Compound Effect of Kidney Donor Profile Index and Cold Ischemic Time on 1-Year Kidney Transplant Recipient Outcomes

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ABSTRACT

Objective. Kidney Donor Profile Index (KDPI) and cold ischemic time (CIT) independently influence recipient outcomes after kidney transplantation; however, the compound effect of these variables on posttransplant outcomes is unknown.

Design. The Scientific Registry of Transplant Recipients database of deceased-donor kidney transplant recipients between January 2012 and December 2016 was reviewed. Recipients were stratified based on their KDPI (0%-20%, 21%-85%, 86%-100%) and then based on CIT (0-12, 13-24, 25-30, 31-36, $\geq$ 37 hours). The primary outcome is 1-year allograft loss. Secondary outcomes include primary nonfunction, delayed graft function, biopsy-proven rejection, and 1-year recipient mortality.

Results. Allograft loss was not affected by CIT for KDPI 0% to 20% ($P = .898$) or KDPI 86% to 100% ($P = .731$), but was significantly different for KDPI 21% to 85% ($P < .001$). The KDPI 21% to 85% group was the only group with a significant difference in primary nonfunction, demonstrating a linear rise with increasing CIT ($P < .001$). CIT did not affect recipient mortality for any KDPI group (KDPI 0%-20%, $P = .306$; KDPI 21%-85%, $P = .098$; KDPI 86%-100%, $P = .774$). Incidence of delayed graft function was greater for each KDPI group ($P < .001$) with increased CIT. Biopsy-proven rejection was not affected by CIT for KDPI 21% to 85% ($P = .244$) or KDPI 86% to 100% ($P = .946$). For KDPI 0% to 20%, there was a significant difference ($P = .024$); however, the incidence was not linear with increasing CIT. For the KDPI 86% to 100% group, incidence of mortality, allograft loss, primary nonfunction, and biopsy-proven rejection did not differ between CIT groups.

Conclusions. Extended CIT alone should not hinder utilization of higher KDPI organs.

THE therapy of choice for end-stage renal disease is kidney transplantation. In the United States, there are currently approximately 95,000 candidates on the kidney transplant waitlist [1]. The demand for a kidney transplant has always exceeded organ availability, with only 18,836 kidney transplants occurring in 2016 [2]. To increase the number of available organs for transplant, multiple efforts have been pursued to increase the donor pool. Strategies for this include accepting organs from donors who are of older age, have a history of hypertension or diabetes, have reversible or temporarily impaired renal function, and have died of a stroke or cardiac event [3].

Historically, priority for kidney transplant in the United States was solely based on wait time [4]. Progressively, more factors were added to the allocation system including, but not limited to, immune system incompatibility, history of prior kidney donation, and donor geography. In December of 2014, the Organ Procurement and Transplantation Network (OPTN) introduced a new component, known as Kidney Donor Profile Index (KDPI), to the organ allocation system to approximate organ longevity, maximize graft potential, and decrease retransplantation rates [5]. The estimated graft half-life is: a KDPI of 0% to 20% confers on average 11.5 years of graft function, 21% to 85% confers 9 years, and > 85% confers 5.5 years [6]. Recipients are also subject to longevity assessment through the Estimated Post-Transplant Survival (EPTS) score. The introduction of KDPI and EPTS facilitates longevity matching between donors and recipients such that candidates with optimal EPTS scores receive priority allocation for low KDPI kidneys, and candidates with shorter expected survival based on their number and severity of comorbidities can receive offers for high-KDPI kidneys, ideally resulting in shorter wait-times and fewer deaths with a functioning allograft.

Although not a component of the KDPI calculation, another important factor in posttransplant outcomes is cold ischemia time (CIT). CIT is defined as the amount of time an organ is preserved on ice, from the time of crossclamping in the donor to the time it is reperfused in the recipient. A longer CIT increases the risks of delayed graft function (DGF), graft failure, recipient cardiac events, and recipient mortality [7,8]. Although higher KDPI and longer CIT independently have been shown to predict worse prognosis, there have been no studies to date assessing the relationship between KDPI, CIT, and clinical outcomes. Kidneys with a KDPI of 81% or higher are subject to a 50% to 70% discard rate, and clinicians may be more inclined to reject a high-KDPI kidney with a long CIT for fear of older donors having a higher susceptibility to the deleterious effects of CIT [9,10]. The purpose of our research is to assess the compound effect, or lack thereof, of CIT and KDPI on kidney allograft outcomes.

DESIGN AND METHODS

This study used data from the Scientific Registry of Transplant Recipients (SRTR). The SRTR data system includes data on all donor, wait-listed candidates, and transplant recipients in the United States, submitted by the members of the OPTN. The Health Resources and Services Administration, US Department of Health & Human Services provides oversight to the activities of the OPTN and SRTR contractors.

Study Population

The study was approved by the Institutional Review Board. Using the SRTR database, we identified adult (≥ 18 years old) patients who underwent deceased-donor kidney transplant between January 1, 2012, and December 31, 2016, inclusive. Although the KDPI-based allocation system went into effect in December 2014, KDPI can be calculated from SRTR data. Children under 18 years of age,

patients who were dual organ recipients, and living-donor transplants were excluded. Recipients were stratified into 3 groups based on KDPI: 0% to 20%, 21% to 85%, 86% to 100%, and 5 groups based on CIT (0-12 hours, 13-24 hours, 25-30 hours, 31-36 hours, and 37 or more hours). The CIT groups were chosen to provide granularity for longer CIT given lack of consistent, previously defined strata. The KDPI was calculated using the variables found in the SRTR database.

Outcomes

The primary outcome is death-censored allograft loss within 1 year posttransplant. Secondary outcomes include incidence of primary nonfunction (PNF), DGF, defined as the need for dialysis within the first 7 days posttransplant, biopsy-proven rejection within 1 year posttransplant, and recipient mortality within 1 year posttransplant. Multivariate analyses were used determine the effect of recipient and donor variables for each KDPI group on death-censored allograft loss and recipient mortality within 1 year posttransplant. Recipient variables include age, sex, race, ethnicity, EPTS score, induction immunosuppression, maintenance immunosuppression at the time of discharge, history of coronary artery disease (CAD), calculated panel reactive antibody, and history of previous transplant. Donor variables include type (brain death or cardiac death), import status, pump status, CIT category, and anastomotic warm ischemic time.

Statistics

Descriptive statistics comprised mean ± SD and medians with interquartile ranges for continuous data. Categorical variables were presented as frequencies using percentages. Inferential statistics comprised analysis of variance, for comparisons of continuous data between the 3 KDPI categories, and utilized a post hoc Scheffé multiple range test to compare individual group differences. Categorical comparisons were performed with a χ^2 test. Logistic regression models were forward, conditional designs that utilized factors shown to have statistically significant univariate differences and potentially clinically meaningful factors. Odds ratios (ORs) and associated 95% confidence intervals (CIs) were calculated for each factor. A priori power analyses were not performed as the data comprised a finite set of available and eligible records. An α level of 0.05 was used for all analyses such that statistically significant results were declared for all findings with $P < .05$. SPSS version 21 (IBM, Armonk, NY, United States) was used for all analyses, with the exception of KDPI calculations, for which Excel 2010 (Microsoft, Redmond, Wash, United States) was used.

RESULTS
Baseline Characteristics

During the study period, 58,318 recipients that met inclusion criteria were identified. Table 1 outlines the baseline characteristics for the study population. In the KDPI 0% to 20% group, there were significant differences between CIT groups for all donor and recipient characteristics except ethnicity, history of CAD, and use of calcineurin inhibitor (CNI) maintenance therapy. For KDPI 21% to 85%, all characteristics differed except history of CAD. For KDPI 86% to 100%, there were fewer recipient characteristics that differed between CIT groups. These included ethnicity, EPTS score, and type of induction therapy. All donor

Table 1. Baseline Characteristics

KDPI 0%-20%	CIT 0-12 (n = 5501)	CIT 13-24 (n = 6282)	CIT 25-30 (n = 1167)	CIT 31-36 (n = 436)	CIT ≥ 37 (n = 306)	P Value
Recipient Characteristics						
Age (y), mean ± SD	42 ± 19	44 ± 17	46 ± 16	46 ± 16	46 ± 16	< .001
Male, n (%)	3399 (61.8)	3794 (60.4)	653 (60)	259 (59.4)	198 (64.7)	.003
African American, n (%)	1539 (28)	1977 (31.5)	380 (32.6)	153 (35.1)	120 (39.2)	< .001
Latino, n (%)	1004 (18.3)	1207 (19.2)	220 (18.9)	81 (18.6)	41 (13.4)	.11
History of CAD, n (%)	123 (2.2)	161 (2.6)	36 (3.1)	13 (3)	11 (3.6)	.27
Previously transplanted, n (%)	743 (13.5)	1247 (19.9)	275 (23.6)	80 (18.3)	55 (18)	< .001
cPRA (%), mean ± SD	19 ± 33	29 ± 40	36 ± 42	27 ± 40	20 ± 35	< .001
EPTS, n (%)						< .001
0%-20%	2994 (54.8)	2951 (47.5)	477 (41.2)	204 (48)	145 (47.9)	
21%-80%	2019 (37)	2612 (42)	533 (46)	168 (39.5)	122 (40.3)	
81%-100%	477 (8.2)	650 (10.5)	149 (12.9)	53 (12.5)	36 (11.9)	
Induction, n (%)						
Antithymocyte globulin (rabbit)	2660 (59.2)	3313 (62.2)	691 (68)	264 (71)	243 (85)	< .001
alemtuzumab	645 (14.4)	853 (16)	140 (13.8)	43 (11.6)	28 (9.8)	.002
basiliximab	1186 (26.4)	1157 (21.7)	185 (18.2)	65 (17.5)	15 (5.2)	< .001
CNI-based maintenance therapy, n (%)	5320 (97.4)	6041 (97.2)	1132 (97.7)	416 (97.9)	297 (98)	.76
Donor Characteristics						
Warm ischemic time (min), mean ± SD	36.11 ± 19.76	36.00 ± 17.89	36.20 ± 18.3	36.57 ± 18.5	45.27 ± 21.15	< .001
National sharing, n (%)	441 (8)	1805 (28.7)	654 (56)	252 (57.8)	163 (53.3)	< .001
Put on pump, n (%)	1249 (22.9)	2353 (37.9)	482 (41.6)	194 (45.6)	188 (62.3)	< .001
DCD, n (%)	414 (7.5)	807 (12.8)	121 (10.4)	41 (9.4)	39 (12.7)	< .001
KDPI 21%-85%	**CIT 0-12 (n = 13075)**	**CIT 13-24 (n = 19383)**	**CIT 25-30 (n = 3876)**	**CIT 31-36 (n = 1704)**	**CIT ≥ 37 (n = 1480)**	**P**
Recipient Characteristics						
Age (y), mean ± SD	52 ± 14	53 ± 13	53 ± 13	54 ± 13	55 ± 13	< .001
Male, n (%)	7939 (60.7)	11547 (59.6)	2266 (58.5)	1005 (59)	908 (61.4)	.05
African American, n (%)	4158 (31.8)	6598 (34)	1368 (35.3)	606 (35.6)	487 (32.9)	< .001
Latino, n (%)	2044 (15.6)	3428 (17.7)	768 (19.8)	342 (20)	327 (22.1)	< .001
History of CAD, yes (%)	487 (3.7)	700 (3.6)	142 (3.7)	70 (4.1)	70 (4.7)	.23
Previously transplanted, n (%)	1803 (13.8)	3149 (16.2)	664 (17.1)	261 (15.3)	159 (10.7)	< .001
cPRA, mean ± SD	22 ± 35	27 ± 38	28 ± 39	23 ± 37	17 ± 32	< .001
EPTS, n (%)						< .001
0%-20%	3034 (23.5)	3983 (20.8)	769 (20.3)	299 (18.5)	274 (18.9)	
21%-80%	7472 (58)	11214 (58.5)	2206 (58.3)	982 (60.8)	860 (59.2)	
81%-100%	2383 (18.5)	3979 (20.7)	812 (21.4)	335 (20.7)	318 (21.9)	
Induction, n (%)						
Antithymocyte globulin (rabbit)	6687 (61.5)	10599 (63.1)	2281 (67.4)	1073 (72.3)	1058 (75.9)	< .001
Alemtuzumab	1654 (15.2)	3034 (18.1)	592 (17.5)	227 (15.3)	201 (14.4)	< .001
Basiliximab	2527 (23.3)	3155 (18.8)	509 (15.1)	184 (12.4)	135 (9.7)	< .001
CNI-based maintenance therapy, n (%)	12476 (96.8)	18450 (96.2)	3668 (96.9)	1571 (97.2)	1403 (96.6)	.02
Donor Characteristics						
Warm ischemic time (min), mean ± SD	36.18 ± 20.28	37.46 ± 19.15	38.88 ± 19.75	40.32 ± 18.21	43.00 ± 18.88	< .001
National sharing, yes (%)	887 (6.8)	4640 (23.9)	2074 (53.5)	1139 (66.8)	1105 (74.7)	< .001
Put on pump, n (%)	3981 (30.9)	9556 (49.9)	1906 (50.3)	875 (54.2)	808 (55.6)	< .001
DCD, n (%)	1804 (13.8)	4687 (24.2)	895 (23.1)	397 (23.3)	315 (21.3)	<.001

KDPI 86-100%	CIT 0-12 (n = 1146)	CIT 13-24 (n = 2652)	CIT 25-30 (n = 699)	CIT 31-36 (n = 362)	CIT ≥ 37 (n = 249)	P
Recipient Characteristics						
Age (y), mean ± SD	61 ± 11	62 ± 10	62 ± 9	62 ± 10	62 ± 11	.09
Male, n (%)	716 (62.5)	1655 (62.4)	438 (62.7)	223 (61.6)	162 (65.1)	.93
African American, n (%)	350 (30.5)	870 (32.8)	246 (35.2)	115 (31.8)	74 (29.7)	.25
Latino, n (%)	177 (15.4)	453 (17.1)	143 (20.5)	75 (20.7)	60 (24.1)	.002
History of CAD, yes (%)	60 (5.2)	145 (5.5)	43 (6.2)	23 (6.4)	12 (4.8)	.84
Previously transplanted, n (%)	79 (6.9)	160 (6)	35 (5)	20 (5.5)	17 (6.8)	.53
cPRA, mean ± SD	13 ± 26	11 ± 25	10 ± 24	9 ± 24	10 ± 24	.18
EPTS, n (%)						.003
0%-20%	94 (8.4)	135 (5.2)	31 (4.7)	21 (6.2)	16 (6.6)	
21%-80%	611 (54.6)	1425 (55)	393 (59.4)	192 (56.5)	148 (61.2)	
81%-100%	415 (37.1)	1033 (39.8)	238 (36)	127 (37.4)	78 (32.2)	
Induction, n (%)						
Antithymocyte globulin (rabbit)	536 (56.5)	1402 (60.3)	399 (64.7)	203 (62.8)	144 (63.2)	.015
Alemtuzumab	178 (18.8)	423 (18.2)	87 (14.1)	71 (22)	59 (25.9)	.001
Basiliximab	235 (24.8)	500 (21.5)	131 (21.2)	49 (15.2)	25 (11)	< .001
CNI-based maintenance therapy, n (%)	1064 (95)	2467 (95.1)	631 (95.3)	325 (95.6)	277 (93.8)	.89
Donor Characteristics						
Warm ischemic time (min), mean ± SD	37.13 ± 23.06	40.32 ± 21.61	38.46 ± 16.77	43.41 ± 15.52	46.25 ± 26.15	< .001
National sharing, yes (%)	123 (10.7)	855 (32.2)	445 (65)	280 (77.3)	202 (81.1)	< .001
Put on pump, n (%)	405 (36.3)	1354 (52.2)	304 (45.9)	160 (47.1)	133 (55.2)	< .001
DCD, n (%)	80 (7)	385 (14.5)	91 (13)	47 (13)	35 (14.1)	< .001

Abbreviations: CAD, coronary artery disease; CIT, cold ischemic time; CNI, calcineurin inhibitor; cPRA, calculated panel reactive antibody; DCD, donation after circulatory death; EPTS, estimated posttransplant survival; KDPI, Kidney Donor Profile Index.

characteristics for this group were found to be significantly different.

Primary and Secondary Outcomes

Death-censored allograft loss within 1 year was not worse with a rising CIT in the KDPI 0% to 20% or 86% to 100% groups; however, a significant difference was found in the KDPI 21% to 85% group, where for each rise in CIT there was an increased incidence of graft failure ranging from 3% in the CIT 0 to 12 group to 5.1% in the CIT ≥ 37 group (*P* < .001; Fig 1). Similarly, PNF was only found to be significantly different in the KDPI 21% to 85% group, demonstrating a linear rise with increasing CIT (0.8%-1.8%; *P* < .001). Recipient mortality within 1 year posttransplant was found to increase with a rising KDPI (KDPI 0%-20% = 2.2%-3.0%; KDPI 21%-80% = 3.3%-4.3%; KDPI 86%-100% = 5.7%-7%), but within a KDPI group, increase in CIT was not associated with a statistically significant difference in survival (Table 2). Incidence of biopsy-proven rejection at 1 year was different in the KDPI 0% to 20% group (*P* = .02); however, it was not linear with rising CIT. Incidence of biopsy-proven rejection did not differ in the KDPI 21% to 85% or 86% to 100% groups. There were statistically significant differences found in incidence of DGF in each KDPI group (*P* < .001).

Multivariate Analyses

Variables contributing to death-censored allograft loss within 1 year for each KDPI group are shown in Table 3. Use of CNI maintenance therapy was protective with an OR (95% CI) of 0.119 (0.047-0.306), 0.223 (0.146-0.342), and 0.278 (0.097-0.793) for KDPI 0% to 20%, 21% to 85%, and 86% to 100%, respectively. EPTS category had a significant association with KDPI 0% to 20% (*P* < .001), while age was significantly associated with KDPI 21% to 85% (OR = 1.024; 95%CI, 1.017-1.032) and 86% to 100% (OR = 1.028; 95% CI, 1.007-1.048). For KDPI 21% to 85%, induction with

antithymocyte globulin (rabbit) was protective (OR = 0.795; 95%CI, 0.638-0.990) while history of previous transplant was associated with graft loss (OR = 1.376; 95%CI, 1.039-1.882).

Variables contributing to recipient mortality within 1 year for each KDPI group are shown in Table 4. Similar to the allograft loss analysis, use of CNI maintenance therapy was a protective factor with an OR (95% CI) of 0.179 (0.11-0.352), 0.276 (0.21-0.361), and 0.496 (0.272-0.907) for KDPI 0% to 20%, 21% to 85%, and 86% to 100%, respectively. Choice of induction therapy was only found to be significant with KDPI 21% to 85%, where use of antithymocyte globulin (rabbit) was found to be protective (OR = 0.827; 95% CI, 0.701-0.976; *P* = .03). History of previous transplant increased risk of mortality for KDPI 21% to 85% (OR = 1.508; 95%CI, 1.205-1.886), but did not play a significant role for the other KDPI groups. A higher EPTS classification was associated with a higher risk of mortality for KDPI 0% to 20% (*P* = .001) and 21% to 85% (*P* = .004); however, this was not seen with KDPI 86% to 100%.

DISCUSSION

This retrospective review of the SRTR database shows that despite being independently associated with mortality [7,11], there is no compound impact of KDPI and CIT on mortality within 1 year after transplant. This finding is especially important for the KDPI 86% to 100% group, because it indicates that even with marginal donors, longer cold ischemic times should not hinder organ utilization in the absence of other significant contributing factors for appropriate recipients. In other words, the results from this study suggest that CIT alone should not be the basis of declining an organ.

The incidence of biopsy-proven rejection was low and only found to be significantly different with different CIT for the KDPI 0% to 20% group despite differences in DGF in all 3 KDPI groups. Interestingly, the incidence of
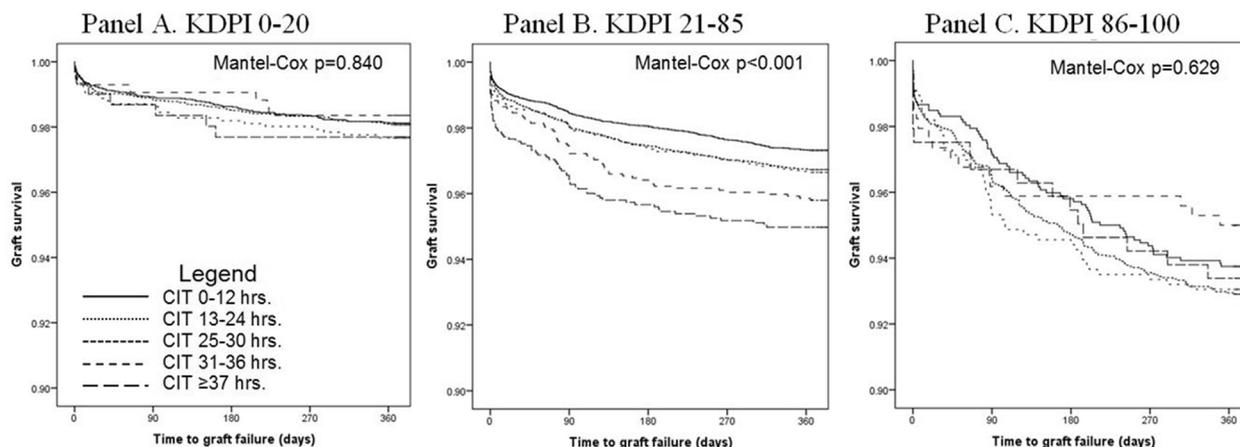

Fig 1. Death-censored allograft loss within 1 year after kidney transplant was not worse with rising CIT in the KDPI 0% to 20% (*P* = .840) or 86% to 100% groups (*P* = .629). For KDPI 21% to 85%, a statistically significant linear rise in allograft loss from 3% in the CIT 0 to 12 group to 5.1% in the CIT ≥ 37 group is seen (*P* < .001). CIT, cold ischemic time; KDPI, Kidney Donor Profile Index.

Table 2. Primary and Secondary Outcomes

KDPI 0%-20%	CIT 0-12 (n = 5501)	CIT 13-24 (n = 6282)	CIT 25-30 (n = 1167)	CIT 31-36 (n = 436)	CIT ≥ 37 (n = 306)	P Value
Primary nonfunction, n (%)	19 (0.3)	14 (0.2)	8 (0.7)	2 (0.5)	2 (0.7)	.1
Incidence of delayed graft function, n (%)	694 (12.6)	1083 (17.2)	240 (20.6)	101 (23.3)	67 (21.9)	< .001
Biopsy-proven rejection within 1 y, n (%)	399 (9.2)	419 (7.9)	65 (6.5)	35 (9.9)	23 (9.3)	.02
Allograft loss within 1 y, n (%)	112 (2)	138 (2.2)	28 (2.4)	9 (2.1)	8 (2.6)	.9
Mortality within 1 y, n (%)	150 (2.7)	136 (2.2)	27 (2.3)	13 (3)	6 (2)	.31

KDPI 21%-85%	CIT 0-12 (n = 13,075)	CIT 13-24 (n = 19,383)	CIT 25-30 (n = 3876)	CIT 31-36 (n = 1704)	CIT ≥ 37 (n = 1480)	P Value
Primary nonfunction, n (%)	99 (0.8)	160 (0.8)	36 (1.0)	27 (1.7)	26 (1.8)	< .001
Incidence of delayed graft function, n (%)	2963 (22.7)	5892 (30.4)	1425 (36.8)	654 (38.4)	571 (38.6)	< .001
Biopsy-proven rejection within 1 y, n (%)	896 (8.4)	1297 (8)	233 (7.3)	104 (7.6)	103 (8.6)	.24
Allograft loss within 1 y, n (%)	390 (3)	680 (3.5)	145 (3.7)	79 (4.6)	76 (5.1)	< .001
Mortality within 1 y, n (%)	437 (3.3)	664 (3.4)	135 (3.5)	74 (4.3)	64 (4.3)	.1

KDPI 86%-100%	CIT 0-12 (n = 1146)	CIT 13-24 (n = 2652)	CIT 25-30 (n = 699)	CIT 31-36 (n = 362)	CIT ≥ 37 (n = 249)	P Value
Primary nonfunction, n (%)	20 (1.8)	70 (2.7)	17 (2.6)	9 (2.6)	6 (2.5)	.56
Incidence of delayed graft function, n (%)	342 (29.8)	976 (36.8)	255 (36.5)	125 (34.5)	82 (32.9)	< .001
Biopsy-proven rejection within 1 y, n (%)	84 (9.2)	211 (9.4)	52 (8.7)	25 (8)	19 (9)	.95
Allograft loss within 1 y, n (%)	80 (7)	203 (7.7)	54 (7.7)	21 (5.8)	19 (7.6)	.73
Mortality within 1 y, n (%)	80 (7)	166 (6.3)	40 (5.7)	23 (6.4)	13 (5.2)	.77

Abbreviations: CIT, cold ischemic time; KDPI, Kidney Donor Profile Index.

Table 3. Death-Censored Allograft Loss Within 1 Year Multivariate Analysis

KDPI 0%-20%	OR (95% CI)	P Value
EPTS	Not applicable	< .001
CNI maintenance therapy	0.119 (0.047-0.306)	< .001

KDPI 21%-85%	OR (95% CI)	P Value
Age	1.024 (1.017-1.032)	< .001
History of previous transplant	1.376 (1.039-1.822)	.03
Antithymocyte globulin (rabbit) induction therapy	0.795 (0.638-0.990)	.04
CNI maintenance therapy	0.223 (0.146-0.342)	< .001

KDPI 86%-100%	OR (95% CI)	P Value
Age	1.028 (1.007-1.048)	.02
CNI maintenance therapy	0.278 (0.097-0.793)	.007

Abbreviations: CI, confidence interval; CNI, calcineurin inhibitor; EPTS, estimated posttransplant survival; KDPI, Kidney Donor Profile Index; OR, odds ratio.

Table 4. Mortality Within 1 Year Multivariate Analysis

KDPI 0%-20%	OR (95% CI)	P Value
Age	1.022 (1.003-1.041)	.03
EPTS 81%-100% vs 0%-20%	4.040 (1.782-9.143)	.001
CNI maintenance therapy	0.197 (0.11-0.352)	< .001
History of CAD	1.795 (1.017-3.17)	.04

KDPI 21%-85%	OR (95% CI)	P Value
Age	1.032 (1.021-1.043)	< .001
Previous transplant	1.508 (1.205-1.886)	< .001
EPTS 81%-100% vs 0%-20%	1.902 (1.231-2.94)	.004
CNI maintenance therapy	0.276 (0.21-0.361)	< .001
Antithymocyte globulin (rabbit) induction therapy	0.827 (0.701-0.976)	.03
Warm ischemic time	1.006 (1.002-1.01)	.001
Male sex	1.249 (1.049-1.487)	.01
DCD	0.77 (0.616-0.963)	.02

KDPI 86%-100%	OR (95% CI)	P Value
Age	1.057 (1.034-1.08)	< .001
CNI maintenance therapy	0.496 (0.272-0.907)	.02
History of CAD	1.772 (1.031-3.043)	.04
Latino	0.546 (0.302-0.987)	.05

Abbreviations: CAD, coronary artery disease; CI, confidence interval; CNI, calcineurin inhibitor; DCD, donation after circulatory death; EPTS, estimated posttransplant survival; KDPI, Kidney Donor Profile Index; OR, odds ratio.

rejection did not rise linearly with increasing CIT; rather, the incidence was higher in CIT 0 to 12 hours and ≥ 37 hours (9.2% and 9.3%), but lower in the CIT 25 to 30 hours group (6.5%). The lack of a significant difference for the other 2 KDPI groups may be a product of greater use of lymphocyte-depleting induction therapy for recipients of kidneys with a longer CIT.

The use of rabbit antithymocyte globulin for organs with a longer CIT is a commonly employed strategy to reduce the incidence of DGF and associated rejection and allograft loss [12–14]. Despite increased use of rabbit antithymocyte globulin in the longer CIT groups, the choice of induction agent was only found to be protective against mortality and allograft loss for the KDPI 21% to 85% group. However, use of a CNI-based maintenance regimen was found to be protective against mortality for all 3 KDPI groups and for allograft loss in KDPI 86% to 100%. This may be indicative of patient disease impacting choice of immunosuppression, but nonetheless should be investigated in future studies.

The linear rise in the incidence of DGF with increased CIT is expected and has been well described in previous studies [15,16]. Despite this rise, however, a similar linear rise for allograft loss and mortality are not consistently seen across all KDPI groups. This suggests the previously described deleterious effect [17–19]. of DGF is multifactorial and not exclusively associated with prolonged CIT, which is consistent with prior studies [20,21]. Rates of allograft loss were low in this cohort, with higher incidence in higher KDPI groups as expected [6]. The only group in which allograft loss was found to significantly increase with a rising CIT was the KDPI 21% to 85% group, although the increase was relatively small (3.0%-5.1%). This finding may be explained by the statistically significant, linear difference in PNF found exclusively in this KDPI group.

Study Limitations

The limitations of this study are largely due to its retrospective design and inherent limitations of the SRTR database. Assessment of 3- or 5-year outcomes would be beneficial; however, given the transplant-era inclusion criteria, these data are largely unavailable at this time. Due to the temporal association between KDPI category and allograft loss, long-term outcomes represent a necessary extension for research in this area when they become available. Additionally, it would have been beneficial to evaluate transplant center volume to see what effect, if any, this has on mortality given the complex management of high-KDPI organs with longer CIT. However, these data are not readily attainable through the SRTR database. Given the nature of the database, it was not possible for us to assess immunosuppression dosing and more precise changes in immunosuppression over time.

The retrospective study design is inherently susceptible to selection bias. This bias is demonstrated by the lower number of kidneys with a CIT of ≥ 25 hours relative to the number with a CIT of ≤ 24 hours in each KDPI group. Therefore, the results of this study do not support utilization of all high-KDPI organs, but rather clinicians should evaluate the donor characteristics as a whole and not simply discard the organ based on a high CIT alone. Despite the limitations of the study design, a strength of utilizing the SRTR database is the volume of records that can be evaluated in this otherwise niche population.

CONCLUSIONS

In conclusion, there is no compound effect of CIT on mortality for kidneys of any KDPI group. Specifically for kidneys with a KDPI of 86% to 100%, there is no compound

effect for CIT on mortality, allograft loss, PNF, or biopsy-proven rejection at 1 year despite differences in DGF. In the setting of an organ shortage, optimization of organ utilization is prudent. Further studies are needed to elucidate the contributing role of DGF in graft and patient loss beyond just the rise in CIT. The results of this study indicate that DGF needs to be expected and managed rather than just avoided by refusal of organs with high CIT.

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