Title

Incidence of Conversion to Active Waitlist Status Among Temporarily Inactive Obese Renal Transplant Candidates

Author

Huang, Edmund

Publication Date

2015

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA

Los Angeles

Incidence of Conversion to Active Waitlist Status Among Temporarily Inactive Obese Renal Transplant Candidates

A thesis submitted in partial satisfaction of the requirements for the degree Master of Science in Clinical Research

by

Edmund Huang

2015

ABSTRACT OF THE THESIS

Incidence of Conversion to Active Waitlist Status Among Temporarily Inactive Obese Renal Transplant Candidates

by

Edmund Huang

Master of Science in Clinical Research

University of California, Los Angeles, 2015

Professor Robert M. Elashoff, Chair

Background: Candidates may be active or temporarily inactive (status 7) on the kidney transplant waiting list. One reason candidates may be inactive is for a "weight currently inappropriate for transplantation". We hypothesized that many of these candidates would not achieve active status.

Methods: Using OPTN/UNOS data from 2006-2012, we used competing risks methods to determine the cumulative incidence of conversion to active status (activation), death, and delisting before conversion among 1679 obese adult kidney candidates designated as status 7 due

to a weight inappropriate for transplantation. Fine and Gray competing risks regression was performed to characterize factors associated with conversion to active status in the overall study population and of eventual transplantation among a subgroup of activated candidates.

Results: At six years, the cumulative incidence of activation was 49%, of death before conversion was 15%, and of delisting was 21%. Higher body mass index (BMI) was strongly associated with a decreased subhazard of activation (BMI ≥45 vs. 30-34.9, sHR: 0.22; 95% CI: 0.16-0.33). Female gender, diabetic end-stage renal disease, history of a previous transplant, panel reactive antibodies <80%, dialysis-dependence at listing, and UNOS region 5 were negatively associated with activation. Among activated candidates, the cumulative incidence of transplantation at six years after initial waitlisting was 61%.

Conclusions: Our findings indicate that half of obese status 7 candidates with a weight inappropriate for transplantation will not achieve active waitlist status. BMI at listing had a strong association with conversion to active status; however, co-morbid factors and regional variation also impact activation.

The thesis of Edmund Huang is approved:

Suphamai Bunnapradist

David Elashoff

Marc Adam Suchard

Robert M. Elashoff, Committee Chair

University of California, Los Angeles

2015

Table of Contents

List of Figures and Tables

Acknowledgements

Chapter 1 is a version of: Huang E, Shye M, Elashoff D, Mehrnia A, Bunnapradist S. Incidence of Conversion to Active Waitlist Status Among Temporarily Inactive Obese Renal Transplant Candidates. *Transplantation*. 2014 Jul 27;98(2):177-86. doi: 10.1097/TP.0000000000000037.

E.H., M.S., and S.B. contributed to the research design, statistical analysis, and writing of the paper; D.E. contributed to the research design and statistical analysis; A.M. contributed to the statistical analysis.

Chapter 2 is a version of: Huang E, Bunnapradist S. Pre-transplant weight loss and survival after kidney transplantation. *Am J Nephrol.* 2015 Jul 25;41(6):448-455. doi: 10.1159/000437341.

E.H. and S.B. contributed to the research design, statistical analysis, and writing of the paper.

This work was supported in part by Health Resources and Services Administration contract 231-00-0115. The content is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. government.

Chapter 1. MANUSCRIPT

Introduction:

Kidney transplant candidates on the United Network for Organ Sharing (UNOS) waiting list may be listed as temporarily inactive (status 7). In contrast to active candidates, status 7 candidates are ineligible for deceased donor organ offers. Historically, candidates designated as status 7 could not accrue waiting time towards kidney transplantation. However, a UNOS policy change was implemented in November, 2003 allowing status 7 kidney candidates to accrue waiting time and resulted in a stark increase in the representation of status 7 candidates on the waiting list (1). Since 2002, the year prior to the UNOS policy change, the number of active candidates increased 23%, from 43,773 candidates in 2002 to 54,047 in 2011. In contrast, the number of status 7 candidates increased almost six-fold over the same time period, from 5,587 candidates in 2002 to 32,501 in 2011, representing 38% of the kidney waiting list (2). This trend suggests that many patients considered inappropriate for transplantation may be prematurely placed on the waiting list in order to take advantage of the waiting time accrual benefits allowed by UNOS.

There are a number of reasons why a candidate may be designated status 7. Among them is a "weight currently inappropriate for transplant". Obesity is associated with increased operative time, cardiovascular events, and delayed wound healing (3). Additionally, obesity has been independently associated with an increased risk of delayed graft function, prolonged hospitalization, acute rejection, and decreased kidney graft survival (4), although a recent analysis demonstrated a survival benefit with kidney transplantation over dialysis among most subgroups of obese patients (5).

Although no formal guidelines have been created to define acceptable weight limits for kidney transplantation, many programs use body mass index (BMI, kg/m^2) as part of their evaluation criteria for transplantation (6). BMI thresholds vary among kidney transplant programs, limiting its utility as a clinical endpoint in studies investigating intentional weight loss among kidney transplant candidates. The designation of "weight currently inappropriate for transplant" may be a better representation of body composition and suitability for transplant surgery than BMI.

This study was performed to address the question of how often do excessively obese kidney transplant candidates achieve a suitable body composition for transplantation. We hypothesized that a large number of obese status 7 kidney candidates with a "weight currently inappropriate for transplant" at initial registration would not achieve active status. In order to examine this hypothesis, data from the Organ Procurement and Transplantation Network (OPTN)/UNOS was analyzed to investigate factors associated with conversion to active status among obese status 7 kidney transplant candidates.

Methods:

Study design:

This was a retrospective observational cohort study using data from the OPTN/UNOS STAR registry files with follow-up to October 19, 2012. All adult (≥18 years) candidates for kidney transplant alone with a body mass index (BMI) ≥30 kg/m^2 were included. In order to identify a population of candidates classified as obese at the time of presentation, we included only candidates designated status 7 due to a "weight temporarily inappropriate for transplantation" within ninety days of initial registration (N=2747). Candidates with multiple listings, missing BMI, and clinically implausible BMI, defined as a BMI ≥65 kg/m^2, were excluded.

The study population was restricted to candidates with an initial registration for kidney transplantation after April 24, 2006, the first recorded date on the STAR registry waitlist history file. In order to allow for a sufficient follow-up period, candidates registered for transplantation up to October 19, 2010 (two years before the date of last follow-up in the database) were included. The final study population consisted of 1679 adult kidney candidates with a BMI ≥30 kg/m^2 designated as status 7 due to a weight inappropriate for transplantation.

Study definitions:

Time to active status was defined as the number of days from initial registration to the first designation of active status on the UNOS waitlist history file. We considered all candidates who were activated at least once to be in the "activated" group, regardless of whether or not the candidate later reverted back to inactive status. A waitlist death was determined if the waitlist file contained record of a date of death and the candidate was removed from the waiting list. A

candidate was considered transplanted if there was record of a transplant date and was assigned a transplant recipient registration identification code. A candidate removed from the waiting list in the absence of death or a transplant was considered delisted.

Statistical analysis:

The study population was stratified into two groups according to whether active status was achieved. Those who did not convert to active status over the study period were classified as "inactive/never activated" and compared to those who achieved active status at least once, defined as "activated". Baseline characteristics were described using proportions for categorical variables and medians with associated inter-quartile ranges (IQR) for continuous variables. An omnibus chi-square test was performed for comparison of categorical variables and Wilcoxon rank sum test for continuous variables. The primary outcome of interest was time to first active status. Because patients who died or were removed from the waiting list (delisted) were no longer able to experience the outcome of interest, death events and waitlist removals were treated as competing events. The time to first active status among the study population was modeled with Fine and Gray competing risks methods (7). The follow-up duration was up to six years and all patients were censored at the end of the study period on October 19, 2012. Candidates with follow-up to the end of the study period who did not experience an outcome (active status, death, or delisting) were considered to be in continued inactive status. Multivariate analysis was performed using backwards stepwise regression, eliminating covariates associated with a $p>0.10$. Candidate predictors tested in the model included age (categorized as <40, 40-49, 50-59, and ≥60), gender, race (white, black, Hispanic, other), BMI at registration

(30-34.9, 35-39.9, 40-44.9, and ≥45), blood type, percent panel reactive antibodies (<80%, ≥80%), dialysis status at registration, education level (high school or below, college or above, unknown), primary cause of end-stage renal disease (diabetes mellitus, hypertension, glomerulonephritis, polycystic kidney disease, and other), UNOS region, primary insurance status (public, private, and other), and history of a previous transplant. Schoenfeld residuals plotted against time did not show a significant violation of the proportional hazards assumption. Tests for interactions were performed and no significant interactions were identified. Model performance was assessed through the calculation of an adapted C-index for competing risks models, as described by Wolbers, et al (8,9). This function accounts for the inability of subjects experiencing competing events to experience the event of interest (in this case, conversion to active status) by treating them as censored at infinity. We performed this function with the R statistical package, version 2.15.3, using the cmprsk package. Coefficients derived from Fine and Gray models were identical using the R statistical software and Stata. The adapted C-index was calculated from the entire study population and internal validity was measured with bootstrapping. The bootstrapping procedure consisted of sampling 1000 consecutive times with replacement for 1679 subjects. The adapted C-index for the bootstrapped samples was reported as the average concordance estimate of the bootstrapped samples.

A subgroup analysis was then performed among all candidates in the activated group to calculate the time to transplantation. For this analysis, living donor transplant, death and removal from the waitlist were considered as competing events and those not experiencing an outcome during the study period (transplant, death, delisting) were considered as still waiting for transplant. Using Fine and Gray competing risks methods to estimate the adjusted subhazard ratio of time to transplant, a multivariate model was performed using backwards stepwise

selection with elimination of covariates associated with a $p>0.10$. Variables tested included the same predictors as above. Two separate models were run to assess time to transplantation as the outcome of interest: 1) the first model defined transplant as a composite of deceased and living donor transplant in the face of death and delisting as competing events; 2) the second model assessed time to deceased donor transplant in the face of living donor transplant, death, and delisting as competing events. For the model of time to deceased donor transplant, plots of scaled Schoenfeld residuals vs. time indicated that the covariate for "A" blood type did not satisfy the proportional hazards assumption. Cumulative incidence curves showed crossing of the deceased donor and living donor transplant incidences at 2.3 years. Therefore, an extended Cox model was performed using a heavyside function for the time intervals < 2.3 years and ≥ 2.3 years.

All p-values were two tailed and a $p<0.05$ was considered statistically significant. Stata version 11 (College Station, TX) was used for all analyses.

Results:

Baseline characteristics:

Table 1-1 describes the baseline characteristics of the study population. A total of 1679 obese candidates were included in the study population. The median BMI at registration was 39.1 kg/m^2 (IQR: 36.8-41.8 kg/m^2). Most patients in the study were classified as obese class II or higher according to World Health Organization criteria (BMI $\geq$35 kg/m^2). A total of 714 candidates (42.5%) were activated at least once over the six year follow-up period; 965 (57.5%) remained inactive during the study period. Of the 714 activated candidates, 332 were transplanted (46.4%). The OPTN/UNOS database only reports BMI at registration and transplant, but does not record BMI at other time points while waitlisted. Of the 332 kidney transplant recipients, BMI at transplant was available in 315. The median BMI change from registration to transplant of the 315 recipients was -2.1 kg/m^2 (IQR: -4.7, -0.14 kg/m^2).

Activated candidates were younger and had a lower BMI at registration than those who remained inactive during the study period. Proportionally more activated patients were white, attained a college level of education or higher, and had private primary insurance. Candidates who were listed inactive/never activated were more likely to be on dialysis at the time of waitlist registration, achieve a high school level education or lower, have diabetes as the primary cause of end-stage renal disease (ESRD), and have public insurance for their primary insurance.

There was variability between UNOS regions in the proportion of candidates converted to active status. A higher proportion of candidates were listed inactive/never activated in UNOS region 5. UNOS region was stratified into low versus high waiting time regions, defined as the five UNOS regions with the lowest median waiting time and the six UNOS regions with the highest median waiting time (10). A smaller proportion of candidates were activated in high

waiting time regions compared to low waiting time regions (38.7% vs. 51.5%, p<0.001; data not shown), but this effect was mostly driven by region 5. When region 5 candidates were excluded from the high waiting time group, the proportion of candidates activated in the high and low waiting time groups was similar (46.1% vs. 51.5%, p=0.07; data not shown).

Cumulative incidence of conversion to active status

Figure 1-1 shows the cumulative incidence of conversion to active status, death, and delisting over six years of follow-up. In this plot, the cumulative incidences of death and delisting reflect occurrences of competing events among inactive candidates and do not reflect events occurring after candidates were activated. The rate of conversion to active status was highest in the first year after registration and then decreased with each subsequent year. Most of the candidates who were activated did so within the first three years of registration (cumulative incidence at three years: 39%). At six years, the overall incidence of conversion to active status was 49%; the cumulative incidence for death was 15% and was 21% for delisting. Only 15% of status 7 candidates remained inactive six years after registration.

Competing risks regression

Table 1-2 shows competing risks regression models for time to active status. Univariate analyses showed decreasing subhazards of conversion to active status with increasing age and BMI at registration. Males, white race, and elevated PRA were associated with increased subhazards of conversion to active status, whereas being on dialysis at registration, lower level of education, diabetes as a cause of ESRD, and public insurance were associated with decreased

subhazards of conversion to active status. Using UNOS region 5 as the reference group, each of the ten other UNOS regions were associated with an increased subhazard of conversion to active status. After backwards stepwise regression, gender, BMI at listing, PRA, dialysis-dependence at listing, cause of ESRD, retransplantation, and UNOS region were associated with conversion to active status. Increasing BMI at registration was a strong predictor of conversion to active status, with a decreasing subhazard associated with each increase in BMI category. Using the univariate model, the predicted cumulative incidence of conversion to active status at six years was 69% for those with a BMI<35 kg/m^2, 54% for BMI 35-39.9 kg/m^2, 41% for BMI 40-44.9 kg/m^2, and 28% for BMI ≥45 kg/m^2 (Figure 1-2).

Predictive discrimination of the multivariate model was assessed using an adapted C-index, which estimates concordance in competing risks models. The concordance estimate for the original sample was 0.67. A bootstrap sampling procedure with replacement was performed to obtain 1000 consecutive samples of 1679 subjects each. The average adapted C-index of the bootstrapped samples was 0.65.

Subgroup analysis: Time to transplant among status 7 candidates converted to active status

Table 1-3 compares baseline characteristics of activated patients who were transplanted to those not transplanted and Figure 1-3 shows the cumulative incidence of deceased and living donor transplantation, accounting for the competing events of death and delisting. For this analysis, death and delisting events occurred after a candidate was converted to active status. The time to event was considered from the date of initial transplant registration.

There were 714 candidates who achieved active status during the study period. The cumulative incidence of kidney transplantation among activated candidates at six years after registration was 61% (deceased donor: 42%; living donor 19%). Most patients were activated well before transplantation (median: 175 days, IQR: 40, 519; data not shown), although the interval between activation and transplantation was shorter for living donor recipients (median: 69 days; IQR: 0, 264) than deceased donor recipients (median: 220 days; IQR: 70, 600).

Univariate and multivariate competing risks regression models for time to overall transplantation (both deceased and living donor) and time to deceased donor transplantation are represented in Tables 1-4 and 1-5. On multivariate analysis, non-white race, elevated panel reactive antibodies (PRA; ≥80%), and high school education or lower was associated with decreased subhazards of overall transplantation and blood types A and AB were associated with increased subhazards relative to blood type O (table 1-4). BMI at registration was not associated with eventual transplantation among activated candidates. When living donor transplantation was considered along with death and delisting as a competing event to deceased donor transplantation, blood type A was associated with an increased subhazard of deceased donor transplantation over the first 2.3 years after registration compared to the reference group of blood type O. Thereafter, blood group A was not associated with deceased donor transplantation. All UNOS regions were associated with an increased subhazard of deceased donor transplantation relative to region 5 except UNOS regions 2 and 9.

The cumulative incidence of death among activated candidates was 6% and delisting was 16%. At the end of the six-year follow-up period, 280 of the 714 activated candidates did not experience an event and underwent administrative censoring. Of these, 202 remained active and 78 returned to inactive status by the end of the study period. The leading reason for return to

status 7 was being temporarily too sick (30 in total, or 4% of all activated candidates) followed by having a weight currently inappropriate for transplant (20 in total, or 3% of all activated candidates).

Discussion:

This study investigated waitlist outcomes among temporarily inactive obese kidney transplant candidates in the United States. Approximately half of obese candidates with a listing weight considered inappropriate for transplantation converted at least once to active status over the span of six years. Factors associated with conversion to active status included male gender, UNOS region, and elevated PRA. Co-morbid factors, including increasing BMI at registration, diabetes as a cause of ESRD, re-transplantation, and dialysis-dependence at registration were associated with a decreased subhazard of conversion to active status. Only 15% remained inactive at the end of six years, and the remainder either died or was removed from the waiting list.

Prior observational studies on obesity in dialysis patients have been limited by an inability to distinguish intentional from unintentional weight loss. Because body weight is influenced by the degree of extracellular volume, muscle mass, and nutritional status, it is not a reliable indicator of adiposity and body composition in ESRD (11). Therefore, studies have used surrogates for muscle mass, such as creatinine, to complement inferences drawn on the effect of body weight on outcomes (12-14). In this study, we limited the inclusion criteria to candidates who were made temporarily inactive due to their weight and applied the condition that they have a BMI $\geq$30 kg/m^2 in order to certify that these patients were indeed obese. We then used conversion to active status as our primary endpoint and considered it to be a surrogate for intentional weight loss. Although we could not confirm the degree of weight change among all candidates because OPTN/UNOS only keeps record of weight at the time of waitlist registration and at transplant, we were able to calculate BMI change in those who received a transplant. In this subgroup of candidates, the median change in BMI was -2.1 kg/m^2, supporting

our assumption that conversion to active status is a reasonable proxy for weight loss.

Approximately half of obese candidates initially considered to have an inappropriate weight for transplantation converted at least once to active status over six years. Most of these candidates achieved active status within the first year of registration and relatively few did so after three years. This observation is supported by data from other studies showing that the highest degree of weight loss generally occurs early after intervention (15-20). The rate of delisting was fairly constant across the study period, suggesting that many transplant centers do not offer a defined period of time for weight loss beyond which the candidate is delisted, although our data argues that such a strategy may be justified.

There was a strong association of BMI at registration with conversion to active status. Patients with the highest BMI ($\geq$45 kg/m^2) were much less likely to be activated than those with a BMI 30-34.9 kg/m^2. Based on the unadjusted model, 69% of candidates with a BMI <35 kg/m^2 are predicted to convert to active status within six years compared to only 28% of candidates with a BMI $\geq$45 kg/m^2. This observation suggests that the heaviest candidates may be given unrealistic weight loss targets for transplantation. These patients might potentially benefit from formal intervention, such as structured weight loss programs, drug therapy, or bariatric surgery.

Co-morbid factors and female gender are also negatively associated with conversion to active status. In particular, diabetes as a cause of ESRD and dialysis-dependence at the time of registration were negatively associated with conversion to active status. These factors have been correlated with decreased physical activity in previous studies of ESRD patients and may be barriers to successful weight loss (21-23). Additionally, it is probable that transplant centers are less likely to activate obese candidates with co-morbidities.

There is geographical variability in conversion to active status, as can be observed with the addition of UNOS region to the model. This variability likely originates at the level of the transplant center, as there is no consensus regarding weight thresholds for transplantation (6). We did not have center-specific data to substantiate this, however. Other factors, such as candidate demographics and local waiting time, also likely contribute to the regional variability, but were not assessed in this study.

Prior observational studies have noted an "obesity paradox" in dialysis patients where higher BMI is associated with lower mortality (24,25). Whereas it may seem logical that weight loss would confer improved survival in obese dialysis patients, some authors have suggested that weight loss may be detrimental (26). Our study did not directly compare intentional versus unintentional weight loss, but does suggest that intentional weight loss is not harmful to obese ESRD patients. Among activated candidates, we observed a remarkably low death rate over the course of the six-year follow-up period (6%), a mortality figure that is considerably lower than that reported in other studies of the waitlist ESRD population (27,28).

Other waitlist outcomes observed in our study were also reassuring, with the majority of activated candidates ultimately receiving a kidney transplant over the study period (61%). Few patients returned to inactive status because of regaining an inappropriate weight for transplant (20 in total, or 3% of all activated candidates). The most common reason for return to inactive status was due to being "temporarily too sick", although only a small percentage of all activated candidates were in this category (30 patients total, or 4% of all activated candidates).

We acknowledge some limitations to our study. No established criteria exist defining what constitutes an appropriate body composition for kidney transplantation, and programs differ in their approach to obese candidates. Therefore, the outcome of conversion to active status was

not based on uniform practice patterns. Nevertheless, the use of this outcome measure allows one to assess the performance of a common strategy of listing obese candidates as temporarily inactive and suggests that this approach may be over-utilized. Second, additional factors beyond the covariates included in our regression model likely impact conversion to active status and were not assessed. Some of these factors include dietary behavior, exercise type, capacity, and frequency, the presence of social support, entry into a weight loss program, and referral to bariatric surgery. Third, the OPTN/UNOS database only lists a single reason for why a candidate is designated status 7; it is possible that a patient may have been designated temporarily inactive due to multiple reasons. Last, this study did not incorporate obese candidates who were evaluated but not listed for kidney transplantation. The incidence of active waitlist registration among these candidates is unknown and may not be extrapolated from the observations gleaned from this study.

In conclusion, this study has shown that half of obese status 7 kidney transplant candidates in the United States with a weight inappropriate for transplant at registration achieved active status within six years, with the majority doing so within the first three years. Male gender, lower BMI at registration, higher PRA, non-diabetic cause of ESRD, pre-emptive dialysis status at registration, and UNOS region were factors associated with conversion to active status. This study suggests that obese ESRD patients should continue to be encouraged to lose weight to achieve an appropriate body composition for transplantation. Further studies are needed to assess the impact of intentional weight loss on waitlist outcomes.

Table 1-1. Baseline characteristics of the overall study population comparing those activated and remaining inactive.

Candidate Characteristic	Overall	Activated	Inactive/Never Activated	P-value
Candidates (%)	1679 (100)	714 (42.5)	965 (57.5)	---
Age - median (25^{th}, 75^{th})	52 (42,59)	51 (41,58)	52 (43,60)	<0.001
Gender				
Male (%)	833 (49.6)	381 (53.4)	452 (46.8)	0.008
Race/Ethnicity (%)				0.03
White	760 (44.1)	344 (48.2)	396 (41.0)	
Black	568 (33.8)	228 (31.9)	340 (35.2)	
Hispanic	277 (16.5)	103 (14.4)	174 (18.0)	
Other	94 (5.6)	39 (5.5)	55 (5.7)	
Blood type				0.37
A	566 (33.7)	229 (32.1)	337 (34.9)	
B	246 (14.7)	113 (15.8)	133 (13.8)	
AB	68 (4.1)	33 (4.6)	35 (3.6)	
O	799 (47.6)	339 (47.5)	460 (47.7)	
BMI at Listing				<0.001
30-34.9 (%)	155 (9.2)	94 (13.2)	61 (6.3)	
35-39.9 (%)	846 (50.4)	396 (55.5)	450 (46.6)	

40-44.9 (%)	493 (29.4)	179 (25.1)	314 (32.5)	
45-64.9 (%)	185 (11.0)	45 (6.3)	140 (14.5)	
Diabetes Mellitus (%)	1018 (60.6)	369 (51.7)	649 (67.3)	<0.001
PRA (%)				
Median (25^{th}, 75^{th})	0 (0, 7)	0 (0, 23)	0 (0, 0)	<0.001
≥80%	139 (8.3)	81 (11.3)	58 (6.0)	<0.001
Dialysis at Listing (%)				
Yes	1188 (70.8)	473 (66.3)	715 (74.1)	<0.001
Education Level				0.01
High school or below	777 (46.3)	313 (43.8)	464 (48.1)	
College or above	755 (45.0)	349 (48.9)	406 (42.1)	
Unknown	147 (8.8)	52 (7.3)	95 (9.8)	
Previous transplantation	103 (6.1)	47 (6.6)	56 (5.8)	0.51
Primary cause of ESRD				<0.001
DM	822 (49.0)	291 (40.8)	531 (55.0)	
HTN	327 (19.5)	143 (20.0)	184 (19.1)	
GN	235 (14.0)	133 (18.6)	102 (10.6)	
PKD	76 (4.5)	45 (6.3)	31 (3.2)	
Other	219 (13.0)	102 (14.3)	117 (12.1)	
Insurance Type (%)				
Public	822 (49.0)	324 (45.4)	498 (51.6)	0.03
UNOS region				<0.001
1	69 (4.1)	28 (3.9)	41 (4.3)	

2	201 (12.0)	96 (13.5)	105 (10.9)	
3	104 (6.2)	63 (8.8)	41 (4.3)	
4	210 (12.5)	91 (12.8)	119 (12.3)	
5	499 (29.7)	143 (20.0)	356 (36.9)	
6	17 (1.0)	10 (1.4)	7 (0.7)	
7	150 (8.9)	73 (10.2)	77 (8.0)	
8	107 (6.4)	69 (9.7)	38 (3.9)	
9	77 (4.6)	30 (4.2)	47 (4.9)	
10	83 (4.9)	42 (5.9)	41 (4.3)	
11	162 (9.7)	69 (9.7)	93 (9.6)	

Table 1-2. Univariate and multivariate competing risks regression for conversion to active status.

Variables (Reference)	**Level**	**Univariate**		**Multivariate**	
		Sub-Hazard Ratio (95% CI)	**P-value**	Sub-Hazard Ratio (95% CI)	**P-value**
Female	Male	1.23 (1.06-1.42)	0.007	1.24 (1.06-1.45)	0.007
Age <40	40-49	0.85 (0.69-1.05)	0.14	---	---
	50-59	0.81 (0.67-0.99)	0.04	---	---
	≥60	0.76 (0.61-0.95)	0.02	---	---
White	Black	0.81 (0.68-0.96)	0.01	---	---
	Hispanic	0.73 (0.59-0.91)	0.006	---	---
	Other	0.83 (0.60-1.15)	0.27	---	---
Blood type					
O	A	0.94 (0.80-1.11)	0.48	---	---
	B	1.13 (0.92-1.40)	0.25	---	---
	AB	1.27 (0.88-1.83)	0.20	---	---

BMI at listing	35-39.9	0.66 (0.52-0.84)	0.001	0.57 (0.44-0.73)	<0.001
(30-34.9 kg/m^2)	40-44.9	0.45 (0.35-0.58)	<0.001	0.37 (0.29-0.49)	<0.001
	≥45	0.28 (0.19-0.39)	<0.001	0.22 (0.16-0.33)	<0.001
PRA <80%	≥80%	1.67 (1.33-2.11)	<0.001	1.69 (1.30-2.20)	<0.001
Dialysis at Listing (No)	Yes	0.75 (0.64-0.87)	<0.001	0.71 (0.61-0.84)	<0.001
Education	High school or below	0.80 (0.69-0.93)	0.004	0.90 (0.77-1.06)	0.21
(College or above)	Unknown	0.65 (0.48-0.86)	0.003	0.66 (0.49-0.89)	0.006
Primary Cause of	Hypertension	1.30 (1.07-1.58)	0.009	1.28 (1.03-1.58)	0.03
ESRD	GN	1.91 (1.55-2.35)	<0.001	1.96 (1.57-2.43)	<0.001
(Diabetes)	PKD	2.19 (1.57-3.06)	<0.001	1.89 (1.31-2.72)	0.001
	Other	1.46 (1.17-1.83)	0.001	1.42 (1.11-1.81)	0.005
Insurance Type					
(Private)	Public	0.83 (0.72-0.96)	0.01	0.87 (0.74-1.03)	0.10
Previous transplant					
(No)	Yes	1.08 (0.81-1.45)	0.59	0.70 (0.52-0.96)	0.03
UNOS Region					

(5)	1	1.73 (1.14-2.64)	0.01	1.76 (1.14-2.70)	0.01
	2	1.95 (1.50-2.54)	<0.001	1.90 (1.45-2.49)	<0.001
	3	2.59 (1.93-3.49)	<0.001	2.45 (1.82-3.31)	<0.001
	4	1.71 (1.32-2.22)	<0.001	1.62 (1.23-2.14)	0.001
	6	2.38 (1.34-4.25)	0.003	2.05 (1.13-3.73)	0.02
	7	1.97 (1.49-2.59)	<0.001	1.78 (1.32-2.41)	<0.001
	8	3.10 (2.32-4.14)	<0.001	2.68 (1.98-3.63)	<0.001
	9	1.50 (1.02-2.22)	0.04	1.65 (1.07-2.54)	0.02
	10	2.15 (1.52-3.05)	<0.001	2.08 (1.43-3.02)	<0.001
	11	1.65 (1.24-2.18)	0.001	1.54 (1.15-2.05)	0.004

Table 1-3. Baseline characteristics comparing those transplanted and not transplanted among the subgroup of candidates achieving active status for kidney transplant.

Candidate Characteristic	Transplanted	Not Transplanted	P-value
Candidates (#,%)	332 (46.5)	382 (53.5)	---
Age - median (25^{th}, 75^{th})	52 (41, 58)	50 (40, 59)	0.79
Gender			
Male (%)	56.3	50.8	0.14
Race/Ethnicity (%)			<0.001
White	57.5	40.1	
Black	28.9	34.6	
Hispanic	10.2	18.1	
Other	3.3	7.3	
Blood Type (%)			<0.001
A	37.4	27.5	
B	13.3	18.1	
AB	7.5	2.1	
O	41.9	52.4	
BMI at Listing			0.78
30-34.9 (%)	14.5	12.0	
35-39.9 (%)	54.2	56.5	

40-44.9 (%)	24.7	25.4	
45-64.9 (%)	6.6	6.0	
Diabetes Mellitus (%)	46.1	56.5	0.005
Dialysis at Listing (%)			
Yes	65.7	66.8	0.76
PRA (%)			
>80%	8.4	13.9	0.02
Education Level			0.77
High school or below	42.5	45.0	
College or above	50.3	47.6	
Unknown	7.2	7.3	
Previous transplantation	5.4	7.6	0.24
Primary cause of ESRD			0.22
DM	37.4	43.7	
HTN	19.3	20.7	
GN	19.6	17.8	
PKD	7.8	5.0	
Other	16.0	12.8	
Insurance Type (%)			0.17
Public	42.2	48.2	
UNOS Region (%)			0.001
1	3.6	4.2	

2	14.5	12.6	
3	9.9	7.9	
4	11.8	13.6	
5	13.3	25.9	
6	2.1	0.8	
7	9.9	10.5	
8	11.5	8.1	
9	3.6	4.7	
10	7.8	4.2	
11	12.1	7.6	

Table 1-4. Univariate and multivariate competing risks regression for time to transplantation (deceased and living donor transplantation combined) with competing events of death and delisting among activated candidates.

Reference Group	**Level**	**Univariate Model**		**Multivariate Model**	
		Hazard Ratio (95% CI)	**P-value**	Hazard Ratio (95% CI)	**P-value**
Age (<40)	40-49	1.00 (0.73-1.38)	0.99	---	---
	50-59	1.16 (0.87-1.55)	0.30	---	---
	≥60	1.17 (0.85-1.63)	0.34	---	---
Gender (Male)	Female	0.88 (0.71-1.09)	0.25	---	---
Race (White)	Black	0.63 (0.50-0.80)	<0.001	0.68 (0.53-0.86)	0.002
	Hispanic	0.48 (0.33-0.69)	<0.001	0.51 (0.35-0.73)	<0.001
	Other	0.39 (0.22-0.70)	0.002	0.42 (0.23-0.75)	0.004
Blood Type (O)	A	1.53 (1.20-1.96)	0.001	1.50 (1.17-1.92)	0.001
	B	0.95 (0.68-1.32)	0.75	0.96 (0.69-1.33)	0.80
	AB	2.77 (1.79-4.27)	<0.001	3.02 (1.92-4.74)	<0.001

BMI at Listing (30-34.9 kg/m^2)	35-39.9 40-44.9 ≥45	0.91 (0.66-1.25) 0.87 (0.61-1.24) 0.86 (0.53-1.40)	0.56 0.46 0.55	--- --- ---	--- --- ---
PRA, % (<80)	≥80	0.63 (0.42-0.94)	0.02	0.62 (0.41-0.94)	0.02
Dialysis at Listing (No)	Yes	0.94 (0.75-1.18)	0.61	---	---
Education (College or above)	High School or Below Unknown	0.80 (0.64-1.00) 0.80 (0.54-1.21)	0.05 0.29	0.77 (0.61-0.97) 0.86 (0.58-1.26)	0.03 0.44
Primary Cause of ESRD (Diabetes mellitus)	HTN GN Polycystic kidney Other	1.04 (0.78-1.40) 1.23 (0.90-1.67) 1.66 (1.07-2.58) 1.35 (0.98-1.84)	0.77 0.19 0.03 0.06	--- --- --- ---	--- --- --- ---
Insurance Type (Private)	Public	0.82 (0.66-1.02)	0.07	---	---
Previous Transplant	Yes	0.75 (0.45-1.24)	0.26	---	---

(No)					
UNOS Region	1	1.82 (0.97-3.41)	0.06	---	---
(5)	2	2.14 (1.41-3.25)	<0.001	---	---
	3	1.87 (1.18-2.96)	0.008	---	---
	4	1.63 (1.05-2.52)	0.03	---	---
	6	2.40 (1.19-4.83)	0.01	---	---
	7	1.73 (1.11-2.71)	0.02	---	---
	8	2.08 (1.38-3.14)	<0.001	---	---
	9	1.46 (0.74-2.88)	0.28	---	---
	10	2.59 (1.60-4.17)	<0.001	---	---
	11	2.15 (1.42-3.27)	<0.001	---	---

Table 1-5. Univariate and multivariate competing risks regression for time to deceased donor transplantation with competing events of living donor transplant, death, and delisting among activated candidates.

Reference Group	**Level**	**Univariate Model**		**Multivariate Model**	
		Hazard Ratio (95% CI)	**P-value**	Hazard Ratio (95% CI)	**P-value**
Age (<40)	40-49	0.87 (0.58-1.30)	0.49	---	---
	50-59	1.21 (0.85-1.72)	0.30	---	---
	≥60	1.25 (0.83-1.87)	0.28	---	---
Gender (Male)	Female	1.08 (0.82-1.41)	0.59	---	---
Race (White)	Black	0.97 (0.72-1.29)	0.82	---	---
	Hispanic	0.55 (0.34-0.88)	0.01	---	---
	Other	0.49 (0.23-1.01)	0.05	---	---
Blood Type (O)	A	1.46 (1.08-1.97)	0.01	<2.3 years: 1.85 (1.23-2.78) ≥2.3 years:	0.003

				1.15 (0.76-1.75)	0.52
	B	0.79 (0.51-1.22)	0.29	0.72 (0.46-1.12)	0.14
	AB	2.38 (1.42-3.99)	0.001	2.20 (1.30-3.73)	0.001
BMI at Listing	35-39.9	0.75 (0.52-1.10)	0.14	---	---
(30-34.9 kg/m^2)	40-44.9	0.69 (0.45-1.05)	0.09	---	---
	≥45	0.54 (0.28-1.05)	0.07	---	---
PRA, %	≥80	0.92 (0.59-1.45)	0.72	---	---
(0-79)					
Dialysis at Listing	Yes	1.70 (1.25-2.30)	0.001	1.69 (1.23-2.32)	0.001
(No)					
Education	High School or Below	1.12 (0.85-1.49)	0.42	---	---
(College or above)	Unknown	1.52 (0.96-2.43)	0.08	---	---
Primary Cause of	HTN	1.06 (0.74-1.51)	0.75	---	---
ESRD	GN	0.97 (0.66-1.42)	0.88	---	---
(Diabetes mellitus)	Polycystic kidney	0.92).50-1.70)	0.79	---	---

	Other	1.27 (0.86-1.88)	0.23	---	---
Insurance Type (Private)	Public	1.23 (0.94-1.61)	0.13	---	---
Previous Transplant (No)	Yes	0.64 (0.33-1.25)	0.19	---	---
UNOS Region (5)	1	2.56 (1.19-5.51)	0.02	2.25 (1.06-4.77)	0.04
	2	1.59 (0.90-2.83)	0.11	1.56 (0.88-2.78)	0.13
	3	2.42 (1.36-4.31)	0.003	2.38 (1.32-4.26)	0.004
	4	1.93 (1.10-3.36)	0.02	1.85 (1.06-3.23)	0.03
	6	2.81 (1.23-6.45)	0.02	2.53 (1.19-5.37)	0.02
	7	2.04 (1.15-3.63)	0.01	2.05 (1.14-3.70)	0.02
	8	2.50 (1.46-4.27)	0.001	2.38 (1.38-4.11)	0.002
	9	1.19 (0.49-2.93)	0.70	1.15 (0.46-2.87)	0.76
	10	2.33 (1.24-4.40)	0.009	2.23 (1.18-4.22)	0.01
	11	3.33 (1.98-5.62)	<0.001	3.19 (1.87-5.44)	<0.001

Figure 1-1. Cumulative incidence of conversion to active status, death, and delisting.

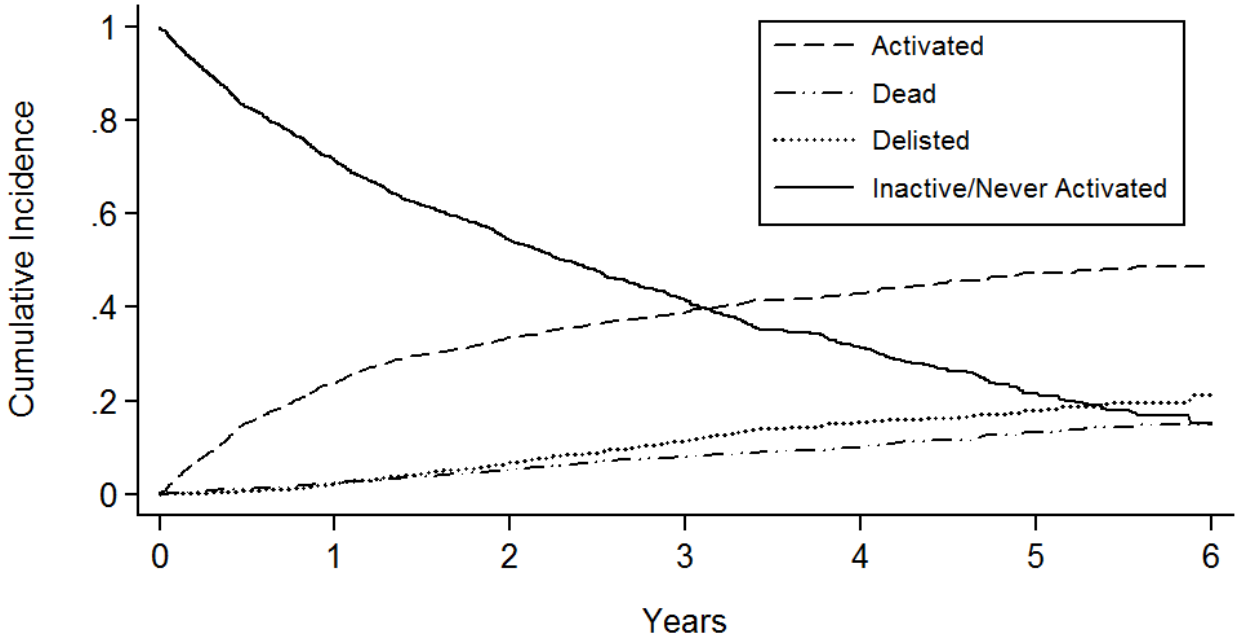


Figure 1-2. Univariate Effect of BMI at registration on the cumulative incidence of conversion to active status.

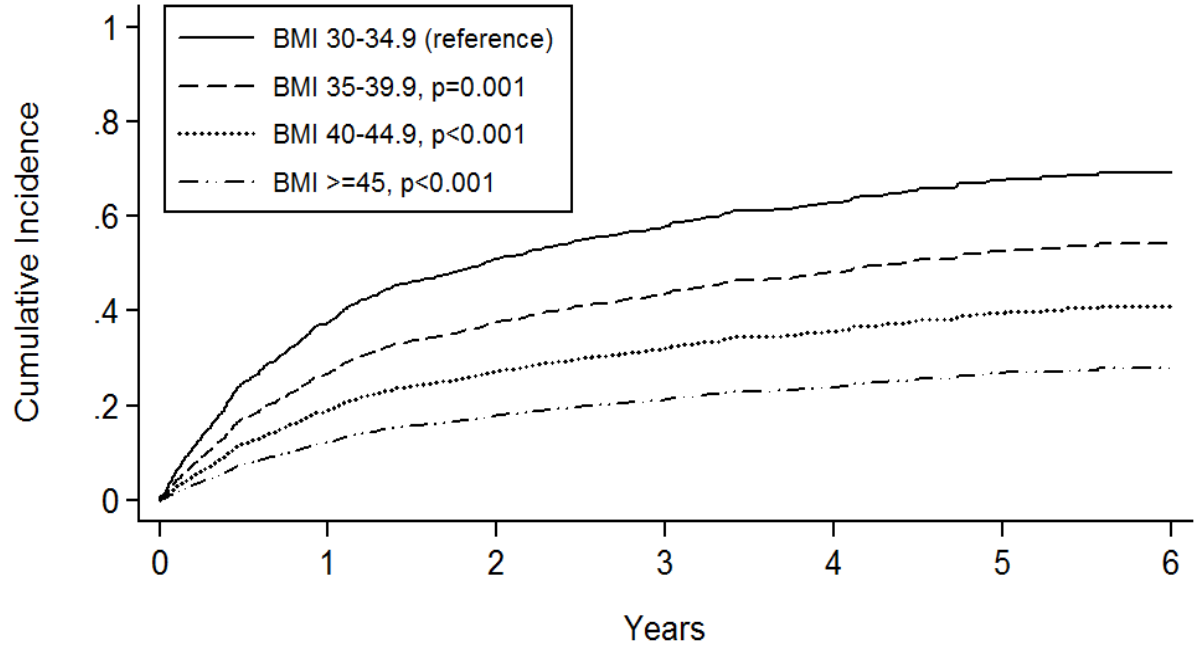
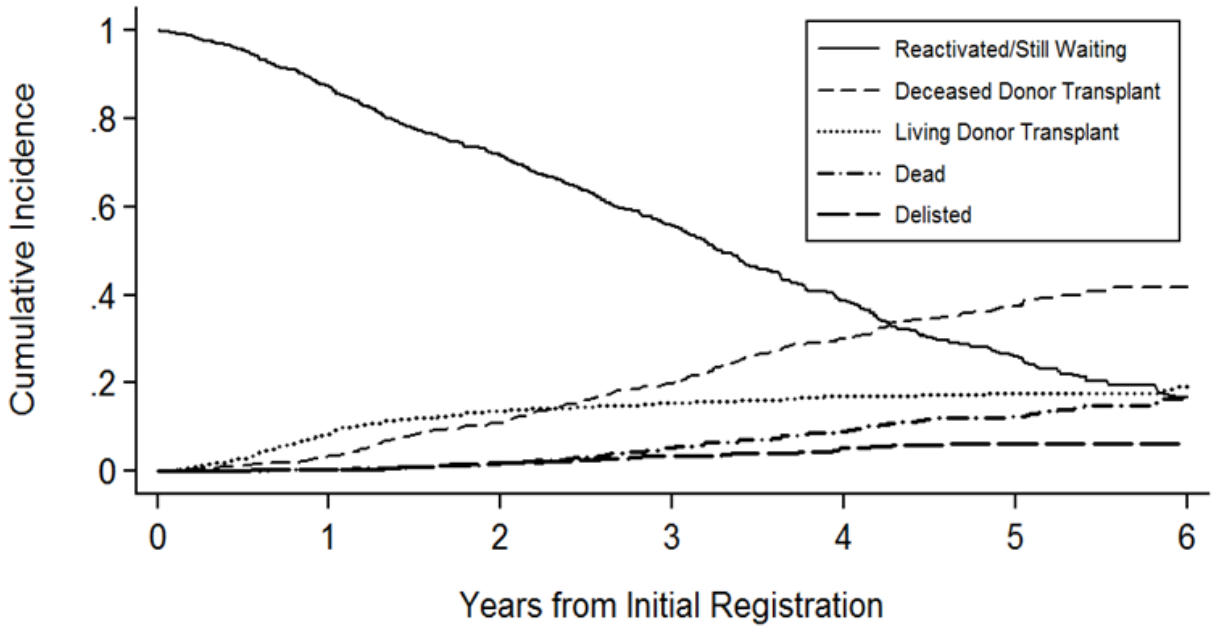


Figure 1-3. Cumulative incidence of deceased and living donor transplant, death, and delisting among a subgroup of activated status 7 candidates from time of initial waitlisting.



CHAPTER 2. STATISTICAL APPENDIX

Chapter 1 was concerned with the waitlist outcomes of transition to active status, transplantation, death, and delisting among obese status 7 kidney transplant candidates. Of equal importance are post-transplant outcomes among status 7 kidney transplant candidates who ultimately receive a kidney transplant. In Chapter 2, we compared patient and allograft survival following transplantation among status 7 kidney transplant candidates who received a kidney transplant to a contemporaneous cohort of kidney recipients. We also examined whether the degree of pre-transplant weight change among status 7 kidney recipients was associated with a difference in post-transplant outcomes.

Of the 332 status 7 candidates who received a kidney transplant in Chapter 1, 328 had at least one post-transplant follow-up record in the OPTN/UNOS dataset and were included in the study. The control group consisted of all adult kidney transplant recipients with an initial registration after April 24, 2006 with at least one follow-up record (n=74,066).

The Kaplan-Meier product limit method was used to compare patient and allograft survival between the two groups. Time to event analyses were performed using Cox proportional hazards models. For multivariate analyses, backwards and forwards stepwise selection was performed, using a significance level of 0.10 for exclusion and inclusion into the model, and yielded no differences in their output. Candidate predictors included: recipient age, gender, race (white, black, Hispanic, other), diabetes, previous transplant (yes/no), donor type (living donor, standard criteria donor, expanded criteria donor), and donor age. There were non-linear effects of recipient and donor age on patient and graft survival; therefore, recipient age was categorized as ≤40, 41-60, >60 years old and donor age was categorized as ≤50 vs. >50 years old. BMI was not included in the model because a large segment of the exposure and

control groups did not overlap in BMI and body habitus was already accounted for in the status 7 definition. An additional multivariate model was performed restricting the control population to recipients with a BMI at registration ≥30 kg/m^2. BMI, categorized as 30-34.9, 35-39.9, and ≥40 kg/m^2, was included in addition to the above covariates to the model. This model did not reveal an appreciable difference in the effect of status 7 compared to the overall population.

Table 2-1 shows the baseline characteristics in the overall population. The median BMI at registration and transplant was higher for the status 7 group compared to controls (38 vs. 27 kg/m^2 and 36 vs. 27 kg/m^2, respectively; $p<0.001$ for both comparisons). There was a larger median percentage decrease in BMI between registration and transplant among Status 7 recipients than controls (-5.0% vs. 0.0%, $p<0.001$).

Figure 2-1 compares patient survival after transplant between status 7 recipients and controls. There was no difference in survival at four years between the two groups (status 7: 87.3%; control: 89.3%; $p=0.90$).

Table 2-2 shows the results of the Cox proportional hazards regression models for patient death. There was no association between status 7 and post-transplant mortality on multivariate analysis (adjusted HR 0.96; 95% CI 0.59-1.57). The absence of effect persisted even after restricting the comparison to controls with a BMI of ≥30 kg/m^2 at initial registration (adjusted HR 0.94, 95% CI 0.42-2.11; data not shown).

Figure 2-2 shows graft survival over time for status 7 and controls. There was no difference in graft survival at four years between the two groups (status 7: 82.9%; control: 81.6%; $p=0.75$).

Table 2-3 shows Cox proportional hazards models for kidney allograft failure. Status 7 was not associated with an increased risk of graft failure compared to controls (adjusted HR

0.95, 95% CI 0.66-1.38). After restricting the control population to those with a BMI ≥30 kg/m^2 at initial registration, there was similarly no association between status 7 and allograft failure (adjusted HR 1.01, 95% CI 0.56-1.84; data not shown).

We then assessed whether the degree of pre-transplant weight change was associated with a difference in post-transplant patient or kidney allograft survival. Status 7 recipients were stratified into quartiles by the degree of weight loss achieved while waitlisted, defined as the percentage change in BMI between registration and transplant. Quartile 1 represented the highest percentage change in waitlist BMI and quartile 4 represented the least. Patient and graft survival were calculated using the Kaplan-Meier product limit method and the log-rank test was used to test for differences between the four quartiles.

Table 2-4 compares the baseline characteristics of the four quartiles. Quartile 1 recipients had the highest BMI at registration (median BMI 40.1 kg/m^2, IQR: 37.0, 42.4) and also experienced the most weight loss while waitlisted, with a median BMI change of -16.5% (IQR: -20.1%, -14.3%). As a result, BMI at transplant was the lowest among recipients in quartile 1 compared to the other three quartiles. Recipients in the first three quartiles lost weight between registration and transplant; however, the majority of recipients in quartile 4 experienced an increase in their BMI while waitlisted (median BMI change +1.6%, IQR 0.4%-4.8%). Baseline characteristics were otherwise similar between recipients in all four quartiles.

Despite the differences in weight loss between the four quartiles, there were no differences in patient survival observed within the first four years after transplant (Figure 2-3). Patient survival at four years was 90.1% in quartile 1, 91.3% in quartile 2, 83.5% in quartile 3, and 84.9% in quartile 4 (log-rank, p=0.94). Univariate Cox proportional hazards regression models showed no association between quartile and death ($HR_{quartile\ 2}$: 0.83, 95% CI 0.21-3.33;

$HR_{quartile\ 3}$: 0.65, 95% CI: 0.14-2.90, $HR_{quartile\ 4}$: 0.98, 95% CI 0.26-3.65; reference: quartile 1). A multivariate analysis could not be performed because of a limited number of deaths overall in the status 7 group (17 deaths total).

There were no differences in graft survival over four years observed between the four quartiles, with a limited number of graft failures occurring overall in the status 7 group (33 total). Graft survival at four years was 80.6% in quartile 1, 86.6% in quartile 2, 81.2% in quartile 3, and 81.4% in quartile 4 (log-rank, p=0.85; Figure 2-4). Univariate Cox proportional hazards regression models showed no association between quartile and graft failure ($HR_{quartile\ 2}$: 1.05, 95% CI 0.38-2.91; $HR_{quartile\ 3}$: 0.65, 95% CI 0.21-2.07; $HR_{quartile\ 4}$: 0.96, 95% CI 0.35-2.67; reference: quartile 1), but because of a limited number of graft failures during the study period, a multivariate analysis could not be performed.

Conclusions:

In summary, this study shows that patient and graft survival of status 7 recipients who were initially temporarily inactive on the waitlist because of their weight was similar to contemporaneous non-status 7 kidney recipients. We were unable to detect a benefit of pre-transplant weight loss among status 7 recipients on graft and patient survival. Our study suggests that the practice of recommending weight loss prior to waitlist activation should be re-examined, particularly because the majority of these recipients remain considerably obese at transplant. In light of our observations and the potential negative consequences of increased time to transplantation, further studies are needed to assess whether recommending weight loss prior to waitlist activation is warranted.

Table 2-1. Baseline characteristics of the overall study population.

Characteristic	Control (n=74,066)	Status 7 (n=328)	p-value
Age at transplant			0.15
≤40	23.9	20.4	
41-60	50.0	55.2	
≥60	26.1	24.4	
Median (IQR)	52 (41, 61)	54 (43, 60)	0.38
Male (%)	61.0	56.7	0.11
Race (%)			0.005
White	57.9	57.6	
Black	22.9	29.0	
Hispanic	13.2	9.8	
Other	6.3	3.4	
BMI at registration, median (IQR)[1]	27 (24, 31)	38 (36, 41)	<0.001
BMI at transplant, median (IQR)[1]	27 (24, 31)	36 (33, 38)	<0.001
% BMI change, median (IQR) [1]	0.0 (-4.2, 4.5)	-5.0 (-11.2, -0.0)	<0.001
Diabetes (%)	38.6	46.0	0.005
Previous transplant (%)	11.1	5.2	0.001
PRA ≥80% (%)	10.6	8.8	0.30
Deceased donor (%)	64.1	63.7	0.88
ECD (%)	9.5	7.3	0.17
DCD (%)	7.7	9.8	0.17
Donor age			
Age >50	24.7	24.1	0.80

Median (IQR)	40 (27, 50)	40 (28, 50)	0.54
Cold ischemic time, median hrs (IQR)[1]	16 (10, 22)	15 (11, 21)	0.68
Time to transplant, median days (IQR)	298 (113, 680)	618 (337, 1106)	<0.001
Length of initial transplant hospitalization stay, median (IQR)	5 (4, 8)	5 (4, 7)	0.01
Delayed graft function (%)[2]	15.1	18.3	0.11
Acute rejection within first year (%)	9.5	11.3	0.26

[1]Deceased donor recipients only.
[2]Defined as requiring dialysis in the first week after transplant.

Table 2-2. Cox proportional hazards regression model assessing factors associated with time to death.

Reference	**Level**	**Univariate**		**Multivariate**	
		HR (95% CI)	**p-value**	**HR (95% CI)**	**p-value**
Control	Status 7	0.97 (0.59-1.58)	0.90	0.96 (0.59-1.57)	0.88
Recipient age ≤ 40	41-60	2.18 (1.97-2.42)	<0.001	1.87 (1.68-2.08)	<0.001
	>60	4.18 (3.77-4.64)	<0.001	3.23 (2.91-3.61)	<0.001
Female	Male	1.22 (1.15-1.30)	<0.001	1.15 (1.08-1.22)	<0.001
White	Black	1.01 (0.94-1.08)	0.86	0.93 (0.86-1.00)	0.06
	Hispanic	0.72 (0.65-0.80)	<0.001	0.76 (0.68-0.84)	<0.001
	Other	0.70 (0.60-0.81)	<0.001	0.65 (0.56-0.75)	<0.001
No diabetes	Diabetes	1.76 (1.66-1.87)	<0.001	1.47 (1.39-1.57)	<0.001
First transplant	Previous transplant	0.98 (0.89-1.08)	0.63	1.19 (1.08-1.31)	0.001
Living donor transplant	SCD	2.31 (2.14-2.50)	<0.001	2.18 (2.01-2.36)	<0.001
	ECD	4.03 (3.65-4.44)	<0.001	2.45 (2.19-2.75)	<0.001
Donor age ≤ 50	>50	1.55 (1.46-1.65)	<0.001	1.21 (1.11-1.31)	<0.001

Table 2-3. Cox proportional hazards regression model assessing factors associated with time to graft loss.

Reference	**Level**	**Univariate**		**Multivariate**	
		HR (95% CI)	**p-value**	**HR (95% CI)**	**p-value**
Control	Status 7	0.94 (0.65-1.37)	0.75	0.95 (0.66-1.38)	0.80
Recipient age ≤ 40	41-60	1.04 (0.98-1.11)	0.17	0.91 (0.86-0.97)	0.004
	>60	1.62 (1.52-1.72)	<0.001	1.25 (1.17-1.34)	<0.001
Female	Male	1.06 (1.01-1.11)	0.01	---	---
White	Black	1.35 (1.28-1.42)	<0.001	1.23 (1.16-1.30)	<0.001
	Hispanic	0.89 (0.82-0.96)	0.002	0.90 (0.83-0.97)	0.006
	Other	0.78 (0.70-0.87)	<0.001	0.72 (0.65-0.81)	<0.001
No diabetes	Diabetes	1.34 (1.28-1.40)	<0.001	1.22 (1.16-1.27)	<0.001
First transplant	Previous transplant	1.13 (1.06-1.22)	<0.001	1.25 (1.17-1.35)	<0.001
Living donor transplant	SCD	1.87 (1.77-1.97)	<0.001	1.82 (1.72-1.93)	<0.001
	ECD	3.30 (3.07-3.55)	<0.001	2.35 (2.16-2.56)	<0.001
Donor age ≤ 50	>50	1.56 (1.49-1.64)	<0.001	---	---

Table 2-4. Baseline characteristics of status 7 recipients stratified into quartiles based on the percentage change in BMI recorded at registration and transplant.

Characteristic	Quartile 1 (n=82)	Quartile 2 (n=82)	Quartile 3 (n=82)	Quartile 4 (n=82)	p-value
Age at transplant					0.18
≤40	24.4	26.8	12.2	18.3	
41-60	52.4	54.9	62.2	51.2	
≥60	23.2	18.3	26.6	30.5	
Median (IQR)	50 (42, 59)	53 (40, 60)	54 (46, 61)	55 (44, 62)	0.20
Male (%)	63.4	61.0	53.7	48.8	0.21
Race (%)					0.79
White	58.5	52.4	63.4	57.3	
Black	29.3	31.7	28.1	26.8	
Hispanic	7.3	13.4	6.1	12.2	
Other	4.9	2.4	2.4	3.7	
BMI at registration, median (IQR)	40.1 (37.0, 42.4)	38.9 (36.3, 41.0)	37.5 (35.6, 40.1)	36.6 (34.9, 38.5)	<0.001
BMI at transplant, median (IQR)	32.6 (30.2, 35.8)	35.5 (33.3, 37.8)	36.5 (34.4, 38.7)	37.6 (35.5, 40.5)	<0.001
% BMI change, median (IQR)	-16.5 (-20.1, -14.3)	-8.2 (-.9.9, -6.7)	-3.2 (-4.1, -1.8)	1.6 (0.4, 4.8)	
Diabetes (%)	45.1	40.2	43.9	54.9	0.28

Previous transplant (%)	6.1	6.1	2.4	6.1	0.64
PRA ≥80% (%)	6.1	8.5	9.8	11.0	0.72
Deceased donor (%)	54.9	64.6	63.4	72.0	0.16
ECD (%)	6.1	2.4	9.8	11.0	0.15
DCD (%)	6.1	13.4	9.8	9.8	0.48
Donor age					
Age >50	30.5	12.2	31.7	22.0	0.01
Median (IQR)	41 (26, 52)	41 (30, 48)	38 (28, 54)	40 (28, 49)	0.81
Cold ischemic time, median hrs (IQR)[1]	17 (13, 20)	16 (12, 21)	12 (10, 19)	16 (10, 23)	0.19

[1]Deceased donor recipients only.

Figure 2-1. Comparison of patient survival among status 7 recipients and contemporaneous kidney transplant recipients.

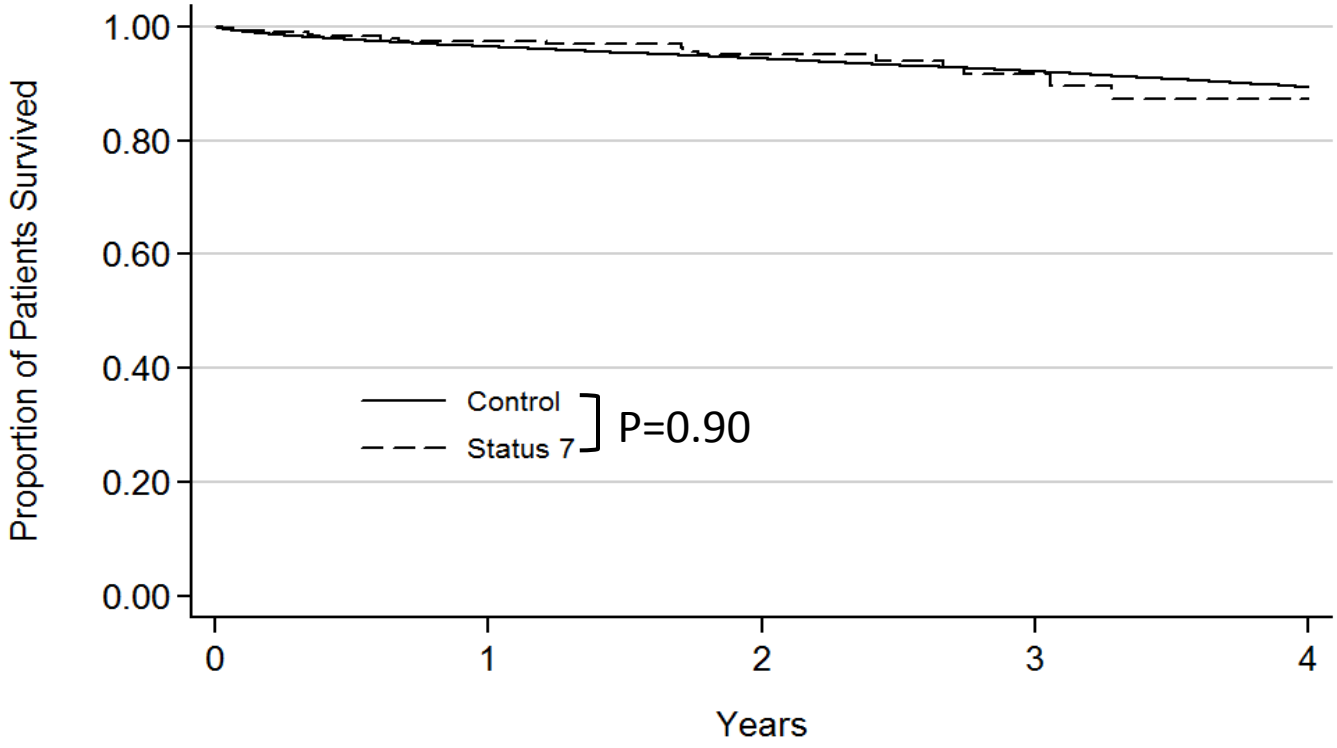


Figure 2-2. Comparison of graft survival among status 7 recipients and contemporaneous kidney transplant recipients.

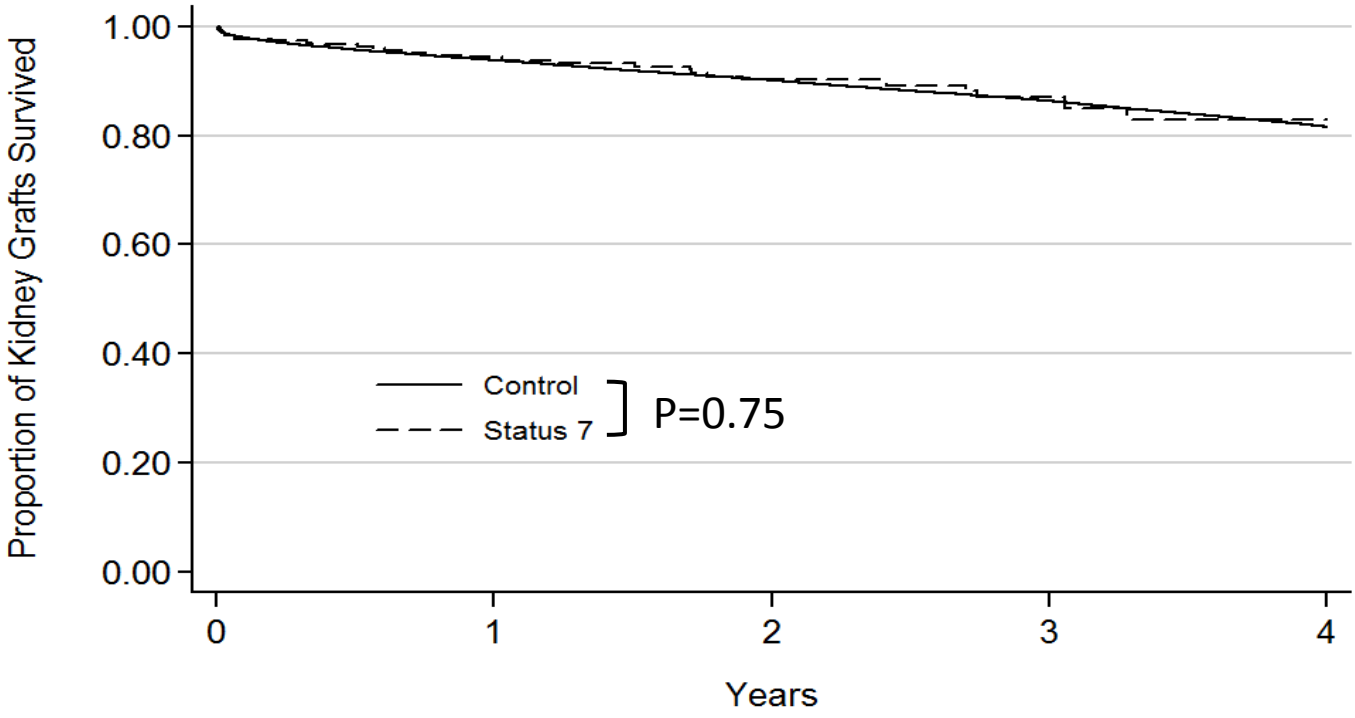

Proportion of Kidney Grafts Survived
1.00
0.80
0.60
0.40
0.20
0.00
Control
Status 7
P=0.75
0
1
2
3
4
Years

Figure 2-3. Comparison of patient survival among status 7 recipients stratified into quartiles according to the degree of weight loss incurred between waitlist registration and transplant.

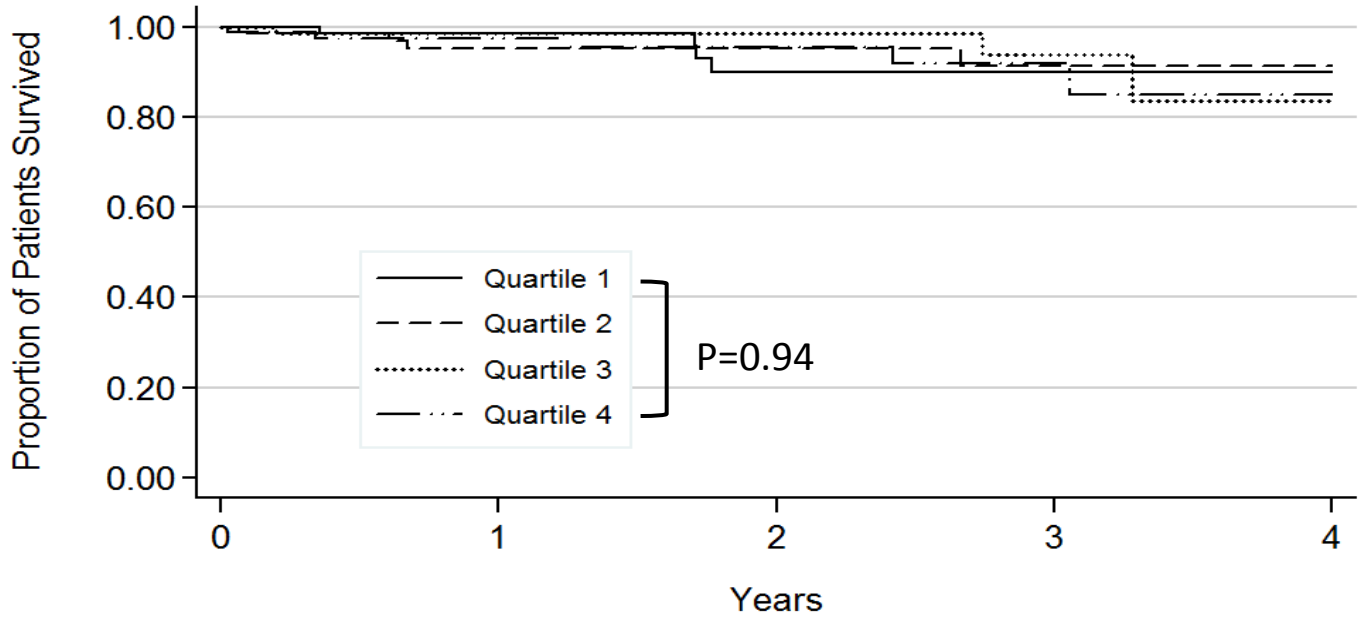
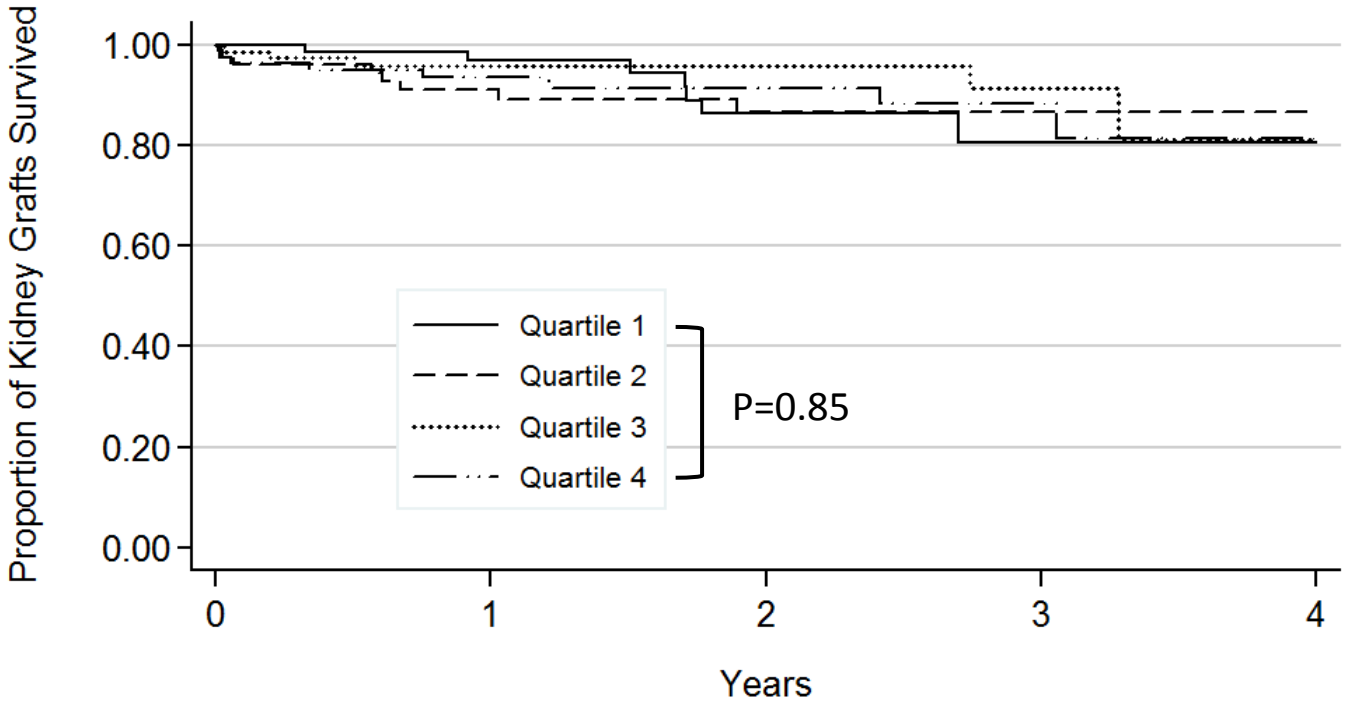


Figure 2-4. Comparison of graft survival among status 7 recipients stratified into quartiles according to the degree of weight loss incurred between waitlist registration and transplant.


Proportion of Kidney Grafts Survived
1.00
0.80
0.60
0.40
0.20
0.00
0
1
2
3
4
Years
Quartile 1
Quartile 2
Quartile 3
Quartile 4
P=0.85

References:

1. Delmonico FL, McBride MA. Analysis of the Wait List and Deaths among Candidates Waiting for a Kidney Transplant. Transplantation 2008;86:1678-83.

2. 2011 Annual Report of the U.S. Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients: Transplant Data 1998-2011. Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation, Rockville, Md; United Network for Organ Sharing, Richmond, Va; University Renal Research and Education Association, Ann Arbor, Mi.

3. Potluri K, Hou S. Obesity in Kidney Transplant Recipients and Candidates. Am J Kidney Dis 2010;56:143-56.

4. Gore JL, Pham PT, Danovitch GM, et al. Obesity and Outcome Following Renal Transplantation. Am J Transplant 2006;6:357-63.

5. Gill JS, Lan J, Dong J, et al. The Survival Benefit of Kidney Transplantation in Obese Patients. Am J Transplant 2013.

6. Pondrom S. The Ajt Report: News and Issues That Affect Organ and Tissue Transplantation. Am J Transplant 2012;12:1663-4.

7. Fine J, Gray RJ. A Proportional Hazards Model for the Subdistribution of a Competing Risk. J Am Stat Assoc 1999;94:496-509.

8. Wolbers M, Koller MT, Witteman JC, Steyerberg EW. Prognostic Models with Competing Risks: Methods and Application to Coronary Risk Prediction. Epidemiology 2009;20:555-61.

9. Wolbers M KM, Witteman JCM, Gerds TA. Concordance for Prognostic Models with Competing Risks. Research Report 13/03. Department of Biostatistics, University of

Copenhagan. Accessed October 28, 2013, https://ifsv.sund.ku.dk/biostat/biostat_annualreport/images/7/72/Research_Report_13-03-ny.pdf.

10. "Health Resources and Services Administration, Organ Procurement and Transplantation Network Data Reports," Last Modified November 5, 2013, Http://Optn.Transplant.Hrsa.Gov/Data/. .

11. Lentine KL, Delos Santos R, Axelrod D, Schnitzler MA, Brennan DC, Tuttle-Newhall JE. Obesity and Kidney Transplant Candidates: How Big Is Too Big for Transplantation? Am J Nephrol 2012;36:575-86.

12. Molnar MZ, Streja E, Kovesdy CP, et al. Associations of Body Mass Index and Weight Loss with Mortality in Transplant-Waitlisted Maintenance Hemodialysis Patients. Am J Transplant 2011;11:725-36.

13. Streja E, Molnar MZ, Kovesdy CP, et al. Associations of Pretransplant Weight and Muscle Mass with Mortality in Renal Transplant Recipients. Clin J Am Soc Nephrol 2011;6:1463-73.

14. Beddhu S, Pappas LM, Ramkumar N, Samore M. Effects of Body Size and Body Composition on Survival in Hemodialysis Patients. J Am Soc Nephrol 2003;14:2366-72.

15. Wadden TA, Berkowitz RI, Womble LG, et al. Randomized Trial of Lifestyle Modification and Pharmacotherapy for Obesity. N Engl J Med 2005;353:2111-20.

16. Unick JL, Beavers D, Bond DS, et al. The Long-Term Effectiveness of a Lifestyle Intervention in Severely Obese Individuals. Am J Med 2013;126:236-42, 42 e1-2.

17. Hamman RF, Wing RR, Edelstein SL, et al. Effect of Weight Loss with Lifestyle Intervention on Risk of Diabetes. Diabetes Care 2006;29:2102-7.

18. Wing RR, Venditti E, Jakicic JM, Polley BA, Lang W. Lifestyle Intervention in Overweight Individuals with a Family History of Diabetes. Diabetes Care 1998;21:350-9.

19. Sacks FM, Bray GA, Carey VJ, et al. Comparison of Weight-Loss Diets with Different Compositions of Fat, Protein, and Carbohydrates. N Engl J Med 2009;360:859-73.

20. MacLaughlin HL, Cook SA, Kariyawasam D, Roseke M, van Niekerk M, Macdougall IC. Nonrandomized Trial of Weight Loss with Orlistat, Nutrition Education, Diet, and Exercise in Obese Patients with Ckd: 2-Year Follow-Up. Am J Kidney Dis 2010;55:69-76.

21. Johansen KL, Chertow GM, Ng AV, et al. Physical Activity Levels in Patients on Hemodialysis and Healthy Sedentary Controls. Kidney Int 2000;57:2564-70.

22. Gutman RA, Stead WW, Robinson RR. Physical Activity and Employment Status of Patients on Maintenance Dialysis. N Engl J Med 1981;304:309-13.

23. Ifudu O, Paul H, Mayers JD, et al. Pervasive Failed Rehabilitation in Center-Based Maintenance Hemodialysis Patients. Am J Kidney Dis 1994;23:394-400.

24. Kalantar-Zadeh K, Block G, Humphreys MH, Kopple JD. Reverse Epidemiology of Cardiovascular Risk Factors in Maintenance Dialysis Patients. Kidney Int 2003;63:793-808.

25. Leavey SF, McCullough K, Hecking E, Goodkin D, Port FK, Young EW. Body Mass Index and Mortality in 'Healthier' as Compared with 'Sicker' Haemodialysis Patients: Results from the Dialysis Outcomes and Practice Patterns Study (Dopps). Nephrol Dial Transplant 2001;16:2386-94.

26. Ikizler TA. Resolved: Being Fat Is Good for Dialysis Patients: The Godzilla Effect: Pro. J Am Soc Nephrol 2008;19:1059-62.

27. Matas AJ, Smith JM, Skeans MA, et al. Optn/Srtr 2011 Annual Data Report: Kidney. Am J Transplant 2013;13 Suppl 1:11-46.

28. Wolfe RA, Ashby VB, Milford EL, et al. Comparison of Mortality in All Patients on Dialysis, Patients on Dialysis Awaiting Transplantation, and Recipients of a First Cadaveric Transplant. N Engl J Med 1999;341:1725-30.