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Beyond Graft Survivl: A National Cohort Study Quantifying the Impact of Increasing Kidney Donor Profile Index on Recipient Outcomes 1 Year Post-transplantation

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Background. The reporting of a locally validated kidney donor profile index (KDPI) began in Australia in 2016. Across diverse populations, KDPI has demonstrated utility in predicting allograft survival and function. A metric that incorporates both elements may provide a more comprehensive picture of suboptimal recipient outcomes. **Methods.** A retrospective cohort study of adult kidney transplant recipients in Australia (January 2009 to December 2014) was conducted. Conventional recipient outcomes and a composite measure of suboptimal outcome (1-y allograft failure or estimated glomerular filtration rate [eGFR] <30 mL/min) were evaluated across KDPI intervals (KDPI quintiles and 5-point increments in the KDPI 81–100 cohort). The impact of increasing KDPI on allograft function (1-y eGFR) and a suboptimal outcome was explored using multivariable regression models, adjusting for potential confounding factors. **Results.** In 2923 donor kidneys eligible for analysis, median KDPI was 54 (interquartile range [IQR], 31–77), and Kidney Donor Risk Index was 1.39 (IQR, 1.03–1.67). The median 1-y eGFR was 52.74 mL/min (IQR, 40.79–66.41 mL/min). Compared with the first quintile reference group, progressive reductions in eGFR were observed with increasing KDPI and were maximal in the fifth quintile (adjusted β-coefficient: –27.43 mL/min; 95% confidence interval, –29.44 to –25.42; $P < 0.001$). A suboptimal outcome was observed in 359 recipients (12.3%). The adjusted odds for this outcome increased across quintiles from a baseline of odds ratio of 1.00 (first quintile) to odds ratio of 11.68 (95% confidence interval, 6.33-21.54, $P < 0.001$) in the fifth quintile cohort. **Conclusions.** Increases in donor KDPI were associated with higher probabilities of a suboptimal outcome and poorer baseline allograft function, particularly in the KDPI > 80 cohort. These findings may inform pretransplant discussions with potential recipients of high-KDPI allografts.

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Introduction

Renal transplantation is considered the optimal treatment modality for many individuals with end-stage renal failure. Access to transplantation is limited by the availability of appropriate donor organs and remains a major constraint. From 2009 to 2019, Australian organ donation rates increased from 11.3 to 21.6 donors per million population.[1] This growth is partly attributable to changes in legislation permitting organ donation after circulatory death (DCD) and an increasing acceptance of older and comorbid donors—trends observed in many transplant jurisdictions.[2,3]

With increasing variability in donor demographics, comorbidities, and perimortem physiology, the introduction of the Kidney Donor Risk Index (KDRI), a metric derived from ten donor variables associated with allograft failure, provided transplant physicians in the United States with some clarity when assessing the relative quality of donor kidneys.[4] The utility of the KDRI, and its practical application, the Kidney Donor Profile Index (KDPI), was acknowledged through its integration into the US Kidney Allocation System in 2014 and is reflected in its use as a comparator across study populations in the literature.

Clinically relevant variations are observed in the distribution of US-based KDRI/KDPI values against non-US study

populations, reflecting broad variability in the characteristics of donor pools across regions.[3] Authors of European studies advocate for the development of KDRI algorithms tailored to local demographics, retrieval practices, and outcome data.[5,6] In Australia a local KDRI/KDPI model (a derivation of the US model via exclusion of hepatitis C status and ethnicity) was validated in 2015,[7] reported alongside organ offers from late 2016, and incorporated in allocation algorithms in April 2020.

Although KDRI/KDPI algorithms are based on the cumulative risk of allograft failure, multiple authors have quantified the intuitive association between increasing KDPI and poorer allograft function.[5,8] Pruett et al[9] argue that failure to achieve sufficient function from transplantation (defined as estimated glomerular filtration rate [eGFR] >30 mL/min 1 y post-transplantation) may negate survival benefits to recipients over remaining on dialysis. Beyond this, impaired allograft function (1-y eGFR <30 mL/min) has been associated with other important recipient outcomes, including increased rates of hospitalization, post-transplant interventions, infection and cardiovascular morbidity and mortality.[10-12]

From this perspective, the predominant reporting of hard outcomes, such as recipient and allograft survival, masks other outcomes that are important for recipients. In a review from the transplant division of the US National Surgical Quality Improvement Program, Amara et al[13] noted that reporting allograft survival alone "fails to capture the impact of poorly functioning grafts and overestimates the success of renal transplant" and proposed a composite outcome measure incorporating recipient death, allograft failure, and poor function.

The study aimed to expand the evidence-base for a range of transplantation outcomes referenced to KDPI, with a specific focus on high-KDPI allografts, to inform pretransplant discussions with potential recipients. In our Australian renal transplant population, we aim to (1) examine and compare recipient outcomes across increasing KDPI strata through the lens of accepted outcome measures and a composite measure of suboptimal outcome—defined as allograft failure (death-censored) or eGFR <30 mL/min 1 y post-transplantation and (2) determine the magnitude of the impact of increasing KDPI on both graft function (eGFR 1 y post-transplantation) and suboptimal outcome, adjusting for clinically relevant donor, recipient, and immunological factors.

MATERIALS AND METHODS

We performed a retrospective cohort study considering all deceased donor kidneys transplanted into adult recipients in Australia from January 2009 to December 2014. This time period was chosen to reflect contemporary donor demographics while avoiding a potential KDPI-labeling bias. Matched deidentified data were accessed from the Australian and New Zealand Dialysis and Transplant Registry and the Australian and New Zealand Organ Donor Registry. Donor-recipient pairs were excluded from analysis if (1) the procedure occurred as multiorgan, en bloc, or dual kidney transplant, (2) there was insufficient data to calculate donor KDRI, (3) recipients were lost to follow-up within 1 y of transplantation, or (4) 1 y eGFR was not recorded. Donation after circulatory death was practiced for the entirety of the study period, machine perfusion was not available, and all recipients had access to medicare-funded immunosuppression.

For each donor, KDRI was calculated retrospectively according to the Australian model, and KDPI was assigned with reference to the Australian donor kidney population from 2016 to 2018 (first available reference period).[14,15] KDPI risk strata were designated as follows: first quintile (lowest risk): KDPI 1–20; second quintile: KDPI 21–40; third quintile: KDPI 41–60; fourth quintile: KDPI 61–80; and fifth quintile (highest risk): 81–100. To investigate the outcome of transplants with the highest-risk allografts in finer detail, the fifth quintile was subdivided at KDPI 5-point increments.

Data were collected across donor and recipient demographics, comorbid conditions, immunological matching parameters, pre-terminal donor management, and post-procurement events (Table 1; definitions, **Table S1, S DC**, http://links.lww.com/

TABLE 1.

Variables examined in this study (excluding those directly involved in the calculation of KDRI)

Variable	Management	Reported Units
Outcome variables		
eGFR	Continuous	mL/min/1.73 m^2
Suboptimal outcome	Binary	Yes = 1
Donor factors		
Donor gender	Binary	Male = 1
Donor smoking history	Binary	Yes = 1
Donor CPR	Binary	Yes = 1
Donor inotropes	Binary	Yes = 1
Donor oliguria	Binary	Yes = 1
Procurement factors		
Transplant out of region[a]	Binary	Yes = 1
Procurement biopsy	Binary	Yes = 1
Ischemic time	Binary	Ischemic time >12 h = 1
Immunological factors		
HLA mismatch	Continuous	Total number HLA mismatches (0–6)
PRA	Continuous	Maximum recorded cPRA (0–100)
Recipient factors		
Recipient gender	Binary	Male = 1
Recipient age	Continuous	Years
Dialysis years	Continuous	Years
<1 y	Binary	Yes = 1
1–10 y	Binary	Yes = 1
>10 y	Binary	Yes = 1
Previous transplant/s	Binary	Yes = 1
Etiology renal disease	Binary	
High-risk GN		Yes = 1
Recipient BMI	Continuous	kg/m^2
<25 kg/m^2	Binary	Yes = 1
25–30 kg/m^2	Binary	Yes = 1
>30 kg/m^2	Binary	Yes = 1
Recipient smoking history	Binary	Yes = 1
CAD	Binary	Yes = 1
PVD	Binary	Yes = 1
CVA	Binary	Yes = 1
Recipient diabetes		
T2DM	Binary	Yes = 1
T1DM	Binary	Yes = 1

[a]Transplant regions in Australia: (1) Queensland, (2) New South Wales/Australian Capital Territory, (3) Victoria/Tasmania, (4) South Australia/Northern Territory, and (5) Western Australia.
BMI, body mass index; CAD, coronary artery disease; CPR, cardiopulmonary resuscitation; cPRA, calculated panel reactive antibody; CVA, cerebrovascular accident; eGFR, estimated glomerular filtration rate; GN, glomerulonephropathy; KDRI, Kidney Donor Risk Index; PRA, panel reactive antibody; PVD, peripheral vascular disease; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

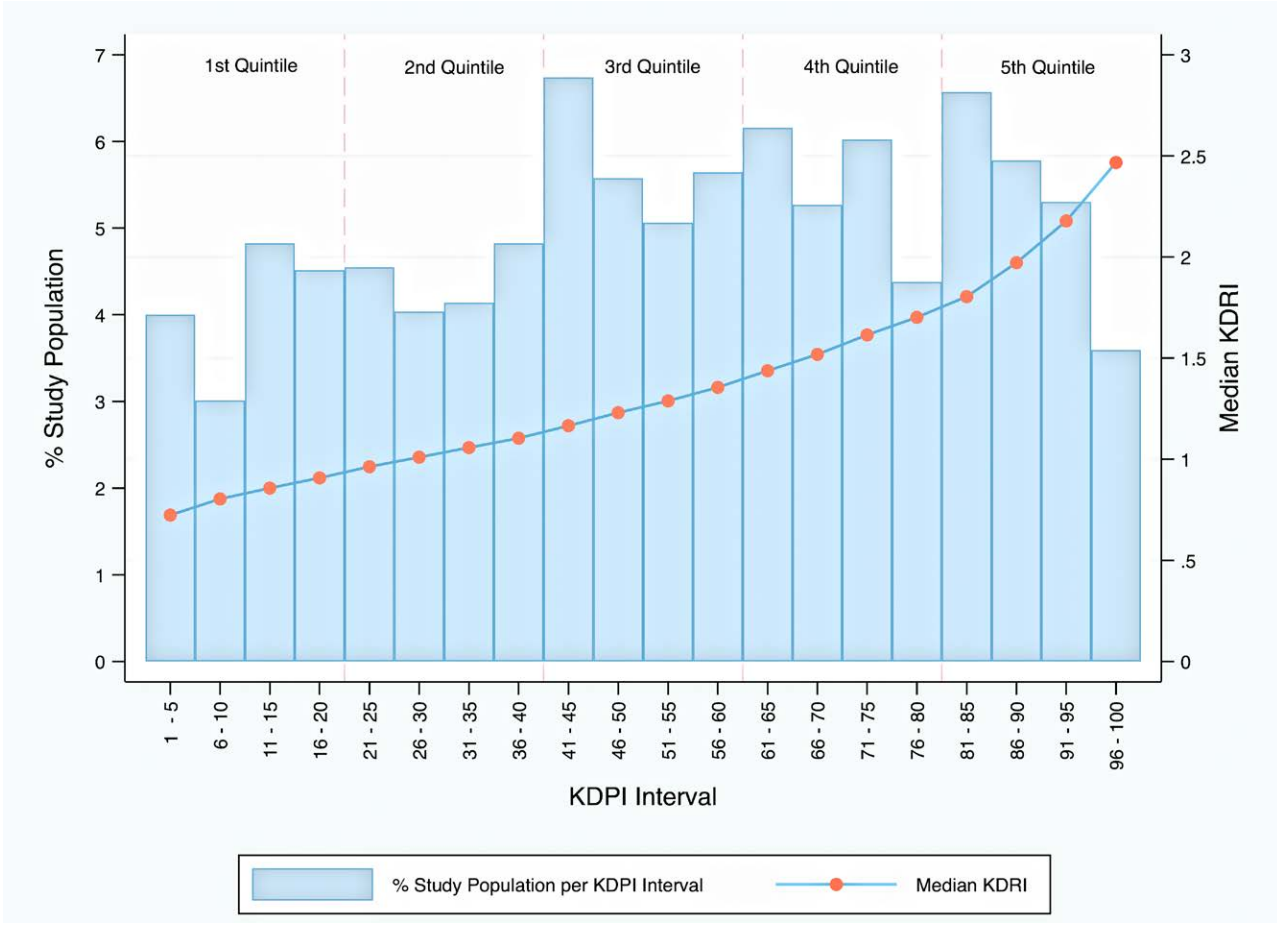

FIGURE 1. Distribution of the study population and median KDRI according to KDPI quintiles and KDPI 5-point increments. KDPI, Kidney Donor Profile Index; KDRI, Kidney Donor Risk Index.

TXD/A409). In addition to previous associations with graft outcomes, these variables were chosen to reflect data reasonably available or approximated before transplantation. Study variables were compared across KDPI cohorts (assuming a non-normal distribution) using the Kruskal-Wallis test by ranks for continuous variables, and Pearson chi-squared test for categorical variables. Differences were considered statistically significant at $P < 0.05$.

The primary outcomes in this study were (1) recipient serum eGFR (Modification of Diet in Renal Disease [relating to the equation used to calculate eGFR]) measured at 1 y post-transplant (1-y eGFR) and (2) suboptimal outcome, defined as death-censored graft failure or eGFR <30 mL/min at the time point 1 y post-transplant. Allograft failure was considered to have occurred if recipients returned to dialysis, or recorded 1-y eGFR <10 mL/min. Across KDPI quintiles, 1-y eGFR was reported as both median eGFR and proportions of recipients falling into each category of renal impairment defined by the Kidney Disease Improving Global Outcomes chronic kidney disease (CKD) classification (2009).[16]

Secondary outcome measures in this study were allograft failure and recipient death at 1 and 5 y post-transplantation. Event rates were reported for delayed graft function and allograft rejection (treated episodes) within 1 y of transplantation. Outcome measures were reported for the entire study cohort, each KDPI quintile, and across 5-point increments in the fifth quintile.

Multivariable regression analyses were performed across the KDPI 1-100 population and in the fifth quintile cohort to determine the effect of increasing KDPI on 1-y eGFR (linear regression) and suboptimal outcome (logistic regression). The effect of increasing KDPI (quintile or 5-point increment) was documented against a baseline comparator group (first quintile or KDPI 81–85) and expressed as reductions in 1-y eGFR (mL/min) or odds ratio (OR; odds of suboptimal outcome) in the nominated group compared to the baseline group. Clinically relevant donor, recipient, immunological, and procurement variables identified as having a potential association with an outcome on univariate analysis ($P < 0.20$) were included in the multivariable analysis for the outcome. Multivariable regression analyses were performed using backward stepwise elimination (exclusion $P > 0.05$). Interaction terms were created and tested for clinically relevant variables. Regression diagnostic procedures were used to identify and examine outliers and high-leverage data points, define nonlinear relationships, and correct variable misspecifications. In each analysis, initial models were constructed using a continuous KDPI variable and compared to a model restricted to the KDPI interval variable (quintiles or 5-point increases) via likelihood ratio testing. Within the logistic regression models, sufficient power was maintained with event-to-variable ratios >10.

This study was approved by the Melbourne Health Human Research Ethics Committee (MH2020.170). Statistical analyses were conducted using Stata 16 MP software (StataCorp, College Station, TX).

TABLE 2.

Distribution of donor variables contributing to the KDRI calculation across KDPI quintiles in the total study population, and 5-point intervals in the fifth quintile cohort.

		Total study population					Fifth quintile cohort			
n	Total 2923	First quintile 478	Second quintile 513	Third quintile 673	Fourth quintile 638	Fifth quintile 621	KDPI 81–85 192	KDPI 86–90 169	KDPI 91–95 155	KDPI 96–100 105
KDRI										
Range	0.62–3.19	0.62–0.93	0.93–1.13	1.13–1.40	1.40–1.74	1.75–3.19	1.75–1.88	1.89–2.06	2.07–2.30	2.31–3.19
Median (IQR)	1.30 (1.03–1.67)	0.84 (0.77–0.89)	1.04 (0.99–1.08)	1.25 (1.19–1.32)	1.55 (1.48–1.64)	2.01 (1.85–2.22)	1.80 (1.77–1.84)	1.97 (1.93–2.01)	2.18 (2.11–2.24)	2.47 (2.38–2.68)
Donor age (y) (IQR)	50 (37–60)	23 (19–29)	39 (30–44)	49 (44–52)	57 (53–61)	66 (62–69)	64 (60–65)	65 (61–67)	68 (64–70)	72 (68–76)
Height (cm) (IQR)	171 (164–179)	177 (170–182)	172 (165–180)	171 (165–179)	170 (163–177)	168 (162–174)	170 (162–176)	168 (160–174)	170 (162–173)	168 (162–170)
Weight (kg) (IQR)	80 (68–90)	75 (68–85)	80 (65–90)	80 (68–92)	80 (70–90)	80 (69–90)	80 (65–90)	80 (70–90)	75 (68–85)	80 (70–87)
Diabetes (%)	185 (6)	3 (0.6)	20 (4)	40 (6)	45 (7)	77 (12)	10 (5)	20 (12)	21 (14)	26 (25)
Hypertension (%)	755 (26)	2 (0.4)	13 (3)	117 (17)	229 (36)	394 (63)	90 (47)	104 (62)	109 (70)	91 (87)
ICH (%)	1428 (49)	45 (9)	174 (34)	343 (51)	407 (64)	459 (74)	141 (73)	116 (69)	125 (81)	77 (73)
DCD (%)	732 (25)	89 (19)	104 (20)	190 (28)	188 (29)	161 (26)	63 (33)	47 (28)	36 (23)	15 (14)
Terminal creatinine (μmol/L) (IQR)	71 (56–96)	68 (56–86)	70 (55–96)	69 (54–96)	72 (57–97)	74 (59–102)	69 (52–83)	73 (57–101)	80 (65–115)	89 (66–121)

DCD, donation after circulatory death; ICH, Intracranial hemorrhage (cause of death); IQR, interquartile range; KDPI, Kidney Donor Profile Index; KDRI, Kidney Donor Risk Index.

RESULTS

Of the 3095 adult recipients of deceased donor kidneys identified within the study period, 37 were excluded because of insufficient data for KDRI calculations, 72 were excluded as recipients of dual or en bloc transplants, and 57 were excluded because the 1-y eGFR was not available. Six recipients were lost to follow-up within 12 mo of transplantation, leaving 2923 donor-recipient pairs (94.4%) eligible for analysis.

Study Population

In this donor population, the median KDPI was 54 (interquartile range, 31–77), and median KDRI was 1.39 (interquartile range, 1.03–1.67). A KDRI of 1.00 and a KDRI of 2.00 mapped to a KDPIs of 27 and 89, respectively (Figure 1). An increase in the gradient of a line plotting the median KDRI against KDPI is observed from the KDPI 81–85 mark, indicating a larger increase in donor risk per KDPI interval from this point.

The summary statistics for the donor variables contributing to KDRI calculations are presented in Table 2. The median donor age increased progressively with KDPI, coarsely dictating KDPI quintile. Differences in the proportions of donors with hypertension, stroke, and diabetes were progressive and marked from the first to fifth quintiles, whereas differences between quintiles for other KDRI component variables (DCD pathway, height, weight, and terminal creatinine) were less consistent. Similar trends continued into the fifth quintile, with increasing terminal creatinine and a decreasing proportion of DCD donors observed across this cohort.

The summary statistics for donor, recipient, procurement, and immunological matching variables not included in the calculation of KDRI are presented in **Tables S2 and S2, SDC**, http://links.lww.com/TXD/A409. Consistent and clinically relevant differences across quintiles were noted in the proportion of male donors (decrease across quintiles), incidence of donor cardiopulmonary resuscitation (decrease), procurement biopsy (increase), median recipient age (increase), duration of dialysis (increase), and incidence of coronary artery disease and type 2 diabetes mellitus in recipients (increase). In the fifth quintile study population, the only significant trend was an increase in the incidence of procurement biopsies.

The proportion of missing data across the study variables was greatest for panel reactive antibody (4.5%), ischemic time (3.7%), and recipient body mass index (3.0%). As a review of missing data revealed no discernible patterns or relationships with outcomes, regression analyses were carried performed as complete case analyses.

Primary Outcomes

Graft Function—1-Y eGFR

The median 1-y eGFR for recipients with a functioning graft was 52.74 mL/min, which decreased with each increment in KDPI quintile (Figure 2, Table 3). Figures 3A and 3B and Table 4 demonstrate the distribution of 1-y eGFR across KDPI quintiles and 5-point increments (fifth quintile allografts). The difference in the proportions of recipients with stage II CKD (mild impairment) and stage IV CKD (severely decreased renal function) was marked across quintiles. Across the fifth quintile, a notable increase in the

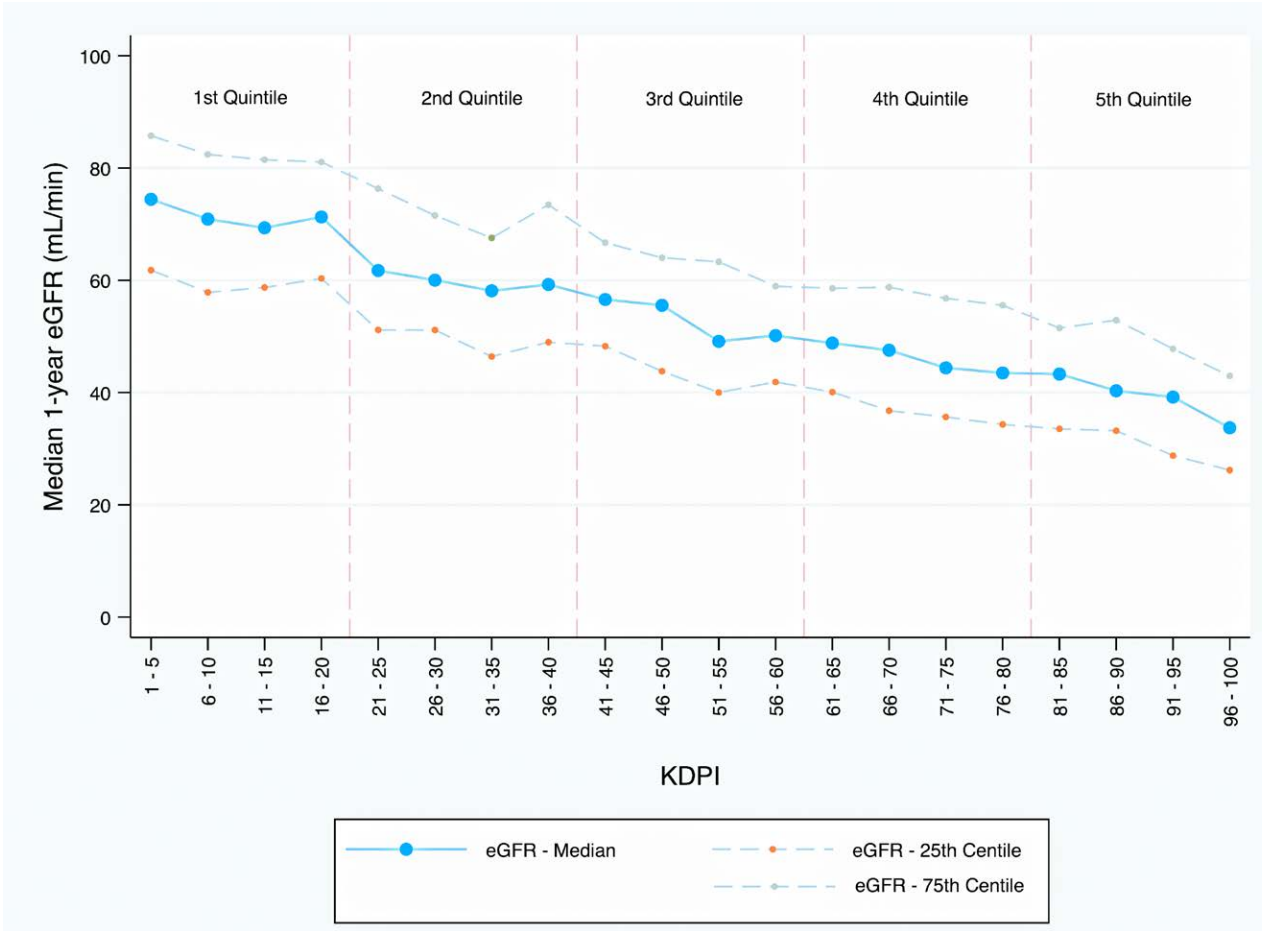

FIGURE 2. Median 1-y eGFR for functioning allografts per KDPI quintile and 5-point increments. eGFR, estimated glomerular filtration rate; KDPI, Kidney Donor Profile Index.

proportion of recipients with stage IV renal impairment was observed.

Univariate linear regression analysis (dependent variable 1-y eGFR) revealed a strong negative correlation between the increasing KDPI quintile and 1-y eGFR when comparing recipients in the second to fifth quintiles (β-coefficients: −9.48 to −28.86 mL/min) against the first quintile group (constant 70.24 mL/min) (**Table S4, SDC,** http://links.lww.com/TXD/A409). An initial multivariable linear regression model was constructed expressing KDPI as a continuous variable and carrying forward variables identified as potential confounders on univariate analysis (Table 5). Regression diagnostics revealed a normal distribution of residuals. There was no evidence of multicollinearity among the included variables or of clinically or statistically significant interactions between variables. High-eGFR data points had significant leverage and were influential. Thus, population eGFR values were capped at 90 mL/min.

Within the final model, each single-point increase in KDPI resulted in a 0.33 mL/min decrease in eGFR. A nested model restricted to KDPI quintiles did not differ from the initial continuous KDPI model (likelihood ratio test χ^2 [3] = −31.95, P = 1.00). Within the restricted model, adjusted decreases in eGFR across KDPI quintiles ranged from 8.76 mL/min (second quintile) to 27.43 mL/min (fifth quintile), based on a first quintile (constant) eGFR of 70.35 mL/min (Table 5). The final models with KDPI expressed as a continuous or categorical (quintile) variable (R^2 = 0.31), accounted for more outcome variability than KDPI (R^2 = 0.29, β-coefficient, −0.36 mL/min/KDPI) and donor age (R^2 = 0.25, β-coefficient −0.56 mL/min/y) alone.

Increases in KDPI across the fifth quintile cohort were also associated with a decrease in 1-y eGFR on univariate analysis. In this smaller population, a statistically sound multivariable linear regression model based on clinically relevant variables could not be constructed, and we reported the unadjusted effect of increasing KDPI in this quintile (Table 5).

Suboptimal 1-Year Outcome: Graft Failure or eGFR <30 mL/min

One year post-transplant, 359 recipients (12.3% of the study population) had either a failed allograft or serum eGFR <30 mL/min. The incidence of this suboptimal outcome increased progressively across KDPI quintiles, reaching 41.6% in allografts with KDPI >95 (Table 3). Using first quintile recipients as a comparator group, univariate logistic regression suggested a strong correlation between increasing KDPI quintile and suboptimal outcome, ranging from OR, 2.56 (95% confidence interval [CI], 1.33-4.91; P = 0.005) in the second quintile to OR, 12.96 (95% CI, 7.26-23.15; P < 0.001) in the fifth quintile (**Table S4, SDC,** http://links.lww.com/TXD/A409).

TABLE 3.

One-Year primary outcomes across KDPI quintiles in the total study population, and 5-point intervals in the fifth quintile cohort

		Total study population					Fifth quintile cohort			
n	Total 2923	First quintile 478	Second quintile 513	Third Quintile 673	Fourth Quintile 638	Fifth Quintile 621	KDPI 81–85 192	KDPI 86–90 169	KDPI 91–95 155	KDPI 96–100 105
Median eGFR (mL/min) (IQR)	52.74 (40.79 - 66.41)	71.22 (60.16 - 83.32)	59.88 (49.79 - 71.59)	52.85 (43.67 - 64.16)	46.74 (37.05 - 57.32)	39.68 (31.34 - 49.51)	43.30 (33.52 - 51.50)	40.31 (33.19 - 52.89)	39.20 (28.77 - 47.79)	33.72 (26.18 - 42.96)
Δ in eGFR[a] (95% CI)		0	−8.76 (−10.82 to −6.70)	−15.17 (−17.11 to −12.22)	−20.79 (−22.78 to −18.80)	−27.43 (−29.44 to −25.42)	0	−0.74 (−3.77 to 2.29)	−4.71 (−7.81 to −1.61)	−8.40 (−11.94 to −4.85)
P			<0.001	<0.001	<0.001	<0.001		0.63	0.003	<0.001
Suboptimal outcome (%)	359 (12)	13 (3)	35 (7)	65 (10)	81 (13)	165 (27)	29 (15)	43 (25)	49 (32)	44 (42)
Allograft failed	111 (4)	9 (2)	17 (3)	21 (3)	22 (3)	42 (7)	7 (4)	15 (9)	10 (6)	10 (10)
eGFR <30 mL/min	248 (8)	4 (0.8)	18 (4)	44 (7)	59 (9)	123 (20)	22 (11)	28 (17)	39 (25)	34 (32)
Adjusted ORs (95% CI)		1.00	2.33 (1.17 - 461)	3.36 (1.77 - 6.37)	4.57 (2.43 - 8.61)	11.68 (6.33 - 21.54)	1.00	1.60 (0.92 - 2.78)	2.60 (1.51 - 4.49)	4.66 (2.60 - 8.36)
P			0.02	<0.001	<0.001	<0.001		0.10	0.001	<0.001
Adjusted probability[b] (95% CI)	0.09 (0.08 - 0.11)	0.03 (0.01 - 0.04)	0.06 (0.04 - 0.08)	0.09 (0.06 - 0.11)	0.11 (0.09 - 0.14)	0.25 (0.21 - 0.28)	0.15 (0.10 - 0.20)	0.22 (0.15 - 0.28)	0.31 (0.23 - 0.39)	0.45 (0.34 - 0.55)
P	<0.001	0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

[a]B-coefficients calculated using data from patients with functioning allografts. Differences in eGFR are referenced to allografts from first quintile (KDPI 1–20) donors, and in the fifth quintile cohort, referenced to allografts from KDPI 81–85 donors.
[b]Adjusted marginal probabilities of multivariable regression model with covariates held at mean values.
CI, confidence interval; eGFR, estimated glomerular filtration rate; IQR, interquartile range; KDPI, Kidney Donor Profile Index; OR, odds ratio.

Inclusion of potential confounders in a multivariable logistic regression model for suboptimal outcome resulted in slight downward adjustment of ORs for each KDPI quintile (Table 6). The predicted probability of a suboptimal outcome using this model (covariates at means) ranged from 0.03 in the first quintile to 0.25 in the fifth quintile. This model was built using a continuous KDPI variable requiring a nonlinear transformation (KDPI ^ 2.99) and an interaction term (type 2 diabetes mellitus and peripheral vascular disease). High-leverage data points, typically observed in recipients with high panel reactive antibody and longer dialysis duration, had low residual values, and were not influential. Exploration of the high residual values observed in recipients with suboptimal outcome and low predicted probability often identified an association with post-transplant events (surgical complications or allograft rejection). The final model had a moderate discriminatory capacity (area under curve = 0.75) and fit the data well (Hosmer-Lemeshow Test χ^2 [8] 8.38, $P = 0.40$). A nested model restricted to KDPI quintiles did not significantly differ from the continuous KDPI model (likelihood ratio test χ^2 [3] = −21.44, $P = 1.00$).

Within the fifth quintile, associations between rising KDPI and an increasing incidence of suboptimal outcome remained strong, although nonsignificant in the KDPI 86–90 interval. Slight reductions in these ORs were observed after adjustment using multivariable logistic regression (Table 6).

Secondary Outcomes

Delayed graft function was observed in 915 recipients (32.0%), and 688 recipients (23.5%) were treated for allograft rejection in the first year after transplantation (Table 7). When compared to allografts from donors with KDPI <80, fifth quintile allografts were associated with increased odds of delayed graft function (unadjusted OR, 1.69; 95% CI, 1.40-2.04; $P < 0.001$) and rejection (unadjusted OR, 1.37; 95% CI, 1.11-1.68; $P = 0.002$).

In this study, 111 recipients (3.8%) had documented allograft failure 1 y post-transplant. The odds of this outcome were higher in the fifth quintile than in the rest of the population (unadjusted OR, 2.35, 95% CI, 1.54-3.54, $P < 0.001$). The incidence of death within 1 y of transplantation was 2.5% (74 recipients), without notable trends across quintiles.

In recipients with a functioning allograft and 1-y eGFR <30 mL/min (248 recipients, 8.5% of the study population), 64 (25.8%) progressed to allograft failure and 37 recipients (14.9%) died within 5 y of transplantation (3 lost to follow-up, 5-y eGFR not recorded for 27 recipients). Compared with recipients with 1-y eGFR >30 mL/min (2504 recipients, 4.2% allograft failure, 7.2% deceased at 5 y), those with 1-y eGFR <30 mL/min had higher odds of allograft failure (unadjusted OR, 8.16; 95% CI, 5.67-11.67; $P < 0.001$) and death (unadjusted OR, 2.27; 95% CI, 1.50-3.35; $P < 0.001$) at 5 y post-transplant.

DISCUSSION

The kidney donor profile index provides a standardized means of communicating allograft quality. Although multiple studies across diverse populations have documented the relationship between KDPI and allograft survival, few have

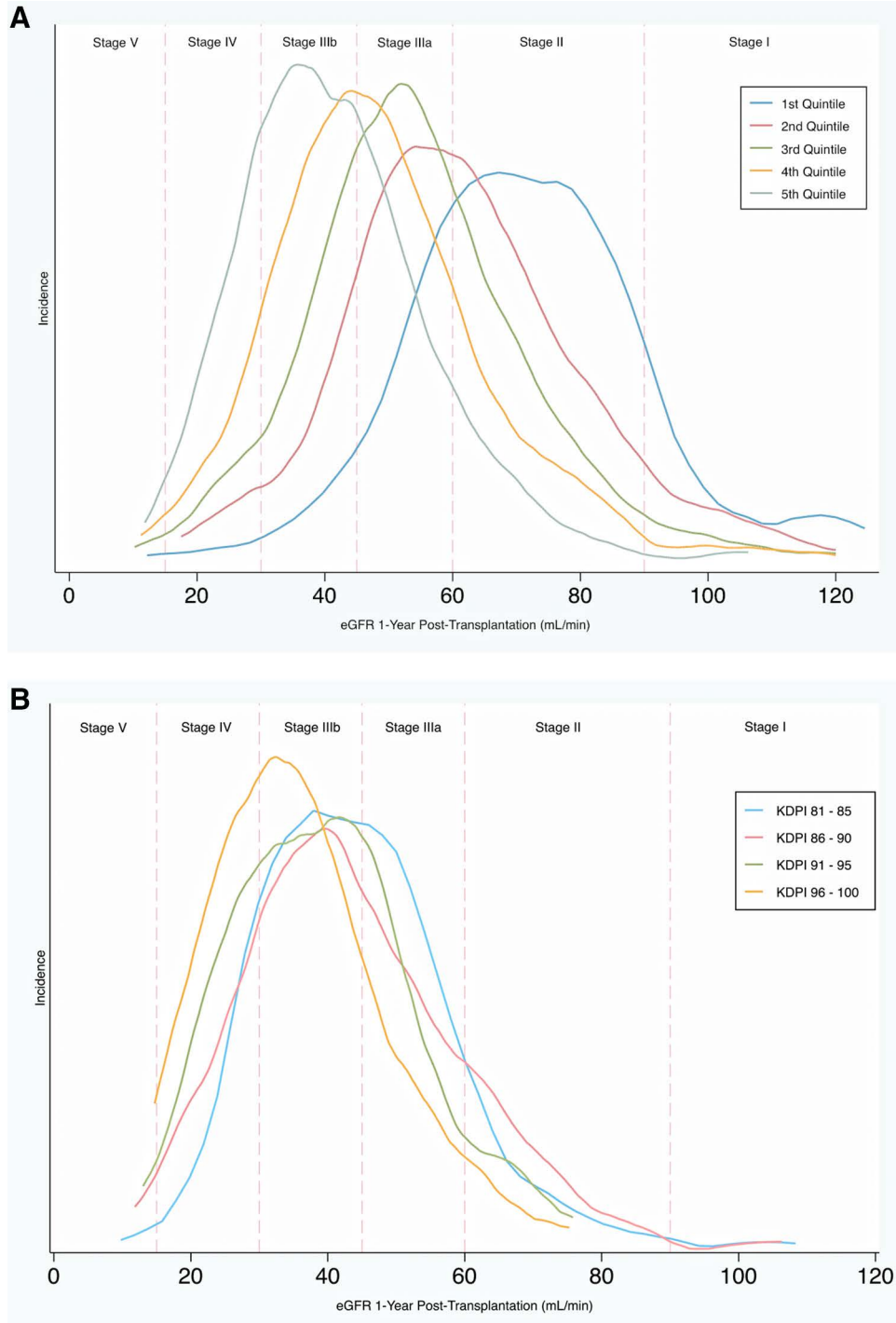

FIGURE 3. Distribution of 1-y eGFR according to KDIGO Classifcation of Chronic Kidney Disease. Incidence across (A) KDPI quintiles and (B) 5-point increments in KDPI >80 allografts. KDIGO CKD stages: stage I—eGFR >90 mL/min; stage II—eGFR 60-90 mL/min; stage IIIa—eGFR 45–60 mL/min; stage IIIb—eGFR 30–45 mL/min; stage IV—eGFR 15–30 mL/min; stage V—eGFR <15 mL/min. CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease Improving Global Outcomes; KDPI, Kidney Donor Profile Index.

reported on the relationship between KDPI and allograft function. This study established a consistent and clinically relevant relationship between increasing donor KDPI and poorer allograft function (1-y eGFR) in our population. Using data from a national transplant registry, this study considers the composite outcome of allograft failure and poor function, identifying significant associations between increasing KDPI and the odds of this suboptimal outcome.

A few single-center European studies have reported 1-y functional outcomes according to KDPI, although the reference intervals differ. German studies with comparable donor demographics (noting an absence of DCD donors), report similar median 1-y eGFR values over equivalent KDPI ranges (KDPI < 20: eGFR 65.8 mL/min, KDPI < 35: eGFR 65 mL/min, KDPI > 85: eGFR 39 mL/min).[5,17] In Dahmen 580-patient cohort, multivariable regression analyses

TABLE 4.
Distribution of eGFR according to KDIGO 2009 CKD classification, per KDPI quintile and 5-point intervals in the fifth quintile cohort

		Total study population					Fifth quintile cohort			
eGFR n	Total 2923	First quintile 478	Second quintile 513	Third quintile 673	Fourth quintile 638	Fifth quintile 621	KDPI 81–85 192	KDPI 86–90 169	KDPI 91–95 155	KDPI 96–100 105
Functioning graft (%)	2752 (94)	460 (96)	484 (94)	642 (95)	602 (94)	564 (91)	180 (94)	153 (91)	140 (90)	91 (87)
CKD stage (%)										
I: >90 mL/min	120 (4)	56 (12)	33 (6)	19 (3)	10 (2)	2 (0.3)	1 (0.5)	1 (0.6)	0 (0)	0 (0)
II: 60–90 mL/min	855 (29)	291 (61)	208 (41)	184 (27)	117 (18)	55 (9)	17 (9)	21 (12)	12 (8)	5 (5)
IIIa: 45–60 mL/min	875 (30)	90 (19)	171 (33)	261 (39)	204 (32)	149 (24)	62 (32)	41 (24)	32 (21)	14 (13)
IIIb: 30–45 mL/min	654 (22)	19 (4)	54 (11)	134 (20)	212 (33)	235 (38)	78 (41)	62 (37)	57 (37)	38 (36)
IV: 15–30 mL/min	234 (8)	4 (1)	18 (4)	41 (6)	54 (8)	117 (19)	21 (11)	26 (15)	37 (24)	33 (31)
V: <15 mL/min	14 (0.4)	0 (0)	0 (0)	3 (0.4)	5 (0.8)	6 (1)	1 (0.5)	2 (1)	2 (1)	1 (1)

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease Improving Global Outcomes; KDPI, Kidney Donor Profile Index.

were used to evaluate the utility of KDPI (against donor age) in predicting allograft function (1-y eGFR). In their models, recipient body mass index was the only additional variable that showed a significant association.[5]

In this study, adjustment for potentially confounding variables resulted in little change in the magnitude of the effect of KDPI in our models, adding minimal explanation of variation in our outcomes beyond KDPI alone. This suggests that of the information reasonably available prior to transplantation, donor KDPI is the key determinant of functional outcomes, with other factors having minimal impact or mediation of this effect. Intraoperative or post-transplant events, including surgical complications, delayed graft function, rejection episodes, immunosuppression regimen, patient compliance, and infection, were not considered in this study. Although these factors undoubtedly contribute to transplant outcomes, our purpose was to produce results using pretransplant data that could inform pretransplant discussions with recipients.

We report the incidence of donor characteristics across KDPI quintiles in the Australian population, noting that complex differences exist in the characteristics of donor populations worldwide. Compared with this study, large donor population studies based on US registry data consist of younger donors (median age 40 y), lower rates of DCD donation (15.2%), and considerably higher incidences of diabetes and hypertension across all KDPI ranges.[18,19] Aside from the aforementioned German studies, European studies reporting donor characteristics according to KDPI are limited. A recent study by Pippias et al[3] outlines significant variations in KDRI between select countries, ranging from KDRI 0.97 in Slovenia to 1.50 in the Basque region (in 2011), and wide-ranging proportions of DCD donors across Europe, from 0% in Slovenia and Denmark to 45% in the United Kingdom and 55% in the Netherlands (2015).

These examples highlight the hazards of drawing direct comparisons between populations using scaled KDPI or population-specific KDRI algorithms. In Pippias et al's[3] report, the median standardized KDRI (across all countries) increased by 13% over the 10-y study period (2005–2015). In an Australian population, Chan et al[20] noted an increase in median KDRI (US algorithm) from 1.02 to 1.32 in the 20 y to 2013. Shifts in donor pool demographics, through alterations in donation practices or precipitated by events such as the coronavirus disease 2019 pandemic, will alter the actual risk (KDRI) represented by the donor KDPI (scaled risk). The perception of risk represented by KDPI values may require periodic recalibration.

Compared with allograft failure alone, the incorporation of allografts with severely impaired baseline function into a composite suboptimal outcome metric identified almost 3.5× more recipients for whom the results of transplantation were (perhaps) poorer than anticipated. In addition to allograft survival, poor allograft function after transplantation is a predictor of various morbidities in recipients. Meier-Kriesche et al published findings of progressive increases in the relative risks of both cardiovascular and infection-related death for transplant recipients with 1-y serum creatinine over 1.5 mg/dL (≈133 μmol/L).[12] Lam et al[21] note significant increases in the risk of myocardial infarction (hazard ratio, 1.85) and cardiovascular disease–related death (hazard ratio, 4.54) in transplant recipients

TABLE 5.

Adjusted coefficients for variables predicting recipient 1-y eGFR (mL/min) in the total study population, as per multivariable linear regression analyses, using models with (1) continuous KDPI predictor variable and (2) KDPI Quintile predictor variable

	KDPI (1–100) continuous[a]		KDPI quintiles	
Variable[b]	Adjusted B-coefficient (95% CI)	*P*	Adjusted B-coefficient (95% CI)	*P*
KDPI	−0.34 (−0.36 to −0.31)	<0.001		
KDPI quintile				
First quintile			0	
Second quintile			−8.76 (−10.82 to −6.70)	<0.001
Third quintile			−15.17 (−17.12 to −13.22)	<0.001
Fourth quintile			−20.79 (−22.78 to −18.80)	<0.001
Fifth quintile			−27.43 (−29.44 to −25.42)	<0.001
Donor male	2.35 (1.14-3.56)	<0.001	2.52 (0.94-4.23)	<0.001
Donor CPR	2.10 (0.88-3.33)	0.001	2.12 (0.89-3.36)	0.001
Transplant out of region	2.77 (0.75-4.79)	0.01	2.86 (0.82-4.89)	0.01
Ischemic time >12 h	−1.46 (−2.71 to −0.21)	0.02	−1.61 (−2.87 to −0.36)	0.01
Procurement biopsy	NS ($P = 0.699$)		NS ($P = 0.699$)	
PRA[c]	−0.05 (−0.09 to −0.03)	<0.001	−0.05 (−0.09 to −0.03)	<0.001
Recipient age[c]	NS ($P = 0.932$)		NS ($P = 0.932$)	
Recipient BMI[d]				
<25 kg/m^3	0		0	
25–30 kg/m^2	−4.00 (−5.41 to −2.59)	<0.001	−3.81 (−5.23 to −2.39)	<0.001
>30 kg/m	−6.51 (−8.06 to −4.97)	<0.001	−6.36 (−7.92 to −4.80)	<0.001
Previous transplant	2.89 (0.85-4.93)	0.01	2.92 (0.87-4.98)	0.005
Dialysis years[c]	NS ($P = 0.460$)		NS ($P = 0.460$)	
High-risk GN	NS ($P = 0.118$)		NS ($P = 0.118$)	
Recipient smoking	NS ($P = 0.066$)		NS ($P = 0.066$)	
Recipient CAD	NS ($P = 0.729$)		NS ($P = 0.729$)	
Recipient T2DM	2.55 (0.92-4.18)	0.002	2.58 (0.94-4.23)	0.002
Constant	73.08 (71.19-74.98)	<0.001	70.35 (68.33-72.37)	<0.001

[a]Total study population model: total observations, 2485; $P < 0.001$.
[b]Refer to **Table S1**, **SDC**, http://links.lww.com/TXD/A409 for definition of variables; refer to **Table S4**, **SDC**, http://links.lww.com/TXD/A409 for a full list of B-coefficients on univariate analysis.
[c]Entered as continuous variable.
[d]Entered as categorical variable.
BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; CPR, cardiopulmonary resuscitation; eGFR, estimated glomerular filtration rate; GN, glomerulonephropathy; KDPI, Kidney Donor Profile Index; NS, nonsignificant; PRA, panel reactive antibody; T2DM, type 2 diabetes mellitus.

with eGFR <30 mL/min, whereas Karthikeyan et al[22] report twice doubling of kidney failure complications below this threshold, noting marked increases in anemia and rates of uncontrolled hypertension.

It is plausible that the improved transparency of outcomes for high-KDPI kidneys afforded by this study might fuel risk-averse acceptance behaviors. The nonutilisation rate of retrieved kidneys in Australia, although low by international standards, is ≈10% (2019).[1] In a review following the introduction of KDPI reporting in Australia, Sypek et al document a 45% increase in offer declines for high-risk kidneys (KDPI > 80), without an increase in nonutilisation in the postreporting period, suggesting the presence of a labeling effect and diversion of high-KDPI kidneys to older recipients.[23] In the US population, Bae et al[24] report a 29% increase in the odds of discard for donor kidneys with KDPI >70 compared with the general population (18.5%), and markedly high discard rates in the KDPI 81–100 (50.6%) and KDPI >95 (71.6%) cohorts.

Despite the high rate of suboptimal outcome observed in our fifth quintile cohort, most recipients in this bracket had acceptable function. Nevertheless, increased risks of poor function and its associated morbidity are important considerations when discussing organ offers with potential recipients, particularly those offered allografts with a KDPI >95. Beyond specific donor circumstances, these discussions may be moderated by multiple factors, including avoidance of antibodies in sensitized patients, likelihood of future offers, and potential morbidity of remaining on dialysis.[25]

The interpretation of the results of this study involves some caveats. We utilized a retrospective methodology and national registry data, subject to error at individual entry points and restricted to data fields collected. As we consider only adult recipients and have donor and recipient populations that are predominantly Caucasian, caution should be exercised when extrapolating the results to pediatric and non-Caucasian recipients. Although the Australian KDRI is a derivation of the US algorithm, the incidence of US donor variables omitted from Australian KDRI calculations was low in our cohort (hepatitis C positive = 0.5%, African-American ethnicity = 0%),[26] and thus, KDRI values in our study would be largely equivalent to those calculated using US KDRI formulae.

The dichotomization of outcomes based on eGFR at a single time point has inherent limitations. It does not consider patients with transiently impaired function (eg. acute rejection), and models based on the resultant binary outcome have impaired discriminatory capacity around the cutoff value. Furthermore, the individual facets of the composite outcome

TABLE 6.

Adjusted OR of variables predicting suboptimal outcome in the total study population and fifth quintile cohort, as per multivariable logistic regression analyses[a]

	Total study population[a]		fifth quintile cohort[b]	
Variable[c]	Adjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
KDPI quintile				
First quintile	1.00		–	
Second quintile	2.33 (1.17-4.61)	0.02	–	
Third quintile	3.36 (1.77-6.37)	<0.001	–	
Fourth quintile	4.57 (2.43-8.61)	<0.001	–	
Fifth quintile	11.68 (6.33-21.54)	<0.001	–	
KDPI interval				
81–85	–		1.00	
86–90	–		1.60 (0.92-2.78)	0.10
91–95	–		2.60 (1.51-4.49)	0.001
96–100	–		4.66 (2.60-8.36)	<0.001
Donor male	NS ($P = 0.172$)		–	
Donor CPR	0.67 (0.51-0.88)	0.004	–	
Inotropes	NS ($P = 0.063$)		NS ($P = 0.374$)	
Oliguria	NS ($P = 0.457$)		–	
Ischemic time >12 h	1.39 (1.08-1.79)	0.01	NS ($P = 0.270$)	
Procurement biopsy	NS ($P = 0.090$)		–	
Transplant out of region	0.41 (0.24-0.69)	0.001	NS ($P = 0.225$)	
HLA mismatch[d]	NS ($P = 0.074$)		1.13 (1.00-1.27)	0.05
PRA[d]	1.01 (1.00-1.01)	0.005	–	
Previous transplant	NS ($P = 0.104$)		–	
Recipient age[d,e]	0.99 (0.98-1.00)	0.02	–	
Recipient BMI				
<25 kg/m^3	1.00		1.00	
25–30 kg/m^2	1.37 (1.01-1.86)	0.04	1.45 (0.90-2.31)	0.12
>30 kg/m	1.59 (1.15-2.19)	0.005	2.30 (1.41-3.76)	0.001
Dialysis years			NS ($P = 0.233$)	
<1 y	0.56 (0.34-0.92)	0.02		
1–10 y	1.00			
>10 y	2.46 (1.28-4.72)	0.01		
High risk GN	1.71 (1.21-2.41)	0.002	2.40 (1.37-4.24)	0.002
Recipient CAD	NS ($P = 0.387$)		–	
Recipient PVD	1.83 (1.17-2.87)	0.01	–	
Recipient CVA	NS ($P = 0.606$)		NS ($P = 0.138$)	
Recipient T2DM	1.45 (1.02-2.08)	0.04	NS ($P = 0.286$)	
Recipient smoking	NS ($P = 0.192$)		–	
Interaction PVD/T2DM	0.53 (0.25-1.11)	0.09	–	
Constant	0.04 (0.02-0.09)	<0.001	0.07 (0.04-0.14)	<0.001

[a]Total study population model: observations: 2577; events: 353; event:variable = 29.4; model $P < 0.001$.
[b]Fifth quintile model: observations: 585; events: 163; event:variable = 32.5; model $P < 0.001$.
[c]Refer to **Table S1**, **SDC**, http://links.lww.com/TXD/A409 for definition of variables; refer to **Table S4**, **SDC**, http://links.lww.com/TXD/A409 for a full list of odds ratios on univariate analysis.
[d]Entered as continuous variable.
[e]Recipient age did not meet inclusion criteria on univariate analysis (0.502); however, it was considered an important potential confounder on clinical grounds and was statistically significant within multivariable regression analysis.
BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; CPR, cardiopulmonary resuscitation; CVA, cerebrovascular accident; GN, glomerulonephropathy; NS, nonsignificant; OR, odds ratio; PRA, panel reactive antibody; PVD, peripheral vascular disease; T2DM, type 2 diabetes mellitus.

(graft failure versus 1-y eGFR <30) have different implications, and as a unified concept, it may be difficult to explain to potential recipients.

As organ donation agencies strive to maximize donation and transplant opportunities, high KDRI kidneys will continue to be offered. The optimal utility of this resource remains an important focus. Allocation algorithms with survival-matching protocols, alongside allowances for preemptive transplantation in older recipients, have demonstrated merit. Tullius et al[27] established that the risk of rejection in allografts from older donors is attenuated in older recipients—a benefit likely afforded through immunosenescence—whereas separate US studies have suggested that preemptive transplantation, in minimizing the accrued morbidity of dialysis, may offset risks associated with high-KDPI allografts in older recipients.[25,28]

Another important focus is risk minimization in high-KDPI allografts. Doshi et al[29] suggested that both procurement biopsies and machine perfusion are unreliable in predicting outcomes in the KDPI >80 population, are resource-intensive, and prolonged ischemic times. Alternatively, consideration of adjunct factors during donor evaluation may be valuable.

TABLE 7.
Secondary outcomes across KDPI quintiles in the total study population, and 5-point intervals in the fifth quintile cohort

		Total study population					Fifth quintile cohort			
n	Total 2923	First quintile 478	Second quintile 513	Third quintile 673	Fourth quintile 638	Fifth quintile 621	KDPI 81–85 192	KDPI 86–90 169	KDPI 91–95 155	KDPI 96–100 105
Delayed graft function (%)	915 (32)	89 (19)	149 (30)	207 (32)	218 (35)	252 (41)	75 (40)	72 (43)	61 (41)	44 (42)
n	2856	467	504	655	621	609	189	166	105	105
Rejection (1 y) (%)	688 (24)	87 (18)	112 (22)	157 (23)	157 (25)	175 (28)	51 (27)	43 (25)	49 (312)	32 (30)
1-y outcomes										
Death (%)	74 (3)	9 (2)	14 (3)	13 (2)	17 (3)	21 (3)	7 (4)	3 (2)	5 (3)	6 (6)
Allograft failed	14 (0.5)	0 (0)	2 (0.4)	3 (0.5)	3 (0.5)	6 (1)	2 (1)	2 (1)	0 (0%)	2 (2)
Allograft functioning	60 (2)	9 (2)	12 (2)	10 (1)	14 (2)	15 (2)	5 (3)	1 (0.6)	5 (3)	4 (4)
Failed allograft (%)	97 (3)	9 (2)	15 (3)	18 (3)	19 (3)	36 (6)	5 (3)	13 (8)	10 (6)	8 (8)
Including death with failed allograft	111 (4)	9 (2)	17 (3)	21 (3)	22 (3)	42 (7)	7 (4)	15 (9)	10 (6)	10 (10)
5-y outcomes										
Lost to follow-up	19	3	4	3	6	3	0	1	2	0
Death (%)	308 (11)	30 (6)	57 (11)	63 (9)	65 (10)	93 (15)	26 (14)	25 (15)	24 (16)	18 (17)
Allograft failed	58 (2)	3 (0.6)	10 (2)	10 (1)	13 (2)	22 (4)	5 (3)	10 (6)	4 (3)	3 (3)
Allograft functioning	250 (9)	27 (6)	47 (9)	53 (8)	52 (8)	71 (11)	21 (11)	15 (9)	20 (13)	15 (14)
Failed allograft (%)	220 (8)	17 (6)	44 (9)	39 (6)	45 (7)	75 (12)	14 (7)	23 (14)	21 (14)	17 (16)
Including death with failed allograft	278 (10)	20 (4)	54 (11)	49 (7)	58 (9)	97 (16)	19 (10)	33 (20)	25 (16)	20 (19)

KDPI, Kidney Donor Profile Index.

Beyond the variables explored in our study, the influence of aberrant donor anatomy, burden of atherosclerosis (on noninvasive imaging), and donor/recipient size mismatch warrants further investigation in this cohort. Redefining the assessment of high-KDPI donors may avoid procurement in those with additional identified risk, or guide the selection of recipients and scenarios with more favorable summative risk profiles.

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