidates in our program participate in a supervised exercise training program pretransplant and 3 months posttransplant with access to nutritional care as needed. Thus, the

TABLE 4.

Change in body weight and exercise capacity over the first-y posttransplant compared with last assessment pretransplant

Parameter	Diagnostic group	Total cohort	High malnutrition risk (Q1)	Low risk (Q2–Q4)	*P*	Mean difference between high malnutrition risk vs low risk (95% CI)[a]	*P*
3 mo post-Tx							
% Median change in body weight	Non-CF (n = 39, 115)	0 (–5.5 to 6.2)	3.9 (–0.5 to 9.5)	–1.5 (–6.5 to 5.8)	0.004	4.5 (1.1–7.9)	0.01
	CF (n = 6; 16)	11 (0.3–16.3)	8.6 (0.2–18.8)	11 (–1.1 to 16.5)	0.91	1.0 (–10.1 to 12.1)	0.85
Median change in 6MWD (m)	Non-CF (n = 31;107)	139 (44–218)	147 (103–273)	135 (33–216)	0.12	52 (0.1–105)	0.0498
	CF (n = 3;14)	133 (97–222)	122 (88–416)	151 (95–220)	0.99	53 (–84 to 189)	0.42
6 mo post-Tx							
% median change in body weight	Non-CF (n = 39;110)	5.5 (–1.3 to 15.1)	14.9 (4.7–21.9)	4.1 (–2.4 to 11.2)	<0.0001	8.7 (4.6–12.9)	0.0001
	CF (n = 7;16)	11.8 (4.9–18.8)	8.7 (6.1–18.8)	14.4 (3.9–19.4)	0.97	–1.4 (–12.8 to 10.0)	0.80
Median change in 6MWD (m)	Non-CF (n = 35;94)	148 (54–235)	156 (88–298)	131 (40–222)	0.13	53 (–5 to 111)	0.08
	CF (n = 3;13)	179 (117–242)	144 (113–503)	179 (99–235)	0.99	76 (–83 to 236)	0.32
12 mo post-Tx							
% median change in body weight	Non-CF (n = 27;107)	9.7 (3.5–19.5)	14.7 (5.7–29.8)	8.9 (2.2–16.6)	0.008	6.8 (1.1–12.4)	0.02
	CF (n = 7;14)	17.2 (5.4–31.8)	18.8 (–4.5 to 38.3)	16.3 (7.1–29.0)	0.86	–3.8 (–21.2 to 13.7)	0.65
Median change in 6MWD (m)	Non-CF (n = 25;98)	129 (44–222)	173 (92–264)	118 (41–221)	0.12	65 (1–128)	0.046
	CF (n = 4;13)	169 (81–274)	113 (–188 to 417)	171 (81–274)	0.62	–51 (–258 to 156)	0.60

Data are presented as median with IQR of 25%–75% and mean difference (95% CI).
[a]Multivariable models adjusted for age, sex, and diagnosis for non-CF group; CF group adjusted for sex.
CF, cystic fibrosis; CI, confidence interval; 6MWD, 6-min walk distance; Tx, transplantation.

effects on malnutrition and BW observed in our program may be different from those without these practices.

In conclusion, the NRI was not prognostic of pre or posttransplant outcomes in LTx patients. Most LTx candidates characterized as having high malnutrition risk were able to maintain or gain weight pretransplant with considerable weight gain posttransplant. There was also an improvement in exercise capacity posttransplant that was comparable or even greater than that of the low-risk malnutrition group. Future prospective studies are needed to evaluate the performance of the NRI as a nutritional marker against previously established nutritional scales and the effectiveness of nutritional interventions in the LTx population.

ACKNOWLEDGMENTS

The authors would like to acknowledge the support of the Toronto Lung Transplant Program and Mr Ramraj Rajakumar and Ms Sharaniyaa Balachandran for their help with data abstraction from the Lung Transplant Database.

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