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Functional Status, Time to Transplantation, and Survival Benefit of Kidney Transplantation Among Wait-Listed Candidates

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Supplementary Material

Table S1: Multivariable competing risk regression analysis of outcome of kidney transplantation.

Table S2: Multivariable Cox regression analysis of outcome of time to first inactivation on kidney transplant waiting list. Figure S1: Flow chart of cohort assembly and analyses.

Figure S2: Lowess plots of change in physical function score while on waiting list.

Item S1: Multivariable Cox regression analysis of outcome of kidney transplantation.

Item S2: Survival benefit associated with kidney transplantation, by quartile of physical function.

Note: The supplementary material accompanying this article (doi: _____) is available at www.ajkd.org

Supplementary Material Descriptive Text for Online Delivery

Supplementary Table S1 (PDF). Multivariable competing risk regression analysis of outcome of kidney transplantation.

Supplementary Table S2 (PDF). Multivariable Cox regression analysis of outcome of time to first inactivation on kidney transplant waiting list.

Supplementary Figure S1 (PDF). Flow chart of cohort assembly and analyses.

Supplementary Figure S2 (PDF). Lowess plots of change in physical function score while on waiting list.

Supplementary Item S1 (PDF). Multivariable Cox regression analysis of outcome of kidney transplantation.

Supplementary Item S2 (PDF). Survival benefit associated with kidney transplantation.

Preliminary results were presented at the World Transplant Congress in San Francisco, July 26-31, 2014.

Abstract

Background—In the context of an aging end-stage renal disease population with multiple comorbidities, transplantation professionals face challenges in evaluating the global health of patients awaiting kidney transplantation. Functional status might be useful for identifying which patients will derive a survival benefit from transplantation versus dialysis.

Study Design—Retrospective cohort study of wait-listed patients using data on functional status from a national dialysis provider linked to United Network for Organ Sharing registry data.

Setting & Participants—Adult kidney transplant candidates added to the waiting list between the years 2000 and 2006.

Predictor—Physical function scale of the Medical Outcomes Study 36-Item Short Form Healthy Survey, analyzed as a time-varying covariate.

Outcomes—Kidney transplantation; Survival benefit of transplantation versus remaining wait-listed.

Measurements—We used multivariable Cox regression to assess the association between physical function with study outcomes. In survival benefit analyses, transplant status was modeled as a time-varying covariate.

Results—The cohort comprised 19,242 kidney transplant candidates (median age, 51 years; 36% black race) receiving maintenance dialysis. Candidates in the lowest baseline physical function quartile were more likely to be inactivated (adjusted HR vs. highest quartile, 1.30; 95% CI, 1.21-1.39) and less likely to undergo transplantation (adjusted HR vs. highest quartile, 0.64; 95% CI, 0.61-0.68). After transplantation, worse physical function was associated with shorter 3-year survival (84% vs. 92% for the lowest vs. highest function quartiles). However, compared to dialysis, transplantation was associated with a statistically significant survival benefit by 9 months for patients in every function quartile.

Limitations—Functional status is self-reported.

Conclusions—Even patients with low function appear to live longer with kidney transplantation versus dialysis. For waitlisted patients, global health measures like functional status may be more useful in counseling patients about the probability of transplantation than in identifying who will derive a survival benefit from it.

Keywords

end-stage renal disease (ESRD); kidney transplantation; dialysis; renal replacement therapy modality; survival benefit; transplant waiting list; physical function; functional status; 36-Item Short Form Health Survey (SF-36); post-transplantation complications; kidney transplant allocation

Over the past two decades, the population of kidney transplant candidates in the United States has grown older. While the waiting list for kidney transplantation rose from 30,010 candidates in 1997 to over 101,000 candidates in 2014, the proportion of candidates 65 years or older increased from 7% to over 21%.¹ Additionally, waiting times have lengthened, requiring candidates to receive several years of maintenance dialysis. Kidney transplant

candidates commonly have multiple comorbidities associated with aging and end-stage renal disease (ESRD), including cardiovascular disease, diabetes, and poor nutrition.² The relative scarcity of organs and heightened scrutiny of center-specific outcomes³ have led transplant professionals to take strong interest in summary measures of global health that may predict important transplant outcomes.^{4,5} A measure of global health such as functional status might be useful to select appropriate patients for placement onto the transplant wait-list, counsel patients about the risk of complications, direct resources such as physical therapy to vulnerable patients, or guide centers about which wait-listed patients should be reevaluated frequently, inactivated, or delisted.

Several studies have revealed that global health measures are independent predictors of post-transplantation complications. Using national cohorts, Kutner et al. and Reese et al. demonstrated that functional status, measured using the physical function (PF) domain of the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36), was strongly associated with post-transplantation survival.^{6,7} The SF-36 instrument is usually self-administered and has been implemented in diverse populations, including dialysis patients and individuals without kidney disease.⁸⁻¹⁰ Frailty, a syndrome of vulnerability to medical stressors, is also common among kidney transplant recipients and was reported to be associated with delayed graft function, early rehospitalization, and mortality in a single center cohort.¹¹⁻¹⁴

Little information, however, is available about the utility of measures of global health to predict outcomes for patients awaiting transplantation. While wait-listed, many candidates suffer infections, vascular complications, or other illnesses that lead to inactive status, permanent removal from the wait-list, or death. Over a third of the kidney transplant list is inactive and, over the past decade, this proportion has grown rapidly. Inactivity is associated with mortality.¹⁵⁻¹⁷ An analysis of Organ Procurement and Transplantation Network (OPTN) data revealed that fewer than half of kidney transplant candidates older than 60 years ever receive a transplant.¹⁸ These findings suggest that global health measures like functional status may worsen for transplant candidates receiving multiple years of dialysis.

The aims of this study were to determine whether functional status is independently associated with the rate of kidney transplantation and if functional status modifies the survival benefit from transplantation in a national cohort of wait-listed candidates. A secondary aim was to determine if poorer physical function is associated with inactivation on the wait-list.

Methods

Study Overview

We performed a retrospective cohort study of US kidney transplant candidates using a linked dataset from the United Network for Organ Sharing (UNOS)/OPTN and Fresenius Medical Care, a provider of maintenance dialysis services.

The OPTN data system includes data on all wait-listed candidates, transplant recipients and donors in the United States, submitted by OPTN members, and has been described

elsewhere.¹⁹ The Health Resources and Services Administration, US Department of Health and Human Services, provides oversight to the activities of the OPTN contractor. The University of Pennsylvania Institutional Review Board approved the study.

Inclusion and Exclusion Criteria

Adult (18 years or older at wait-listing) patients who had received 12 consecutive months of dialysis provided by Fresenius Medical Care were included if they were added to the kidney transplant wait-list from June 1, 2000, through May 31, 2006. Patients were required to have completed at least one SF-36 form on or after June 1, 2000. We excluded individuals who were never active on the wait-list, or wait-listed for multi-organ transplants other than kidney-pancreas.⁷ The observation period was June 1 2000 until September 3 2010.

Exposure Assessment

The primary exposure was the PF subscale of the SF-36. The protocol at Fresenius dialysis centers was to administer the SF-36 instrument to patients each year as part of routine care. The PF scale consists of 10 questions that assess difficulties with common physical activities requiring varying levels of exertion, such as bathing and dressing or walking a hundred yards.²⁰ PF scores were transformed into a scale from 0 to 100, by convention.²¹ To make the results clinically intuitive, we empirically divided the study population into quartiles defined by baseline PF scores. We selected the PF score collected closest in time to the wait-listing date for the baseline value.

Outcomes Assessment

The primary outcomes were 1) time to kidney transplantation, and 2) the net survival benefit of kidney transplantation vs. remaining wait-listed across strata of physical function. To avoid immortal time bias, follow-up time started at each patient's 'index date,' which was the date of wait-list registration or the date of PF measurement, whichever was later (range: June 1, 2000 until November 22, 2008). For the transplant outcome, we assumed complete follow-up from wait-listing until transplantation, death, or the end of study (September 3, 2010).

Death was ascertained through center reports and linkage to the Social Security Death Master file. For mortality, we assumed complete follow-up from the index date until death or end of study. For the outcome of inactivation, patients were followed up until transplantation, death, inactivation, delisting, or end of study.

Covariate Assessment

We obtained data on the following covariates submitted to the OPTN by transplant centers at wait-listing: age (<35, 35-<45, 45-<55, 55-<65, and ≥65 years), sex (Male/Female), race (White, Black, Hispanic, Asian, Other), Primary insurance type (Private, vs. Medicare, vs. Other), diabetes (Yes/No), prior kidney transplant (Yes/No), peripheral vascular disease (Yes/No), glomerulonephritis as cause of ESRD (yes/no), polycystic disease as cause of ESRD (Yes/No), congenital or reflux disease as cause of ESRD (Yes/No), hypertension as cause of ESRD (Yes/No), blood type (AB, A, B and O). We also estimated waiting time to kidney transplantation in the donor service area (DSA) where the candidate was listed.

Because <50% of candidates undergo transplantation in some areas, we calculated time until 25% of candidates underwent transplantation during the years 2000-2010 (using data for all adult waitlisted candidates, not just this cohort) and used these times to categorize the donor service areas into quartiles. We obtained Fresenius Medical Care data on body mass index (BMI, in kg/m²), time since dialysis initiation (years), and dialysis modality (hemodialysis vs. peritoneal dialysis), measured at each patient's index date.

Statistical Analysis

We conducted analyses using Stata (version 13.0; StataCorp LP, College Station, TX) with a 2-sided p-value <0.05 as the criterion for statistical significance. Medians are reported with the interquartile range (IQR). We used Kruskal Wallis to compare continuous variables and chi-square tests to compare categorical variables across PF quartiles. We modeled change in PF scores using Lowess plots. Because of variation in the number of PF scores (measured only during waiting list time), we also used mixed effects models to estimate individual level slopes of PF score during the first two years after index dates for the subset of patients with ≥ 2 PF measurements.

Analysis of Time to Transplantation—We used the Kaplan–Meier product-limit estimate of the survivor function to estimate the median of the time to transplantation for each quartile of baseline PF function and used the log-rank test to compare outcomes across quartiles. The estimated failure represents 1 minus the Kaplan–Meier estimate of the survivor function for each PF quartile. We first fit multivariable Cox regression models and used baseline PF quartile as the primary exposure. We next analyzed PF quartile as a time-updated exposure. The primary models censored for death. We performed four secondary analyses in which 1) we treated PF score as a continuous variable; 2) we treated death as a competing risk; 3) we restricted the analyses to individuals never inactive on the waiting list; and 4) we censored for living donor kidney transplantation. The rationale for censoring at living donor transplantation was that living donor recipients often have brief waiting time, and different demographic and clinical characteristics, than deceased donor kidney recipients.^{22,23}

Outcome of Time to First Inactivation—We fit a multivariable Cox regression model for time to first inactivation. This analysis was restricted to patients who were active when added to the waiting list.

Outcome of Survival Benefit From Kidney Transplantation—We employed a time-dependent Cox regression model in which transplantation was treated as a time-updated covariate and death was the outcome. All patients were followed up from the index date until death, removal from the waiting list, undergoing kidney transplantation, or end of follow-up. We also treated inactive status as a time-varying covariate.

Patients undergoing transplantation ‘switched’ therapies and after transplantation contributed time to the transplant therapy group.²⁴ We calculated hazard ratios (HRs) with 95% confidence-intervals (CIs) associated with transplantation at discrete time intervals (<1, 1-<3, 3-<6, 6-<9, 9-<12, 12-<18, 18-<24, and ≥ 24 months). The models were fit within each

quartile of PF. Next, a model was fit that included indicator variables for PF quartile and time interval, along with interaction terms between each PF quartile and time interval. A likelihood ratio test confirmed that there were no significant interactions between PF quartile and time interval. We performed a secondary analysis restricted to never-inactive patients.

Covariate selection for multivariable models was guided by clinical judgment and prior literature about attributes likely to affect time to transplantation and survival.^{2,24-27} All models adjusted for the variables listed in the “covariate assessment” section. The model that examined time to inactivation also adjusted for era (before versus on or after 11/1/2003, when the OPTN implemented a policy to permit waiting time accrual when a candidate is inactive.)

We assessed model fit using the Cox-Snell residuals and a graphical display of the Nelson-Aalen function to confirm that the cumulative hazard function conditional on the covariate vector has an exponential distribution with a hazard rate of one, indicating good fit.

Missing Data—Less than 0.1% of the cohort had missing data for any covariate, with the exception of peripheral vascular disease (missing in 6.9%) and body mass index (missing in 0.5%). Individuals with missing data were not included in regression models for primary analyses. We performed sensitivity analyses in which individuals with missing data on peripheral vascular disease were first assigned as having the disease, then not having the disease, and analyses in which individuals with missing BMI data were assigned extreme values. We also performed secondary analyses of the outcomes of transplantation and transplant survival benefit with adjustment for panel-reactive antibody (PRA, missing in 30%).

Results

We identified 150,843 adults who had received ≥12 consecutive months of dialysis, among whom 114,133 (76%) had completed ≥1 SF-36 questionnaires. We linked this file of maintenance dialysis patients to a file from the OPTN and identified 19,609 adults wait-listed for kidney transplantation. After applying exclusion criteria, the cohort was composed of 19,242 kidney transplant candidates at 227 transplant centers. A total of 11,050 candidates (57%) received a kidney transplant; 90% received deceased donor transplants. Median follow-up was 5.8 (IQR, 4.2-7.5) years. Cohort generation is displayed in **Figure S1** (provided as online supplementary material).

As shown in **Table 1**, the median age was 51 (IQR, 41-59) years; 36% were black and 60% were male. Compared to candidates in the lowest PF quartile, the candidates in the highest PF quartile were more likely to be <35 years of age (23% vs. 8%), male (68% vs. 53%), and less likely to have diabetes (28% versus 54%).

The cohort had wide variation in baseline PF score, with a median of 55 (IQR, 35-80). The median number of PF score measurements was 3 (IQR, 2-5). Over time, PF scores showed a pattern of general decline that was most evident in the highest PF quartile (**Figure S2**). Among patients with ≥2 measurements in the first two years after the index date (n=11,645),

the median estimated slope per year was -0.5 (IQR, -9.1 to 5.9). The median estimate slope per year was -4.2 (IQR, -14.0 to 0.2) for candidates in the highest baseline PF quartile, -2.9 (IQR, -12.8 to 4.0) in the next highest quartile, -0.2 (IQR, -8.3 to 8.2) in the second-to-lowest quartile, and 4.0 (IQR, -2.2 to 15.2) in the lowest quartile.

Figure 1 shows that worse functional status was strongly associated with lower rates of kidney transplantation. The median time to transplantation was 1000, 1170, 1252, and 1606 days in the quartiles 1 through 4, where quartile 1 is has the highest baseline PF.

In multivariable Cox regression (**Table 2; table a of Item S1**), candidates in the lowest baseline PF quartile had a 26% lower rate of kidney transplantation than candidates in the highest quartile (adjusted HR, 0.74; 95% CI, 0.70-0.79). When analyzed as a time-updated covariate, candidates with PF in the lowest quartile had a 36% lower transplantation rate.

Table b of Item S1 reveals similar results when PF score was treated as a continuous exposure. Using a competing risks approach, results (reported as sub-HRs) were consistent with the primary approach (**Table S1**). Results were also similar when patients were censored at living donor transplantation and in the sub-cohort of never-inactive patients (**tables c and d of Item S1**).

Among the 19,242 candidates, 516 were inactive on the index date. An additional 8129 (43%) became inactive during follow-up. Lower baseline functional status was independently associated with a greater risk of inactivation on the waiting list (adjusted HR versus candidates in highest PF quartile, 1.3; 95% CI, 1.21-1.39). These results are presented in **Table 3 and Table S2**.

Among candidates who received a kidney transplant, better function was associated with lower post-transplantation mortality. Using the Kaplan-Meier method, the survival rate for kidney transplant recipients after three years was 92% (95% CI, 91%-93%), 89% (95% CI, 88%-90%), 87% (95% CI, 86%-89%), and 84% (95% CI, 82%-86%) for recipients in quartiles 1 through 4, respectively (arranged in order of decreasing PF; $p < 0.001$).

Figure 2 shows the survival benefit of transplantation versus remaining on the waiting list. Transplantation was associated with a higher risk of death compared to remaining wait-listed in the immediate post-transplantation period, followed by a gradual improvement in survival over time. Most notably, transplantation was associated with significantly lower hazard of death by 9 months post-transplantation for patients in every PF quartile. For candidates in the lowest PF quartile, the survival benefit was evident by 6 months after transplantation. In order to detect differences in time to a lower hazard of death with transplantation by PF quartile, we examined for time-by-PF quartile interactions. These interaction terms were neither significant nor included in final models.

Additional sensitivity and secondary analyses showed results similar to the primary results (**tables e-i of Item S1; tables a and b of Item S2**).

Discussion

In a diverse national cohort of kidney transplant candidates, lower physical function was independently associated with a greater risk of inactivation on the waiting list, a substantially lower rate of transplantation and worse post-transplantation survival. Yet, even for patients in the lowest functional status quartile, kidney transplantation instead of receiving dialysis was associated with better long-term survival. Taken in the context of other research, these findings suggest that global health measures such as physical function may be useful predictors of meaningful transplant outcomes and may enrich the process of counseling patients about their prospects of ever receiving a transplant.^{6,12} Functional status may have less utility in identifying which wait-listed patients will not derive a survival benefit from kidney transplantation.

Kidney transplant candidates in this cohort showed wide variation in functional status and a substantial proportion had poor function. Additionally, among patients in the highest baseline quartile of function, loss of function was evident in the first two years. These findings are consistent with a robust body of research showing that severity of chronic kidney disease is strongly associated with poor functional status, frailty, and poor physical performance;^{8,10,28-30} these adverse outcomes are driven by vascular, immunological, and endocrine etiologies. Advanced kidney disease promotes vascular calcification with smooth muscle apoptosis and up-regulation of osteoblast related transcription factors.³¹ Dialysis patients commonly have systemic inflammation with anorexia, protein energy wasting, and sarcopenia.^{32,33} Hypertension and anemia may lead to left ventricular hypertrophy and compromised functional status.³⁴ Delays in evaluation for transplantation, and the ever-lengthening waiting time for a transplant, usually expose candidates to multiple years in which these pathological mechanisms can worsen health.³⁵ Because of the challenges of fully summarizing the comorbidities of ESRD patients, transplant leaders have articulated the need for global measures of health status such as functional status.⁵

The most important finding in this study is that candidates with the lowest functional status have a greater death rate after transplantation compared to candidates with higher function, but still achieve a survival benefit from transplantation compared to dialysis.⁷ Complementary studies that have examined functional status as well as frailty among kidney transplant recipients suggest that post-transplantation complications such as early rehospitalization will also be more common among patients with worse global health.⁶

These results have direct ethics implications for the question of whether candidates with poor global health should undergo transplantation. From the patient perspective, the survival benefit of kidney transplantation must be weighed against the probability of complications. Patients with low functional status should be counseled about their risk of inactivation, longer time to transplantation, lesser likelihood of ever receiving a transplant, and the risk of lower post-transplantation survival. From the societal perspective, the allocation of kidneys to patients with low functional status will improve survival compared to dialysis but not maximize post-transplantation survival compared to allocation of kidneys to patients with better function.

These results also have implications for how transplant professionals practice. Particularly when low function is accompanied by older age or multiple comorbidities, wait-listed patients may benefit from reevaluation at shorter intervals and proactive communication between the center and referring physicians to address dialysis complications including infections, cardiovascular events, or hospitalizations.³⁶ Reevaluations and communication will necessarily involve more work and costs for providers, patients, and payers. However, for providers and patients willing to accept these outcomes, kidney transplantation offers a highly effective alternative to dialysis.

Given these findings, transplant professionals need guidance about optimal management of kidney transplant candidates with poor functional status, particularly those patients at risk for prolonged waiting time due to geographic region, immunological reactivity, or other factors.^{37,38} These strategies might include physical therapy (“prehabilitation” before transplantation), tailored nutrition programs, or potentially, novel anti-inflammatory therapies that address the effects of dialysis. While self-reported functional status is currently measured in all maintenance dialysis patients, and feasibly assessed by transplant centers, there is evidence that some groups – such as older adults – may overestimate their function.³⁹ Therefore, observed tests of physical function such as the short physical performance battery may provide more objective measures of declining global health status.⁴⁰ Future studies should compare these observed measures with self-reported function.

The study methods had a number of advantages. The cohort comprised patients at 227 transplant centers, with a sample size sufficient to implement robust analyses of survival benefit from transplantation vs. dialysis in subgroups defined by functional status. The dataset included repeat measurements of global health. We also examined inactivation as an outcome, which supplies a mechanism for why poor functional status is associated with lower probability of transplantation.¹⁵ The rising prevalence of inactive wait-listed patients is a pressing problem for transplant centers. Our results were robust in secondary analyses such as in the subset of patients who were never inactivated (and were presumably healthy enough for transplantation throughout the observation period).

We acknowledge study limitations. First, the findings about survival benefit among patients with poor baseline functional status may have limited generalizability for patients who were never accepted to the transplant waiting list. Second, unmeasured confounding is possible. The OPTN/UNOS dataset provided information about important clinical attributes such as cause of ESRD and diabetes, but lacked high quality data on potential confounders such as cardiovascular disease or arthritis.² Third, our analyses focusing on change in functional status over time may be susceptible to bias. Some patients may have had fewer assessments of functional status for different reasons including transplantation, death, or, potentially, health deterioration. We attempted to address this limitation by calculating slopes only during the first two years after wait-listing. Additionally, analyses that focused only on baseline function and those using repeated measures yielded similar results. The patterns of functional status change may also reflect regression to the mean. Lastly, results related to inactivation pose some challenges to interpretation because the reason for inactivation is unknown. Some inactivation events may take place due to illness, while others may be

driven by required medical testing such as a cardiac stress test that is not necessarily a signal of poor health.¹⁶

In conclusion, lower functional status had robust associations with higher risk of inactivation and longer time to kidney transplantation. In a diverse national cohort, kidney transplant candidates across a range of function enjoyed a survival benefit from transplantation. Given organ scarcity, these results underscore the need to identify novel management strategies that can support vulnerable candidates during prolonged waiting times for transplantation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Unadjusted association of baseline functional status quartile with the outcome of receiving a kidney transplant, using the Kaplan-Meier method. For analyses of the outcome of transplantation, we assumed complete follow-up from the index date until transplantation, death, or the end of study (September 3, 2010). *Log-rank test P-value < 0.001.

Figure 2.

Survival benefit associated with kidney transplantation (versus remaining wait-listed and receiving dialysis), by quartile of physical function. For analyses of mortality, we assumed complete follow-up from wait-listing until death or the end of the study

Table 1

Patient characteristics, by quartile of baseline physical function score

	PF Score Quartile					
	Total (N=19242)	Q1 (Highest; n=4253)	Q2 (n=5287)	Q3 (n=4492)	Q4 (Lowest; n=5210)	p-value
PF Score	50 (35,80)	90 (85,95)	70 (65,75)	50 (45,50)	20 (10,30)	<0.001
Range	0-100	85-100	60-80	40-55	0-35	
Age (y)	51 (41,59)	46 (36,56)	50 (40,59)	52 (42,60)	54 (45,61)	<0.001
Follow Up Time (y)	5.8 (4.2,7.5)	6.3 (4.9,7.9)	6.0 (4.4,7.6)	5.7 (4.0,7.4)	5.3 (3.0,7.0)	<0.001
Age category						<0.001
<35 y	2692 (14)	966 (23)	796 (15)	508 (11)	422 (8)	
35-<45 y	3671 (19)	1001 (24)	1020 (19)	857 (19)	793 (15)	
45-<55 y	5391 (28)	1109 (26)	1491 (28)	1299 (29)	1492 (29)	
55-<65 y	5165 (27)	797 (19)	1361 (26)	1242 (28)	1765 (34)	
65 y	2323 (12)	380 (9)	619 (12)	586 (13)	738 (14)	
Sex						
Female	7732 (40)	1344 (32)	2030 (38)	1902 (42)	2456 (47)	<0.001
Male	11510 (60)	2909 (68)	3257 (62)	2590 (58)	2754 (53)	
Race						
White	7676 (40)	1689 (40)	2120 (40)	1716 (38)	2151 (41)	<0.001
Black	6939 (36)	1569 (37)	1968 (37)	1688 (38)	1714 (33)	
Hispanic	3531 (18)	751 (17)	892 (17)	805 (18)	1083 (21)	
Asian	694 (4)	144 (3)	192 (4)	179 (4)	179 (3)	
Other	402 (2)	98 (2)	116 (2)	105 (2)	83 (2)	
Cause of ESRD						<0.001
Diabetes	6170 (32)	922 (22)	1518 (29)	1525 (34)	2205 (42)	
Hypertension	4719 (25)	1164 (27)	1347 (26)	1118 (25)	1090 (21)	
Glomerulonephritis	3093 (16)	896 (21)	921 (17)	637 (14)	639 (12)	
Polycystic Kidney	1039 (5)	288 (7)	318 (6)	213 (5)	220 (4)	
Congenital/Reflux	225 (1)	68 (2)	62 (1)	50 (1)	45 (1)	
Other or Unknown	3996 (21)	915 (22)	1121 (21)	949 (21)	1011 (19)	
Diabetes						<0.001
No Diabetes	11357 (59)	3077 (72)	3320 (63)	2560 (57)	2400 (46)	
Diabetes	7885 (41)	1176 (28)	1967 (37)	1932 (43)	2810 (54)	
Median BMI						<0.001
Underweight	490 (3)	88 (2)	152 (3)	109 (2)	141 (3)	
Healthy Weight	6263 (33)	1551 (37)	1760 (33)	1402 (31)	1550 (30)	
Overweight	6222 (33)	1458 (35)	1689 (32)	1447 (32)	1628 (31)	
Obese	3874 (20)	726 (17)	1060 (20)	935 (21)	1153 (22)	
Severely Obese	2295 (12)	408 (10)	601 (11)	575 (13)	711 (14)	
Peripheral vascular disease						

		PF Score Quartile				
	Total (N=19242)	Q1 (Highest; n=4253)	Q2 (n=5287)	Q3 (n=4492)	Q4 (Lowest; n=5210)	p-value
Disease	1087 (6)	137 (3)	235 (4)	258 (6)	457 (9)	
No Disease	16830 (88)	3789 (89)	4723 (89)	3917 (87)	4401 (85)	
Unknown/Missing	1312 (7)	323 (8)	327 (6)	315 (7)	347 (7)	
Prior Kidney Tx						0.06
No Prior Tx	17015 (88)	3739 (88)	4672 (88)	3946 (88)	4658 (89)	
Prior Tx	2227 (12)	514 (12)	615 (12)	546 (12)	552 (11)	
Blood type						0.9
AB	627 (3)	131 (3)	182 (3)	150 (3)	164 (3)	
A	5895 (31)	1313 (31)	1630 (31)	1341 (30)	1611 (31)	
B	2915 (15)	649 (15)	804 (15)	702 (16)	760 (15)	
O	9805 (51)	2160 (51)	267 (51)	2299 (51)	2675 (51)	
Insurance Type						<0.001
Private	6556 (34)	1736 (41)	1872 (35)	1410 (31)	1538 (30)	
Medicare	10982 (57)	2165 (51)	2986 (57)	2646 (59)	3185 (61)	
Other	1697 (9)	350 (8)	428 (8)	435 (10)	484 (9)	
Time since dialysis initiation						<0.001
<1 y	5887 (31)	1437 (34)	1629 (31)	1359 (30)	1462 (28)	
1-3 y	8344 (43)	1779 (42)	2323 (44)	1893 (42)	2349 (45)	
>3 y	4997 (26)	1033 (24)	1333 (25)	1238 (28)	1393 (27)	
Dialysis modality						<0.001
Hemodialysis	17231 (90)	3773 (89)	4690 (89)	4011 (89)	4757 (91)	
Peritoneal dialysis	2011 (10)	480 (11)	597 (11)	481 (11)	453 (9)	
Wait-listed before UNOS policy change*						0.3
Yes	4566 (39)	1639 (39)	2056 (39)	1771 (39)	2100 (40)	
No	11676 (61)	2614 (62)	3231 (61)	2721 (61)	3110 (60)	
Geographic quartile of time to kidney Tx* (%)						0.02
Shortest	2496 (13)	561 (13)	711 (14)	580 (13)	644 (12)	
Near Shortest	3388 (18)	788 (19)	960 (18)	790 (18)	850 (16)	
Near Longest	7043 (37)	1568 (37)	1930 (37)	1614 (36)	1931 (37)	
Longest	6304 (33)	1333 (31)	1685 (32)	1504 (34)	1782 (34)	
Any Kidney Tx Outcome[#]	11,050 (57)	2886 (68)	3247 (61)	2516 (56)	2401 (46)	<0.001
Deceased Donor Tx	9207 (90)	2351 (87)	2732 (90)	2108 (91)	2016 (93)	<0.001
Living Donor Tx	1843 (10)	535 (13)	515 (10)	408 (9)	385 (7)	<0.001

Note: Missing data was <1% for all variables except peripheral vascular disease. Values for categorical variables are given as number (percentage); for continuous variables, as median [interquartile range], except as noted.

BMI, body mass index; ESRD, end-stage renal disease; PF, physical function; Tx, transplant or transplantation; UNOS, United Network for Organ Sharing

* November 1, 2003 allowing priority to accrue during inactive time.

* Calculated among all kidney Tx candidates in each donor service area (geographic region defined by Organ Procurement and Transplantation Network that is strongly associated with organ availability through allocation)

Living or deceased donor.

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Table 2

Multivariable Cox regression analysis of receipt of kidney transplant

Physical Function	Unadjusted * (n=19,242)		Adjusted * (n=17,821)		Adjusted ** (n=17,821)	
	HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
Q1: Highest	1.00 (reference)		1.00 (reference)		1.00 (reference)	
Q2	0.89 (0.85-0.94)	<0.001	0.95 0.90, 1.00	0.04	0.94 0.89, 0.99	0.01
Q3	0.81 0.77, 0.86	<0.001	0.91 0.86, 0.96	0.001	0.81 0.76, 0.86	<0.001
Q4: Lowest	0.66 0.63, 0.70	<0.001	0.74 0.70, 0.79	<0.001	0.64 0.61, 0.68	<0.001

Note: Model adjusted for age, sex, race, primary insurance type, diabetes, prior kidney transplant, peripheral vascular disease, glomerulonephritis as cause of ESRD, polycystic disease as cause of ESRD, congenital or reflux disease as cause of ESRD, hypertension as cause of ESRD, blood type, body mass index, time since dialysis initiation, dialysis modality and geographic quartile of time to transplantation defined at level of the donor service area where the candidate was listed.

CI, confidence interval; ESRD, end-stage renal disease; HR, hazard ratio; Q, quartile

* Physical function categories defined at baseline without time-updates.

** Time-updated physical function categories.

Table 3

Multivariable Cox regression analysis of time to first inactivation on kidney transplant waiting list

Physical Function	Unadjusted * (n=18,726)			Adjusted * (n=17,331)			Adjusted ** (n=17,331)		
	HR (95% CI)		p	Adjusted HR (95% CI)		p	Adjusted HR (95% CI)		p
Q1: Highest	1.00 (reference)			1.00 (reference)			1.00 (reference)		
Q2	1.10 (1.04-1.17)		0.002	1.11	1.04, 1.19	0.003	1.12	1.05, 1.20	0.001
Q3	1.15	1.08, 1.23	<0.001	1.16	1.08, 1.24	<0.001	1.22	1.13, 1.31	<0.001
Q4: Lowest	1.29	1.22, 1.38	<0.001	1.27	1.18, 1.36	<0.001	1.30	1.21, 1.39	<0.001

Note” Model adjusted for age, sex, race, primary insurance type, diabetes, prior kidney transplant, peripheral vascular disease, glomerulonephritis as cause of ESRD, polycystic disease as cause of ESRD, congenital or reflux Disease as cause of ESRD, hypertension as cause of ESRD, blood type, body mass index, time since dialysis initiation, dialysis modality, geographic quartile of time to transplantation defined at level of donor service area where candidate was listed, and era (defined as before or after United Network for Organ Sharing policy change allowing priority to accrue during inactive time)

CI, confidence interval; ESRD, end-stage renal disease; HR, hazard ratio; Q, quartile

* Physical function categories defined at baseline without time-updates

** Time-updated physical function categories