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Association Between Waiting Times for Kidney Transplantation and Rates of Live Donation

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A deceased donor (DD) allocation system incorporating net life survival benefit has been proposed. In this system, many kidneys will be shifted to younger recipients, thereby decreasing their waiting times. The goal of this study was to determine the potential effects of altering waiting times on the likelihood of live donor kidney transplantation (LDKT). We analyzed 93 727 waiting list candidates to determine the association of various patient factors with likelihood of LDKT. The proportion of patients receiving LDKT was compared by the median DD waiting time at that patient's transplant center for someone of that patient's age category and race. LDKT was consistently higher as waiting times became longer. After adjusting for all other factors associated with likelihood of LDKT, waiting time remained a significant, independent predictor. Patients with the longest DD waiting times had 2.3-fold higher odds of LDKT (95% CI 2.11–2.58, $p < 0.001$). In planning the new DD allocation policy, we must account for resulting alterations in LDKT. It is possible that shifting DD kidneys to younger recipients may decrease LDKT or shift it to older recipients, net effects not consistent with the goal of net life survival benefit.

Key words: Kidney transplantation, live donation, organ allocation

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Recently, changes to the deceased donor (DD) kidney allocation policy have been proposed. These include recommendations from the UNOS Kidney Allocation Review Subcommittee (KARS), presented at a forum in Dallas on February 8, 2007. KARS has designed a DD allocation system incorporating net life survival benefit as measured by life years from transplant, attempting to maximize the number of person-years gained from each DD kidney (1). In this system, the allocation of many ideal DD kidneys will be shifted to younger recipients, thereby decreasing waiting times for younger patients and, as a result, increasing waiting times for older patients (2).

However, concerns have been raised that changing the way DD kidneys are allocated might change the attitudes and decrease the willingness of live donors. This would be profoundly problematic, as live donor kidney transplantation (LDKT) represents the most promising modality for addressing the organ crisis. Despite significant efforts to increase public awareness, deceased kidney donation has increased only 15% in the last 10 years, while LDKT has nearly tripled (3). Furthermore, LDKT offers considerably better graft survival (4,5), less waiting time, improved patient survival by decreasing dialysis time before transplantation (6) and a higher potential for preemptive transplantation.

The goal of this study was to determine the potential effects of altering DD waiting times on the likelihood of LDKT. We have shown that, for any patient characteristics, a longer waiting time is associated with a higher likelihood of LDKT.

Methods

This was a secondary data analysis of a prospective cohort of primary kidney-only waiting list candidates, evaluating the association between various risk factors and likelihood of LDKT. A total of 93 727 adult patients who registered at 247 transplant centers for first-time kidney-only transplants between January 1, 1995, and December 31, 2002, and were available for analysis in the UNOS Kidney Standard Transplant Analysis and Research (STAR) waiting list file were analyzed. Follow-up was available through June 6, 2006. Our study focused on the likelihood of receiving LDKT after registering for the waiting list. However, we also analyzed 13949 patients who received LDKT but were never registered for the waiting list, to see if waiting times would also influence LDKT rates for these patients who did not experience the wait for a DD kidney.

A logistic regression model for the odds of LDKT was designed in the following manner. First, unadjusted analyses were performed of the following biologically relevant candidate variables from the STAR file: age, race, blood type, diagnosis, panel reactive antibody (PRA), insurance, education, body mass index (BMI), cerebrovascular disease (CVD), chronic obstructive pulmonary disease (COPD), hypertension (HTN), prior malignancy, diabetes, peptic ulcer disease (PUD), peripheral vascular disease (PVD), dialysis, gender, hospitalization and year of listing. The appropriate functional form of model covariates was determined by exploratory data analysis in unadjusted models. All biologically relevant variables found to be statistically significant on univariate analysis were included in a forced multivariate model. The appropriateness of the forced model was confirmed with forward stepwise and backward stepwise testing for a reduction in the Akaike's Information Criterion (AIC), demonstrating that all variables included in the model contributed explanatory power. The absence of collinearity between covariates was confirmed by examination of variance inflation factors (mean VIF 1.72). Goodness-of-fit was confirmed by the Hosmer-Lemeshow test ($p = 0.18$) and Receiver Operating Characteristic curve (area under curve = 0.72).

Subgroups were selected based on the two most significant, well-known factors determining likelihood of LDKT: candidate age (7) and race (8,9). For the purposes of minimizing the number of subgroups while describing as much relevant information as possible, age was categorized as 18–39, 40–59 and ≥60 years, and race was categorized as Caucasian (as reported to UNOS by the transplant center) and non-Caucasian (any other race reported to UNOS). Median waiting time for patients awaiting DD transplants in each of the six subgroups, for each transplant center, was calculated using Kaplan–Meier estimates, modeling waiting time in active status as time-to-event data with DD transplantation as an event and death or end-of-study as censored observations. Each patient was assigned a 'median center/subgroup-specific' waiting time to indicate what the median waiting time at that patient's transplant center would be for someone of that patient's age category and race. A similar process was utilized to develop 'median center/race-specific' waiting times, categorizing only on race and not age subgroup. These waiting times were also divided into quintiles, within each subgroup. As a result, each patient was assigned a score, which indicated how long that particular patient's subgroup (either age/race-specific or just race-specific) could expect to wait at his particular transplant center for a DD transplant.

Unless otherwise specified, all tests were 2-sided with statistical significance set at $\alpha = 0.05$. All analyses were performed using multiprocessor Stata/SE 9.1 for Linux (StataCorp, College Station, TX).

Results

Of 93 727 adults registered for first-time kidney-only transplants between January 1, 1995, and December 31, 2002, and followed through June 6, 2006, a total of 13 785 (15%) received LDKT, 41 096 (44%) received DD kidneys and 38 846 (41%) remained un-transplanted; in addition, 13 949 patients received live donor kidneys without registering (Table 1). Consistent with previous reports, the proportion of patients who received DD kidneys differed very little over the years of the study (range 11.3–13.1%). Similarly, little difference was seen in patients who received live donor kidneys without registering (range 10.4–14.1%). However, the proportion of patients who received LDKT after listing nearly tripled over the course of the study, from 6.9% in 1995 to 18.5% in 2002. When compared with DD recipients, those who received LDKT after listing were more likely to be young (34.2% vs. 23.8%), Caucasian (63.7% vs. 51.2%), low PRA (91% vs. 85.8%), privately insured (63.3% vs. 42.2%), college educated (51.7% vs. 40.7%) and preemptively transplanted (31.1% vs. 14.9%). By multivariate logistic regression, notable factors associated with likelihood of LDKT after listing included age, race, PRA, insurance, education, diabetes, dialysis and year listed (Table 2).

Table 1: Characteristics of patients registered for or receiving first-time kidney-only transplants

	Registered for deceased donor waiting list			Not registered
Donor type	Deceased donor	Live donor	Not transplanted	Live donor
N	41096	13785	38846	13949
Age (%)				
18–39	23.8	34.2	19.9	41
40–59	55	50.7	53.7	45.6
≥60	21.2	15.1	26.3	13.4
Race (%)				
Non-Caucasian	48.8	36.3	54.3	27
Caucasian	51.2	63.7	45.7	73
Blood type (%)				
A	39.4	35.9	27.6	40.8
B	11.9	13.5	16.9	11.9
AB	5.4	3.2	2.5	4.1
O	43.3	47.4	52.9	43.2
Diagnosis (%)				
GN	9.8	10.9	4.8	16.2
IgA	3.4	7	1.4	9.8
FSGS	5.5	7.3	2.6	9.3
Reflux	1.7	2.3	0.6	5.1
PKD	10	10.5	4.1	12.9
Diabetes	27.4	23	45.4	35.8
Lupus	2.8	3.8	2.6	6
HTN	6.9	5.1	4.7	4.9
Misc	32.5	30.3	33.9	0
PRA (%)				
0–19	85.8	91	73.9	NR
20–79	9.6	7.4	15.1	NR
≥80	4.7	1.6	10.9	NR
Insurance (%)				
Private	42.2	63.3	36.2	58.8
Medicare	48.3	28.4	51.1	33.4
Medicaid	6.9	5.6	9.4	4.3
Other	2.6	2.8	3.4	3.5
Education (%)				
Pre-college	59.3	48.3	61.5	50.3
College or beyond	40.7	51.7	38.5	49.7
BMI (%)				
<25	39.8	41.4	39.4	NR
25–29.9	35.1	34.3	33.4	NR
30–34.9	17.7	16.8	17.4	NR
35–39.9	5.4	5.4	6.7	NR
≥40	1.9	2.1	3.1	NR
CVD (%)	2.8	2.1	3.8	1.8
COPD (%)	1	0.9	1.4	0.9
Hypertension (%)	82.6	83.2	83.5	79.8
Prior malignancy (%)	2.8	2.8	3.2	2.3
Diabetes (%)	31.8	26.3	53	27.4
PUD (%)	5.4	4.5	6.5	4.5
PVD (%)	4.3	3.7	8.2	3.5
Dialysis (%)	85.1	68.9	77.8	69.3
Female (%)	38.4	39.6	42.3	42.2
Hospitalized (%)	0.4	0.6	1	1.2
Year listed (%)				
1995	11.8	6.9	9.2	10.4
1996	12.7	7.7	10.1	11.1
1997	13	10	10.4	11.4
1998	13.1	11.1	11.5	12.9
1999	12.8	13.5	11.7	12.7
2000	13.1	16	14.4	13.8
2001	12.2	16.3	15.1	14.1
2002	11.3	18.5	17.6	13.6

NR = not reported; GN = glomerulonephritis; FSGS = focal segmental glomerulosclerosis; PKD = polycystic kidney disease; HTN = hypertension; PRA = panel reactive antibody; BMI = body mass index; CVD = cerebrovascular disease; PUD = peptic ulcer disease; PVD = peripheral vascular disease.

Table 2: Candidate factors associated with odds of live donation

	Univariate OR		Multivariate OR	
Age				
18–39	Reference		Reference	
40–59	0.60 (0.57–0.62)	$p < 0.001$	0.60 (0.57–0.63)	$p < 0.001$
≥60	0.41 (0.39–0.43)	$p < 0.001$	0.44 (0.41–0.48)	$p < 0.001$
Race				
Non-Caucasian	Reference		Reference	
Caucasian	1.86 (1.79–1.93)	$p < 0.001$	1.59 (1.51–1.67)	$p < 0.001$
Blood type				
A	Reference		Reference	
B	0.89 (0.84–0.94)	$p < 0.001$	1.05 (0.97–1.13)	$p = 0.22$
AB	0.74 (0.67–0.83)	$p < 0.001$	0.77 (0.67–0.87)	$p < 0.001$
O	0.92 (0.89–0.96)	$p < 0.001$	0.98 (0.93–1.04)	$p = 0.52$
Diagnosis				
GN	Reference		Reference	
IgA	1.96 (1.78–2.16)	$p < 0.001$	1.38 (1.22–1.56)	$p < 0.001$
FSGS	1.20 (1.09–1.31)	$p < 0.001$	1.06 (0.95–1.19)	$p = 0.31$
Reflux	1.38 (1.20–1.58)	$p < 0.001$	1.12 (0.94–1.33)	$p = 0.20$
PKD	1.00 (0.92–1.08)	$p = 0.92$	0.79 (0.72–0.88)	$p < 0.001$
Diabetes	0.43 (0.40–0.46)	$p < 0.001$	0.82 (0.71–0.95)	$p = 0.008$
Lupus	0.94 (0.84–1.05)	$p = 0.25$	1.15 (1.00–1.32)	$p = 0.06$
HTN	0.59 (0.54–0.65)	$p < 0.001$	0.80 (0.70–0.91)	$p < 0.001$
Misc	0.62 (0.58–0.66)	$p < 0.001$	0.79 (0.72–0.86)	$p < 0.001$
PRA				
0–19	Reference		Reference	
20–79	0.53 (0.50–0.57)	$p < 0.001$	0.60 (0.55–0.66)	$p < 0.001$
≥80	0.18 (0.16–0.21)	$p < 0.001$	0.21 (0.18–0.25)	$p < 0.001$
Insurance				
Private	Reference		Reference	
Medicare	0.35 (0.34–0.37)	$p < 0.001$	0.46 (0.44–0.49)	$p < 0.001$
Medicaid	0.43 (0.39–0.46)	$p < 0.001$	0.52 (0.46–0.57)	$p < 0.001$
Other	0.58 (0.52–0.64)	$p < 0.001$	0.57 (0.49–0.67)	$p < 0.001$
Education				
Pre-college	Reference		Reference	
College or beyond	1.63 (1.56–1.69)	$p < 0.001$	1.23 (1.17–1.29)	$p < 0.001$
BMI				
<25	Reference		Reference	
25–29.9	0.96 (0.92–1.00)	$p = 0.041$	0.99 (0.93–1.04)	$p = 0.60$
30–34.9	0.92 (0.87–0.96)	$p < 0.001$	1.00 (0.94–1.07)	$p = 0.99$
35–39.9	0.85 (0.78–0.92)	$p < 0.001$	0.90 (0.82–1.00)	$p = 0.06$
≥40	0.79 (0.70–0.90)	$p < 0.001$	0.82 (0.70–0.96)	$p = 0.016$
CVD	0.62 (0.55–0.71)	$p < 0.001$	0.83 (0.71–0.98)	$p = 0.024$
COPD	0.74 (0.61–0.89)	$p = 0.002$	0.90 (0.71–1.14)	$p = 0.38$
Hypertension	1.01 (0.96–1.06)	$p = 0.61$		
Prior malignancy	0.94 (0.84–1.05)	$p = 0.27$		
Diabetes	0.49 (0.47–0.51)	$p < 0.001$	0.60 (0.53–0.68)	$p < 0.001$
PUD	0.75 (0.69–0.82)	$p < 0.001$	0.93 (0.83–1.03)	$p = 0.17$
PVD	0.58 (0.52–0.63)	$p <0.001$	0.92 (0.81–1.03)	$p = 0.15$
Dialysis	0.50 (0.48–0.52)	$p < 0.001$	0.73 (0.69–0.77)	$p < 0.001$
Female	0.97 (0.94–1.01)	$p = 0.14$		
Hospitalized	0.84 (0.66–1.06)	$p = 0.13$		
Year listed				
1995	Reference		Reference	
1996	1.03 (0.94–1.13)	$p = 0.56$	0.94 (0.83–1.05)	$p = 0.26$
1997	1.30 (1.19–1.42)	$p < 0.001$	1.20 (1.07–1.34)	$p = 0.001$
1998	1.39 (1.28–1.52)	$p < 0.001$	1.31 (1.17–1.46)	$p < 0.001$
1999	1.69 (1.55–1.84)	$p < 0.001$	1.59 (1.43–1.77)	$p < 0.001$
2000	1.79 (1.65–1.94)	$p < 0.001$	1.83 (1.65–2.03)	$p < 0.001$
2001	1.84 (1.70–2.00)	$p < 0.001$	1.91 (1.72–2.11)	$p < 0.001$
2002	1.98 (1.83–2.15)	$p < 0.001$	2.10 (1.90–2.32)	$p < 0.001$

OR = odds ratio; GN = glomerulonephritis; FSGS = focal segmental glomerulosclerosis; PKD = polycystic kidney disease; HTN = hypertension; PRA = panel reactive antibody; BMI = body mass index; CVD = cerebrovascular disease; PUD = peptic ulcer disease; PVD = peripheral vascular disease.

The proportion of patients receiving LDKT after listing was compared by 'median center/subgroup-specific' waiting time, i.e. the median DD waiting time at that patient's transplant center for someone of that patient's age category and race. Median DD waiting times varied widely, ranging from 384 days in the centers with the shortest waiting time to 1351 days in the centers with the longest waiting times for non-Caucasian candidates and 240–901 days for Caucasian candidates (Figure 1). In contrast, LDKT recipients at centers with the longest DD waiting times had relatively similar waiting times for their live donor transplants as LDKT recipients at centers with the shortest DD waiting times (317 vs. 225 in non-Caucasians, 226 vs. 160 in Caucasians).

For almost every age and race subgroup, candidates at transplant centers with longer waiting times were more likely to receive LDKT after listing (Figure 2). For example, 14.1% of Caucasian candidates over 60 received LDKT at transplant centers with long DD waiting times, while only 6.7% received LDKT at centers with short DD waiting times. Similarly, 33.0% of younger Caucasian candidates (18–39 years old) received LDKT at centers with long waiting times, versus 16.8% at centers with short waiting times. In general, non-Caucasians had lower rates of LDKT when compared to Caucasians. Additionally, the difference between LDKT rates at centers with long- and short-waiting times was insignificant in non-Caucasians over 60 (7.1% vs. 6.7%).

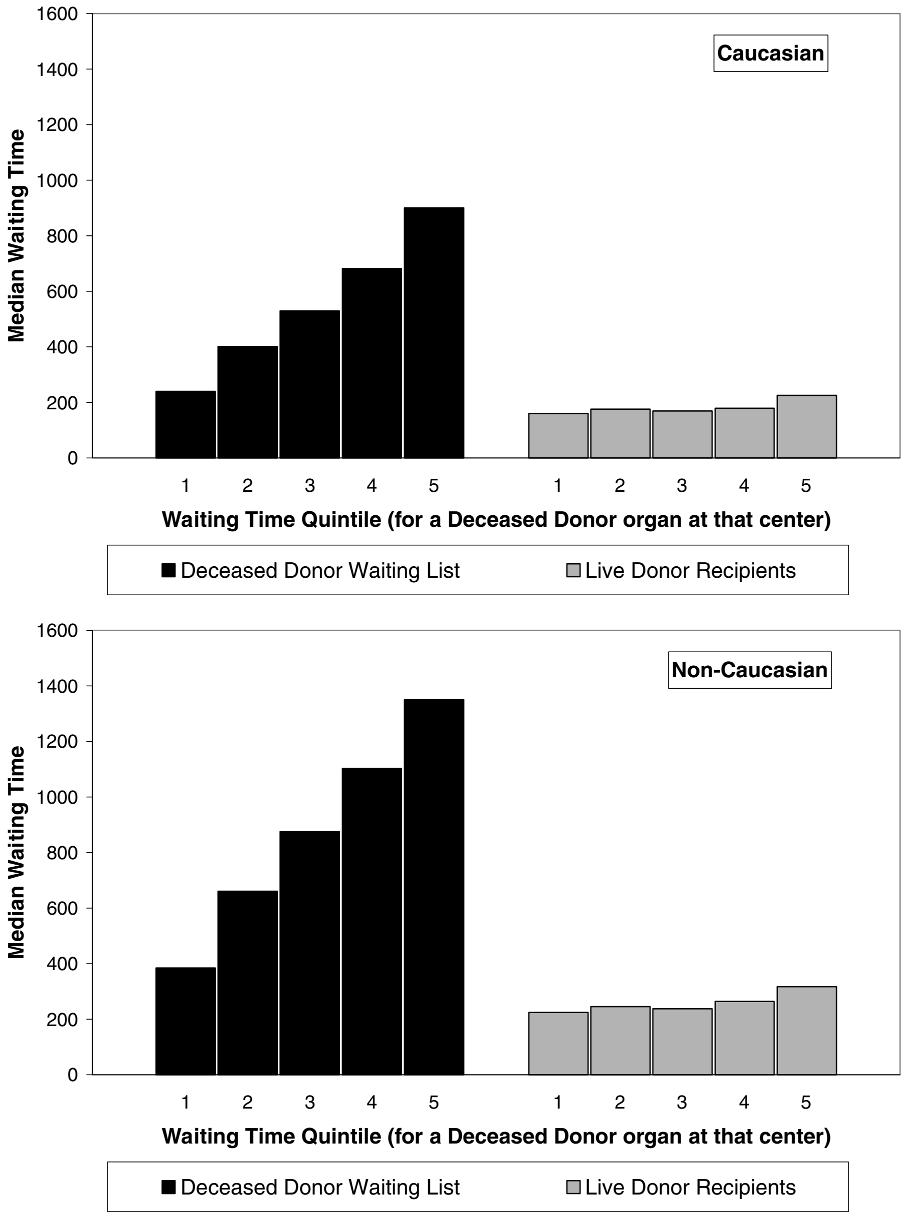

Figure 1: Median waiting times for deceased donor and live donor kidney transplantation after listing, stratified by quintile of median waiting time for a deceased donor organ at the candidate's transplant center for the candidate's race subgroup.

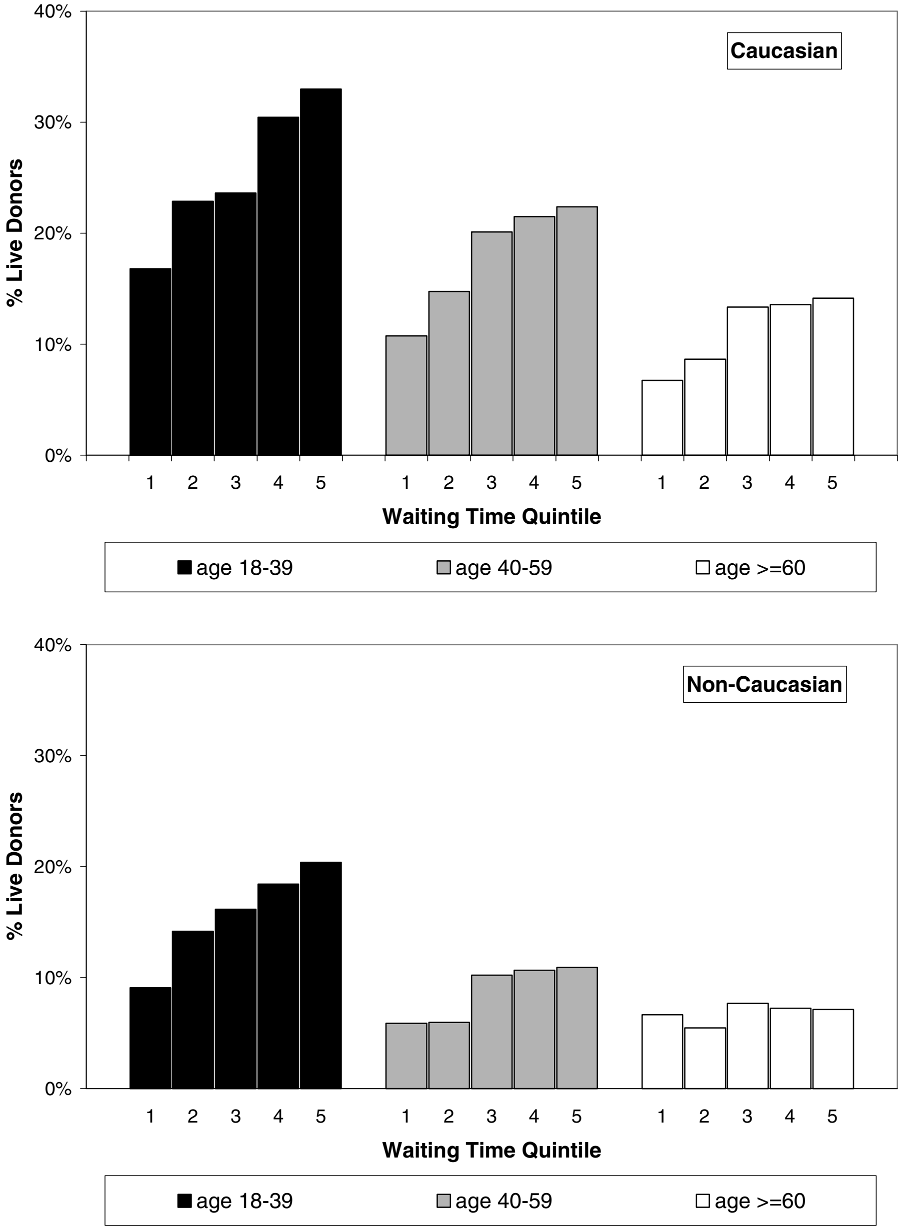

Figure 2: Differences in rates of live donor transplant after listing, between centers with various median waiting times, by race and age subgroups. Median waiting times were calculated by center, for each age/race subgroup.

Because of the limitations of stratified analysis, the above comparisons could account only for differences in age and race. However, other factors discovered to be associated with the likelihood of LDKT included blood type, diagnosis, PRA, insurance, education, BMI, CVD, COPD, diabetes, PUD, PVD, dialysis and year listed. After accounting for all of the above factors in a multivariate logistic regression model, the median DD waiting time at a patient's transplant center for someone of that patient's subgroup remained a significant, independent predictor (Figure 3). In all subgroups of Caucasians and in the youngest subgroup of non-Caucasians, patients at centers with the longest waiting times had >2.5-fold higher odds of LDKT when compared with patients at centers with the shortest waiting times. In older non-Caucasians, this difference was attenuated.

As expected, overall odds of receiving a DD transplant decreased significantly across quintiles of waiting time (Table 3). The odds of LDKT before registering for the waiting list decreased across quintiles of waiting time in a similar manner. However, being registered at a transplant center with the longest waiting times for one's race/age subgroup was associated with 2.33-fold higher odds of LDKT after listing (95% CI 2.11–2.58, $p < 0.001$), a 2.61-fold

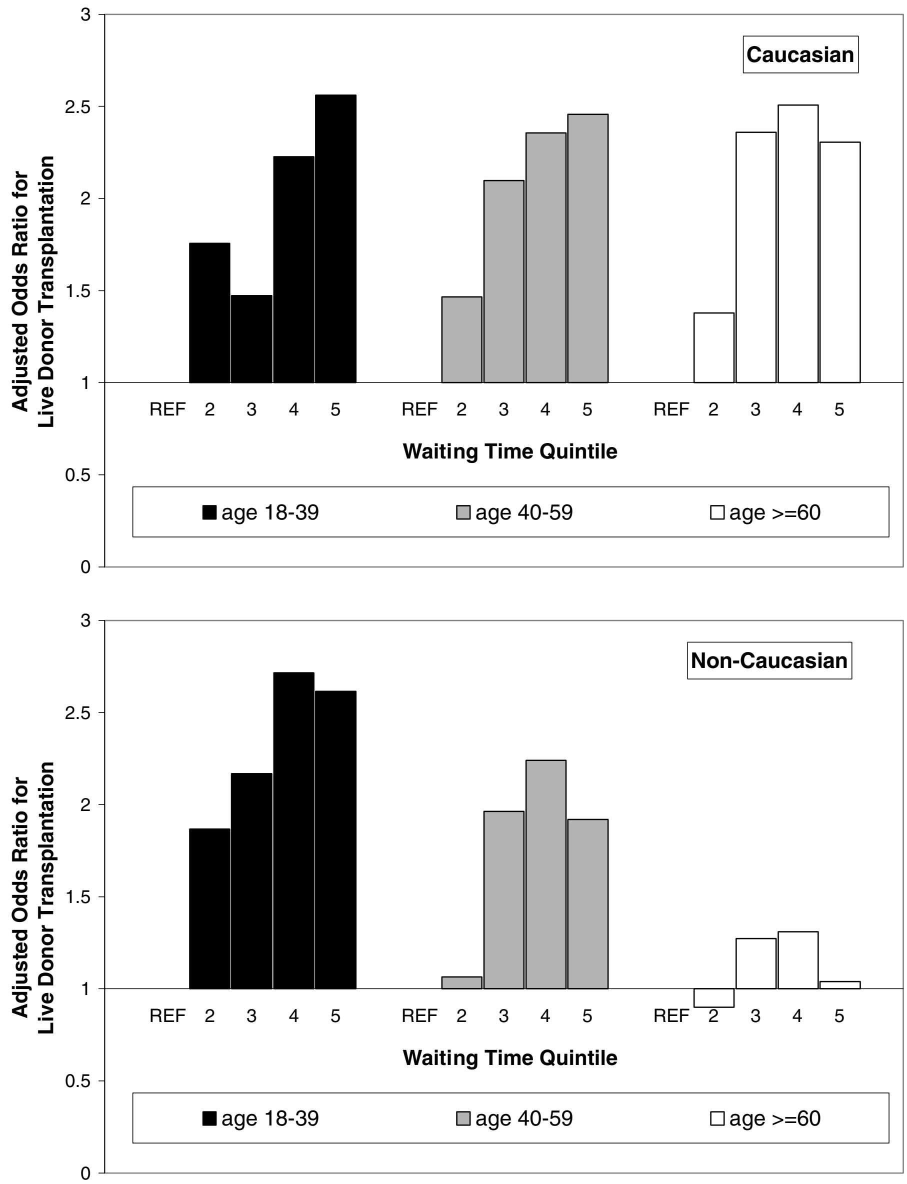

Figure 3: Adjusted odds ratios of receiving a live donor transplant after listing, by median waiting times. Adjusted for age, race, blood type, diagnosis, PRA, insurance, education, comorbidities (BMI, CVD, COPD, diabetes, PUD, PVD), dialysis and year listed. Median waiting times were calculated by center, for each age/race subgroup.

higher odds after waiting for more than 6 months (95% CI 2.30–2.98, $p < 0.001$), a 3.18-fold higher odds after waiting for more than 12 months (95% CI 2.65–3.81, $p < 0.001$) and a 6.23-fold higher odds after waiting more than 24 months (95% CI 4.40–8.82). This likely indicates that the upfront availability of live donation in a given geographic area was driven by general donor awareness in a manner similar to deceased donation, but that longer waiting times once registered for the waiting list inspired increased interest in live donation. The pressure of the waiting list seemed stronger than that of dialysis, with 2.33-fold higher odds of receiving a LDKT after listing and after starting dialysis (95% CI 2.10–2.60, $p < 0.001$), and 1.84-fold higher odds of receiving a LDKT after listing but before starting dialysis (95% CI 1.43–2.37, $p < 0.001$).

Discussion

We have shown that patients with longer waiting times for DD kidneys are more likely to undergo LDKT. Even after adjusting for all factors discovered to be associated with the likelihood of LDKT, patients at centers with the longest DD waiting times (median 1351 days for non-Caucasians and 901 days for Caucasians) had more than 2-fold higher odds of being transplanted with a live donor when compared with patients at centers with the shortest DD waiting times (median 384 days for non-Caucasians and 240 days for Caucasians).

It is possible that the search for a live donor widens with each day that a patient is on dialysis, explaining the highest

Table 3: Odds ratios of receiving a kidney transplant, by median deceased donor waiting time specific to the patient's age/race subgroup and transplant center. Multivariate model adjusted for age, race, blood type, diagnosis, PRA, insurance, education, comorbidities (BMI, CVD, COPD, diabetes, PUD, PVD), dialysis and year listed

	Multivariate odds ratio (95% confidence interval; p < 0.001 for all comparisons)			
Waiting time quintile (1 = Reference)	2	3	4	5 (longest)
Deceased donor	0.74 (0.70–0.78)	0.56 (0.53–0.59)	0.46 (0.44–0.49)	0.3 (0.28–0.32)
Live donor before listing	0.71 (0.67–0.76)	0.54 (0.50–0.57)	0.47 (0.43–0.50)	0.33 (0.30–0.36)
Live donor after listing	1.53 (1.39–1.68)	1.98 (1.80–2.17)	2.38 (2.17–2.62)	2.33 (2.11–2.58)
Live donor after listing, pre-dialysis	1.80 (1.44–2.26)	2.27 (1.82–2.83)	2.46 (1.97–3.09)	1.84 (1.43–2.37)
Live donor after listing, post-dialysis	1.45 (1.31–1.60)	1.84 (1.66–2.03)	2.25 (2.03–2.49)	2.33 (2.10–2.60)
Live donor >6 months after listing	1.52 (1.34–1.72)	1.9 (1.68–2.15)	2.35 (2.07–2.66)	2.61 (2.30–2.98)
Live donor >12 months after listing	1.57 (1.31–1.89)	2.09 (1.75–2.50)	2.69 (2.26–3.20)	3.18 (2.65–3.81)
Live donor >24 months after listing	2.16 (1.51–3.10)	3.16 (2.23–4.47)	4.33 (3.07–6.10)	6.23 (4.40–8.82)

likelihood in the centers with highest DD waiting time and the increasing likelihood of LDKT for patients who have waited longer periods of time on the waiting list. However, the waiting times for patients who receive DD kidneys are much greater than for those who receive LDKT, and the differences are much more pronounced in centers with higher DD waiting times. This could indicate that the perception or knowledge of long waiting times for a DD kidney for a given patient's age category and race at a given patient's transplant center encourages the search for live donation and inspires the participation of potential live donors even before long waits ensue.

One aim in changing organ allocation is to increase the net lifetime survival benefit of transplantation. If the association between shorter DD waiting times and lower likelihood of LDKT holds true under a new allocation system, patients who derive shorter DD waiting times as a result of the new system (i.e. younger patients) may be less likely to undergo LDKT than they are at present, and those who suffer longer waiting times (i.e. older patients) may be more likely. In other words, it is possible that, although the utility of ideal DD kidneys will be improved by allocation to younger patients, the utility of live donor kidneys will be decreased by shifting LDKT to older recipients. Since live donor kidneys are predicted to function nearly twice as long as DD kidneys, the net benefit of improving DD utility but harming live donor utility could be negative.

Our data suggest that the upper bound of LDKT likelihood for younger candidates (33.0% for Caucasian and 20.4% for non-Caucasian) is considerably higher than the comparable best-case scenario for older candidates (14.1% for Caucasian and 7.1% for non-Caucasian). In fact, even the lower bound of LDKT likelihood for younger candidates is higher than the best-case scenario for older candidates. Depending on the subgroups most affected by a net benefit policy, and the degree to which their waiting times are affected, a shift in DD waiting times could even decrease LDKT rates altogether. As an example, shifting younger candidates from the upper quintile to the middle quintile of DD waiting times (i.e. decreasing waiting times for this subgroup), and reciprocally shifting older candidates from the lowest quintile to the middle quintile of DD waiting times (i.e. increasing waiting times for this subgroup) would be predicted to lower net live donation by 3% for both Caucasians and non-Caucasians. A more extreme shift (from the highest quintile to the lowest quintile in younger candidates and from the lowest quintile to the highest quintile in older candidates) would be predicted to lower net live donation by 9% for Caucasians and 11% for non-Caucasians.

Inferences from our findings and subsequent generalization of these inferences are limited by a number of assumptions that merit discussion. Most importantly, even if our model accurately captures the associations in the patients that we analyzed, these data describe past behavior, which for many reasons may not necessarily predict future behavior. Second, waiting time and its association with LDKT may represent a surrogate for donor and recipient attitudes, and a change in the DD allocation policy may affect donor and recipient attitudes independently of how the waiting times in any particular system in ongoing operation would affect such attitudes. Finally, it is not straightforward to establish the true effect of the proposed allocation system on waiting times for various patient subgroups. Without a discrete event simulation to characterize the changes in waiting times under the proposed allocation system, we cannot accurately predict the resulting change in live donation rates. However, our findings suggest that changes would occur in LDKT that might offset some of the net utility gained through DD reallocation.

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