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Procurement Biopsy Findings Versus Kidney Donor Risk Index for Predicting Renal Allograft Survival

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Background. Efforts to maximize transplantation by matching organ quality to recipient longevity require reliable tools. The US kidney allocation system uses the Kidney Donor Risk Index (KDRI) for this purpose, and many centers additionally rely on donor biopsies. The Leuven score combines donor age with procurement histology (glomerulosclerosis and interstitial fibrosis/tubular atrophy) to predict allograft survival. **Methods.** We compared KDRI with Leuven scores for associations with kidney discard, delayed graft function, and allograft function and survival. We used Cox, modified Poisson, and linear regression to calculate risks based on KDRI and (separately) Leuven scores, adjusting for important transplant and recipient variables. **Results.** From 890 donors, 1729 kidneys were procured and biopsied. Five hundred eighty-five (34%) kidneys were discarded. Median donor age was 53 years (interquartile range [IQR], 44-61 years). Median KDRI and Leuven scores were 1.56 (IQR, 1.28-1.90) and 59 (IQR, 49-69). Relative risk for discard was 1.21 (95% confidence interval [CI], 1.17-1.24) per 0.2-unit increase in KDRI and 1.38 (1.31-1.46) per 10-unit increase in Leuven score. Adjusted relative risks for delayed graft function were 0.98 (95% CI, 0.94-1.02) and 0.94 (95% CI, 0.90-0.99), adjusted hazard ratios for graft failure were 1.10 (95% CI, 1.04-1.16) and 1.11 (95% CI, 1.02-1.21), and adjusted linear regression coefficients for 3-year estimated glomerular filtration rate were -3.88 (-4.63 to -3.13) and -5.18 (-6.19 to -4.18). **Conclusions.** In kidneys clinically selected for procurement biopsy, the Leuven score was more strongly associated with discard but performed similarly to KDRI for predicting transplant outcomes, suggesting the need to reevaluate current procurement biopsy practices. Given modest associations for both tools; however, neither KDRI nor the Leuven score should be used in isolation for individual organ acceptance decisions.

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Approximately 100 000 individuals currently await kidney transplantation in the United States. Roughly 30 000 adults are added to the waiting list each year, but the number of transplants has remained steady over the past decade at around 17 000 annually, leading to increasing mortality on the waiting list.¹ To expand the number of kidneys for transplantation, organ procurement organizations (OPOs) have increasingly used less than ideal deceased donors. In addition, the Organ Procurement and Transplantation Network (OPTN) sought to improve matching between organ quality and expected recipient survival in hopes of reducing retransplantation rates by initiating a new kidney allocation system in December 2014. The OPTN now uses the Kidney Donor Risk Index (KDRI) as the measure of organ quality for the matching algorithm; however, many transplant centers in the United States also request procurement kidney biopsies to aid in kidney offer decision-making.

The primary concerns about performing procurement biopsies are that they delay decisions and prolong cold ischemia, which could further injure already “marginal” kidneys, encourage unnecessary discards, and increase healthcare costs. There is also a lack of standardization in how procurement biopsies are performed, processed, examined, and reported, as well as uncertainty about their predictive utility.^{2,3} Procurement kidney biopsies are rarely performed in Europe despite higher transplantation rates for “marginal” kidneys with similar outcomes compared with the United States.⁴ These and other concerns have led some to suggest abandoning procurement biopsies altogether.⁵ Prior studies have evaluated donor kidney biopsy features but have reported inconsistent results for associations with posttransplant outcomes.⁶

Despite their limitations, procurement biopsies are being performed more often in the United States and are associated with increasing rates of discard. For example, Stewart et al⁷ demonstrated that much of the rise in kidney discards during the last decade (from 13% in 1999 to 19% in 2009) can be attributed to more biopsies in addition to changing donor characteristics. Primary reasons to request a procurement biopsy are likely linked to underlying clinical concerns about donor quality. Because these underlying indications for biopsy may confound relationships with posttransplant outcomes, we performed a large cohort study of kidneys selected for procurement biopsy to compare the utility of a well-described clinicohistopathological score to that of KDRI itself primarily for predicting kidney discard. We secondarily compared its performance for the development of delayed graft function (DGF) and 3-year allograft function and survival.

MATERIALS AND METHODS

Cohort and Data Sources

This is an ancillary study to an ongoing multicenter deceased organ donor cohort (ClinicalTrials.gov identifier: NCT01848249). Details regarding donor enrollment and data collection are available in prior publications.⁸⁻¹³ Briefly, 5 participating OPOs enrolled donors between May 2010 and December 2013. Detailed donor and organ characteristics were extracted from OPO charts. We excluded donors younger than 5 years and those that were not biopsied or had missing data necessary for the analysis.

This study also used data from the OPTN. The OPTN data system includes information on all donors, waitlisted

candidates, and transplant recipients in the United States, submitted by the members of the OPTN and is more fully described elsewhere.¹⁴ The Health Resources and Services Administration, US Department of Health and Human Services provides oversight to the activities of the OPTN contractor. Recipient characteristics and outcomes were ascertained using data submitted by transplant centers to the United Network for Organ Sharing (UNOS), the current OPTN contractor, through routine transplantation and follow-up forms.

Based on individual OPO practices, wedge or needle biopsies were performed on ex vivo kidneys immediately after procurement. Tissue samples were not collected for this study. On-call donor hospitals evaluated frozen sections from procurement biopsies to generate reports that were uploaded to the secure, Web-based DonorNet maintained by UNOS for review by transplant centers during kidney allocation. Data from these clinically available pathology reports were abstracted to calculate the previously described “3-year prediction” Leuven Donor Risk Score (Leuven score).¹⁵

The Leuven score is calculated from donor age (years), percent glomerulosclerosis (GS) and interstitial fibrosis/tubular atrophy (IFTA) grade according to the Banff ‘07 classification¹⁶ using the following equation: $\text{age} + (2 \times \text{GS}) + (10 \times \text{IFTA})$, where $\text{GS} < 10\% = 0, \geq 10\% = 1$; and $\text{IFTA} \leq 5\% = 0, 6-25\% = 1, 26-50\% = 2, > 50\% = 3$. We specifically chose this clinicohistopathological score for the following reasons. First, the score was initially developed using multivariable modeling in a cohort of 181 procurement biopsies that were not clinically available for allocation or discard decisions. Second, the score was validated in a separate group of 367 procurement biopsies and found to provide “sufficient predictive performance to guide kidney allocation” with an area under the receiver-operating characteristic curve (AUC) for 3-year allograft survival of 0.70. Third, we could calculate the score from clinically available procurement kidney biopsy reports, which provided variable summary information about the degree of GS, IFTA, arteriosclerosis, and acute tubular necrosis. Thus, based on current practices in the United States, transplant centers can similarly calculate the Leuven score from procurement kidney biopsy reports without requesting additional morphologic measurements.

We chose kidney discard (ie, kidneys procured for the purpose of transplantation but not transplanted) and time to allograft failure (defined as initiation/return to chronic dialysis, retransplantation, or death of the recipient) as coprimary outcomes. Secondary outcomes of interests were DGF (defined as any dialysis in the first week of transplant), allograft survival at 3 years, and allograft function at 1 and 3 years. Allograft function was assessed via estimated glomerular filtration rate (eGFR) calculated from serum creatinine values reported to UNOS using the Chronic Kidney Disease Epidemiology Collaboration equation.¹⁷ We carried forward the last eGFR reported for recipients that died with functional allografts and imputed eGFR as 10 mL/min per 1.73 m² after instances of death-censored graft failure.

We adhered to the ethical principles of the Declaration of Helsinki,¹⁸ and the institutional review boards and/or scientific committees for all participating organizations approved the study. Data for deceased donors were collected if donor surrogates agreed to research, and institutional review board waiver of consent was approved for recipient outcomes given our use of deidentified OPTN data. The clinical and research

activities reported here are also consistent with the principles outlined in the Declaration of Istanbul on Organ Trafficking and Transplant Tourism.¹⁹

Statistical Analyses

We calculated descriptive statistics and reported values as mean (SD) or median [interquartile range] for continuous variables and as frequency (percentage) for categorical variables. We used Wilcoxon rank-sum tests to compare continuous variables between groups and χ^2 or Fisher exact tests as appropriate for categorical comparisons. We calculated the KDRI as described by Rao et al²⁰ with mapping to the Kidney Donor Profile Index (KDPI) relative to all US deceased donors in 2010.²¹

Using modified Poisson regression to estimate relative risk (RR) and control for possible correlation of outcomes between kidneys from the same donor, we fit separate models using KDRI and then the Leuven score for the dichotomous outcomes of kidney discard, DGF, and 3-year allograft survival. We fit Cox proportional hazards models for time to allograft failure and linear mixed regression models for 1- and 3-year eGFRs. Based on the cohort distribution of KDRI and Leuven scores, we calculated risk for each outcome per 0.2-unit increase in KDRI and per 10-unit increase in Leuven score. Because the aim of this study was to compare these clinical summary measures of donor/organ quality, no additional characteristics were used to adjust the models for kidney discard. Models for all other (posttransplant) outcomes, however, were subsequently adjusted for the use of machine perfusion, cold ischemia time (hours) and the following recipient variables: age (years), black

race, sex, previous kidney transplant, diabetes as the cause of end stage renal disease, need for pretransplant blood transfusion, number of HLA mismatches, percent panel-reactive antibody (PRA), body mass index (weight/height², kg/m²), and preemptive transplant status. For kidney discard and allograft survival, we additionally controlled for KDRI to assess potential independent associations for the Leuven score.

Recipient follow-up was calculated from the date of transplant to all-cause allograft failure and administratively censored at the end of the study period on July 6, 2016. For dichotomous outcomes, we used each regression model to calculate AUCs. Analyses were completed using SAS 9.4 statistical software for Windows (SAS Institute, Cary, NC) and R 3.1.2 (R Foundation for Statistical Computing, Vienna, Austria). We used a 2-tailed significance value less than 0.05 and controlled for possible correlation of outcomes between kidneys from the same donor for all statistical tests.

RESULTS

Figure 1 depicts the cohort generation. Table S1 (SDC, <http://links.lww.com/TXD/A119>) shows the characteristics for the 1729 kidneys from 890 donors included in the analysis (ie, procured for the purpose of transplantation and biopsied) compared with the 1469 kidneys from 774 donors that were excluded (ie, no procurement biopsy). Kidneys from donors enrolled in the parent cohort that underwent biopsy tended to come from older donors with more comorbidities. There was substantial variation in procurement biopsy rate between OPOs (range, 16-87%; Table S2, SDC, <http://links.lww.com/TXD/A120>).

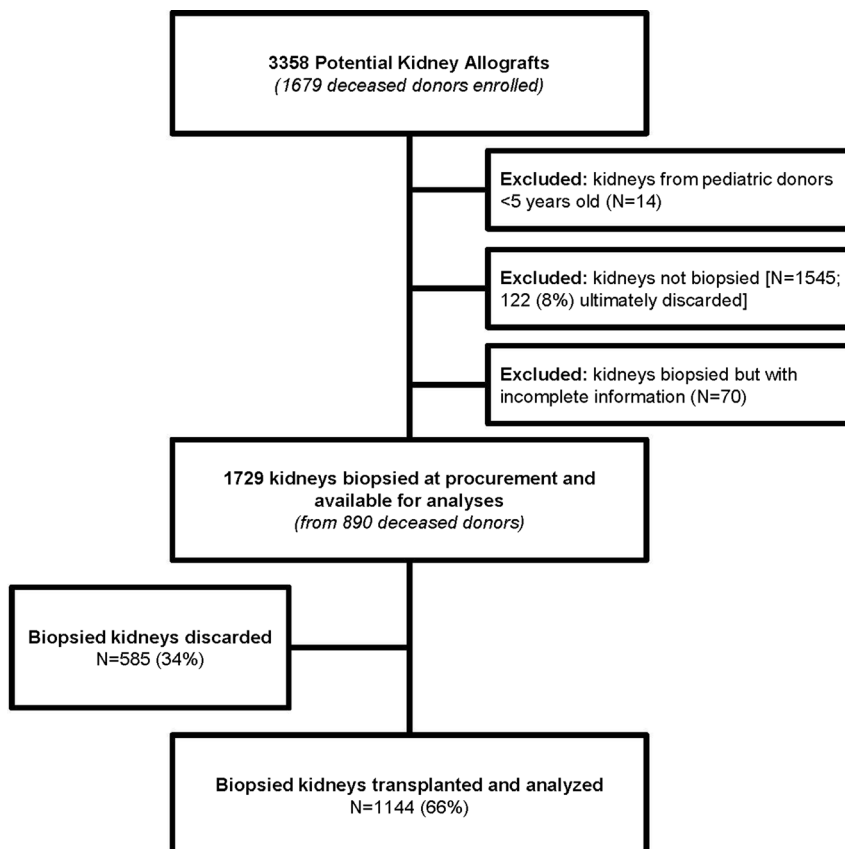


FIGURE 1. Cohort generation.

However, there were no clear correlations between OPO biopsy rates and severity of reported findings. One hundred twenty-two (8%) of the kidneys that were not biopsied (excluded from further analyses) were eventually discarded compared with 585 (34%) kidney discards for those that were biopsied and included in subsequent analyses ($P < 0.001$).

A total of 1144 (66%) biopsied kidneys were transplanted. Table 1 provides donor characteristics according to the number (0, 1, or 2) of resulting transplants. Median donor age was 53 years (44-61 years), 56% were male, 18% were black, 15% donated after cardiovascular determination of death, and 29% had KDPI greater than 85%. Median KDRI and Leuven score were 1.57 (1.29-1.91) and 59 (49-69), respectively. There was overlap between KDRI and Leuven scores as shown in Figure 2.

Median recipient age was 60 [50-66] years, 41% were male, 27% were black, 7% were preemptive transplants, 4% had prior transplants and 10% had PRA >80%. Table 2 provides recipient and transplant characteristics by median KDRI. Table S3 (SDC, <http://links.lww.com/TXD/A121> provides the same information by median Leuven score. Of transplanted kidneys, 458 (40%) developed DGF and 251 (22%) failed by 3 years, including 25 (2%) with primary nonfunction, 130 (11%) with death-censored graft failure, 96 (8%) deaths with functioning grafts, and 37 (3%) deaths after graft failure. Median follow-up was 3.5 [3-4.5] years.

Kidney Discard

Compared with KDRI, there was a stronger association between increasing Leuven score and kidney discard risk. RR (95% confidence interval [CI]) for discard was 1.20 (95% CI, 1.17-1.24) and 1.38 (95% CI, 1.31-1.46) for each

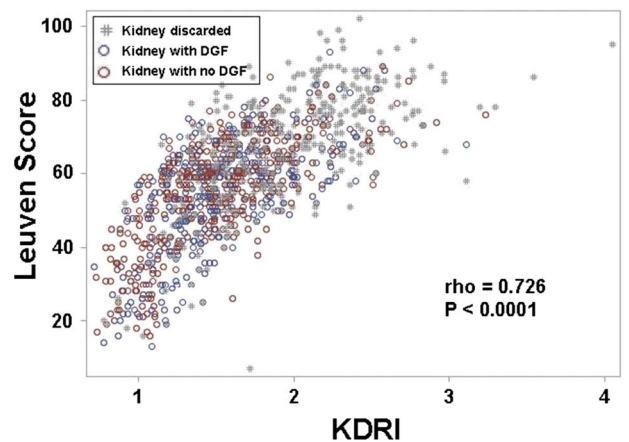


FIGURE 2. Scatterplot of Leuven scores and KDRI.

0.2-unit increase in KDRI and each 10-unit increase in Leuven score. Controlling for KDRI, adjusted RR (aRR) for discard decreased to 1.22 (1.13-1.31) with each 10-unit increase in Leuven score. For predicting discard, AUCs for KDRI and Leuven score were no different at 0.72.

Allograft Failure

Increasing values for either KDRI or the Leuven score were independently associated with allograft failure with adjusted hazard ratios (aHR) of 1.10 (1.04-1.16) for each 0.2-unit increase in KDRI and 1.11 (1.02-1.21) for each 10-unit increase in Leuven score (Table 3). The aRRs for 3-year allograft failure were also similar for KDRI and Leuven score at 1.08 (1.03-1.14) and 1.10 (1.03-1.19) and with AUCs of 0.62 and 0.61, respectively. The baseline clinical model of

TABLE 1.

Donor demographics by number of kidneys transplanted

	All (N = 890)	No kidney transplant (n = 231)	1 kidney transplant (n = 138)	2 kidney transplants (n = 521)	P	
Age, y	53 (44-61)	60 (52-68)	54 (47-60)	50 (40-58)	<0.001	
Male	500 (56%)	125 (54%)	73 (53%)	302 (58%)	0.432	
Black race	157 (18%)	43 (19%)	22 (16%)	92 (18%)	0.809	
Hispanic	116 (13%)	19 (8%)	13 (9%)	84 (16%)	0.005	
Body mass index, kg/m ²	28 (24-34)	28 (25-34)	29 (25-34)	28 (24-33)	0.326	
Hypertension	497 (56%)	167 (72%)	81 (59%)	249 (48%)	<0.001	
Diabetes	121 (14%)		34 (25%)	87 (17%)	<0.001	
Cause of death	Head Trauma	153 (17%)	29 (13%)	21 (15%)	103 (20%)	<0.001
	Anoxia	284 (32%)	56 (24%)	52 (38%)	176 (34%)	
	Stroke	426 (49%)	142 (62%)	61 (45%)	223 (44%)	
	Other	13 (1%)	2 (1%)	2 (1%)	9 (2%)	
Hepatitis C seropositive	29 (3%)	13 (6%)	11 (8%)	5 (1%)	<0.001	
Expanded criteria donor	396 (44%)	160 (69%)	61 (44%)	175 (34%)	<0.001	
Donation after cardiac death	130 (15%)	21 (9%)	21 (15%)	88 (17%)	0.02	
KDRI	1.56 [1.28-1.9]	1.92 [1.56-2.31]	1.64 [1.37-1.9]	1.45 [1.17-1.72]	<0.001	
KDPI	73 [54-88]	88 [72-96]	76.5 [60-88]	66 [44-81]	<0.001	
Terminal serum creatinine, mg/dL	1.1 [0.79-1.6]	1.22 [0.9-1.8]	1.1 [0.8-1.7]	1 [0.7-1.5]	<0.001	
Year of procurement	2010	138 (16%)	31 (13%)	19 (14%)	88 (17%)	0.130
	2011	272 (31%)	70 (30%)	33 (24%)	169 (32%)	
	2012	282 (32%)	84 (36%)	48 (35%)	150 (29%)	
	2013	198 (22%)	46 (20%)	38 (28%)	114 (22%)	

Values are N (%) or median [IQR].

TABLE 2.
Recipient, transplant, and kidney characteristics and outcomes by KDRI median

Recipient and transplant characteristics		All (N = 1144)	KDRI ≤ 1.56 (n = 692)	KDRI > 1.56 (n = 452)	P
Age, y		60 [50, 66]	56 [47, 64]	63 [56, 69]	<0.001
Male		706 (62%)	425 (61%)	281 (62%)	0.798
Black race		473 (41%)	290 (42%)	183 (40%)	0.633
Hispanic		141 (12%)	86 (12%)	55 (12%)	0.896
Body mass index, kg/m ²		28 [25, 32]	28 [24, 32]	28 [25, 32]	0.813
Cause of ESRD	Other or unknown	210 (18%)	130 (19%)	80 (18%)	<0.001
	Diabetes	375 (33%)	218 (32%)	157 (35%)	
	Hypertension	323 (28%)	174 (25%)	149 (33%)	
	Glomerulonephritis	169 (15%)	122 (18%)	46 (10%)	
	Graft failure	68 (6%)	48 (7%)	20 (4%)	
ESRD duration, months		47 [21, 68]	46 [19, 70]	49 [26, 66]	0.473
Preemptive transplant		121 (11%)	78 (11%)	43 (10%)	<0.001
Kidney machine perfusion used		731 (64%)	472 (68%)	259 (57%)	<0.001
Kidney cold ischemia time, hours		16.5 [12.1, 22]	16.7 [12.1, 22.3]	16.5 [12.1, 21]	0.214
HLA mismatches	0	57 (5%)	45 (7%)	12 (3%)	<0.001
	1	10 (1%)	7 (1%)	3 (1%)	
	2	31 (3%)	23 (3%)	8 (2%)	
	3	128 (11%)	87 (13%)	41 (9%)	
	4	274 (24%)	165 (24%)	109 (24%)	
	5	431 (38%)	243 (35%)	188 (42%)	
	6	211 (18%)	121 (18%)	90 (20%)	
PRA	0%	799 (70%)	474 (68%)	325 (72%)	<0.001
	1-20%	86 (8%)	45 (7%)	41 (9%)	
	21-80%	142 (12%)	80 (12%)	62 (14%)	
	>80%	117 (10%)	93 (13%)	24 (5%)	
DGF		458 (40%)	282 (41%)	176 (39%)	0.480
1-y eGFR, mL/min per 1.73 m ²		48 [35, 63]	54 [40, 67]	43 [30, 53]	<0.001
3-y eGFR, mL/min per 1.73 m ²		46 [30, 61]	51 [35, 67]	38 [24, 51]	<0.001
Kidney Characteristics		All (N = 1729)	KDRI ≤ 1.56 (n = 866)	KDRI > 1.56 (n = 863)	P
GS	<10%	1307 (76%)	754 (87%)	553 (64%)	<0.001
	10%-20%	226 (13%)	72 (8%)	154 (18%)	
	>20%	196 (11%)	40 (5%)	156 (18%)	
IFTA	None (≤5%)	810 (47%)	418 (48%)	392 (45%)	0.011
	Mild (6-25%)	815 (47%)	410 (47%)	405 (47%)	
	Moderate (26-50%)	99 (6%)	38 (4%)	61 (7%)	
	Severe (>50%)	5 (0%)		5 (1%)	
Kidney Leuven score		59 [49, 69]	51 [39, 59]	67 [59, 75]	<0.001
Kidney discarded		585 (34%)	174 (20%)	411 (48%)	<0.001

Values are N (%) or median [IQR].

ESRD, end-stage renal disease; IFTA, interstitial fibrosis/tubular atrophy.

transplant and recipient factors (ie, excluding donor factors) provided an AUC for 3-year allograft failure of 0.60. Statistical significance for the Leuven score was lost

after controlling for KDRI in each clinical model (aHR, 1.04; 95% CI, 0.93-1.15; aRR for 3-year allograft failure, 1.05; 95% CI, 0.96-1.15).

TABLE 3.
Risk of allograft failure by KDRI or Leuven score

Algorithm	Cox proportional hazards		Modified Poisson regression—3-yr allograft failure			
	Unadjusted HR (95% CI)	aHR ^a (95% CI)	Unadjusted RR (95% CI)	AUC	aRR ^a (95% CI)	AUC
KDRI ^b	1.10 (1.05-1.16)	1.10 (1.04-1.16)	1.09 (1.04-1.13)	0.58	1.08 (1.03-1.14)	0.62
Leuven score ^c	1.12 (1.04-1.22)	1.11 (1.02-1.21) ^d	1.12 (1.05-1.20)	0.56	1.10 (1.03-1.19) ^d	0.61

^a Adjusted for use of pump perfusion, cold ischemia time (hours) and the following recipient variables: age (years), black race, gender, previous kidney transplant, diabetes as the cause of end stage renal disease, need for pretransplant blood transfusion, number of HLA mismatches, PRA (%), body mass index, and pretransplant dialysis.

^b Per 0.2 unit increase.

^c Per 10 unit increase.

^d In addition to the covariates listed above, further controlling for KDRI resulted in an aHR of 1.04 (0.93-1.15) and an aRR of allograft failure at 3 years of 1.05 (0.96-1.15).

TABLE 4.
Risk of DGF by KDRI or Leuven score

Algorithms	Unadjusted RR (95% CI)	AUC	aRR ^a (95% CI)	AUC
KDRI ^b	1.00 (0.96-1.04)	0.50	0.98 (0.94-1.02)	0.66
Leuven score ^c	0.97 (0.92-1.01)	0.53	0.94 (0.90-0.99)	0.66

^a Adjusted for use of pump perfusion, cold ischemia time (hours) and the following recipient variables: age (years), black race, gender, previous kidney transplant, diabetes as the cause of end stage renal disease, need for pretransplant blood transfusion, number of HLA mismatches, PRA (%), body mass index, and pretransplant dialysis.

^b Per 0.2 unit increase.

^c Per 10 unit increase.

Secondary Outcomes

Neither KDRI nor the Leuven score predicted DGF in this cohort with unadjusted AUCs of 0.5 and 0.53, respectively (Table 4). The aRRs for DGF with KDRI and the Leuven score were 0.98 (0.94-1.02) and 0.94 (0.90-0.99), respectively. However, both scores were independently associated with worse allograft function at 1 and 3 years posttransplant (Table 5). Based on linear regression R^2 values, either score accounted for 10% to 11% of the variation in 1- and 3-year eGFRs, whereas multivariable models using either score and adjusting for transplant and recipient factors accounted for 12% to 15% of eGFR variation.

DISCUSSION

Current deceased-donor kidney transplant practices, on average, improve and prolong the lives of recipients, but the process to consider kidney offers involves individualized and often complex clinical decisions. In this large, multicenter study of deceased-donor kidneys selected to undergo biopsy, we found that the Leuven score (1) can be easily calculated from donor age and 2 histopathological findings available from procurement kidney biopsy reports and (2) performs no better than the 10-variable KDRI for predicting kidney discard as well as posttransplant allograft survival and function. Neither the Leuven score nor KDRI accurately predicted DGF in this cohort. We believe these findings support the notion that procurement biopsies, at least as they are currently performed and reported in the United States, lead to more kidney discards and provide no added value for predicting transplant outcomes.

It is important to note that over half of the donors enrolled in the parent cohort were biopsied with wide variation between OPOs. Kidneys from donors that underwent biopsy

tended to have more unfavorable clinical characteristics and were much more likely to result in discard compared with those that did not undergo procurement biopsy. Because we cannot know the clinical outcomes for discarded kidneys had they instead been transplanted, theoretical arguments against discarding kidneys because of biopsy findings can be quite tenuous. Consequently, some OPOs obtain procurement kidney biopsies from most donors, and many centers request biopsies if not already available as permitted by OPTN Policy 2.11.A(2).²² In fact, Stewart et al⁷ noted an increase in biopsies from about 23% in 1999 to 50% in 2009—a substantial increase despite concomitant decreases in median donor age and KDRI over the same period.

In some transplant centers, GS is the primary donor biopsy information consistently reviewed because it provides a convenient cutoff (eg, >10%) for automatic offer turndowns. However, Banff guidelines for procurement biopsies discourage the use of “rigidly defined histologic cutoffs” during organ allocation.² This seems appropriate given the analyses by Massie et al,²³ which showed selected candidates experience improved survival with early acceptance of lower-quality (ie, high-KDPI) offers. Notwithstanding, whether a center should accept a lower-quality offer for an individual patient can be a challenging question, and there are high-volume centers that use procurement biopsies as part of their decision making process for select offers. Centers have also used standardized procurement biopsies to calculate histopathology scores to determine whether to transplant lower-quality kidneys from 1 donor into 2 recipients versus 1 as a dual-kidney transplant, resulting in acceptable outcomes.^{24,25}

With regard to organ utilization at the national level, however, medical environments for transplantation in the United States are complex. Thus, variables affecting organ discard are complex and likely include regulatory oversight and diverse geographic, reimbursement, ethnosocioeconomic, and even behavioral economic issues, such as loss and risk aversion.²⁶ Nevertheless, procurement kidney biopsy is an important factor.⁷ We noted a 34% discard rate for kidneys that underwent procurement biopsy—substantially higher than the 8% discard rate for nonbiopsied (excluded) kidneys. Although these divergent rates were comparable to national averages (31.4% for biopsied kidneys vs 6.8% for nonbiopsied kidneys),¹ the tendency to request procurement biopsies based on donor quality complicates analyses of organ utilization because of confounding by indication.

Confounding by indication in this setting was supported by our finding of reduced RR for discard with increasing

TABLE 5.
Linear regression coefficients on allograft function by KDRI or Leuven score

Outcome	Algorithm	Unadjusted			Adjusted ^a		
		Number available	Beta-coefficient (95% CI)	R^2	Number available	Beta-coefficient (95% CI)	R^2
1-y eGFR	KDRI ^b	1125	-3.54 (-4.15 to -2.94)	0.11	1112	-3.27 (-3.92 to -2.62)	0.15
	Leuven score ^c	1125	-4.86 (-5.70 to -4.02)	0.10	1112	-4.44 (-5.33 to -3.55)	0.15
3-y eGFR	KDRI ^b	1063	-3.75 (-4.44 to -3.06)	0.10	1051	-3.88 (-4.63 to -3.13)	0.13
	Leuven score ^b	1063	-5.20 (-6.15 to -4.26)	0.10	1051	-5.18 (-6.19 to -4.18)	0.12

^a Adjusted for use of pump perfusion, cold ischemia time (hours) and the following recipient variables: age (years), black race, gender, previous kidney transplant, diabetes as the cause of end stage renal disease, need for pretransplant blood transfusion, number of HLA mismatches, PRA (%), body mass index, and pretransplant dialysis

^b Per 0.2 unit increase

^c Per 10 unit increase.

Leuven score after adjusting for KDRI. Decreasing from an unadjusted RR of 1.38, the aRR of 1.22 remained statistically significant, however, indicating a persistent independent association between the Leuven score (ie, procurement biopsy) and kidney discard. Moreover, we were interested to find that the utility of the procurement biopsy Leuven score was essentially no different than that of KDRI for predicting allograft failure. In fact, both scores performed only modestly in this cohort with unadjusted AUCs that were less than the KDRI C-statistic reported as 0.62 for all deceased-donor kidney-only transplants in the OPTN database from 1995 to 2005.²⁰ Lending further support for confounding by biopsy indication, statistical significance for the Leuven score for predicting allograft failure was abolished after controlling for KDRI.

There are limitations to this study. Though we controlled for factors known to associate with allograft survival, residual confounding is possible given our observational design and use of OPTN data. Although the Banff Working Group recommended using frozen sections from wedge biopsies, the guidelines also described the limitations to this approach, including limited interobserver concordance for GS and IFTA.² Without biopsy slides, we could not assess other histologic scores from the literature, such as the chronic allograft damage index,²⁷ the Remuzzi score,²⁸ all chronic changes described in the Banff '97 classification,²⁹ or the Maryland aggregate pathology index.³⁰ Although prior studies have suggested that renal vascular changes based on these and other scoring systems have prognostic value,³¹⁻³⁴ the procurement biopsy reports used for the current study contained inadequate information for meaningful analyses on vessel pathology. Although independent, standardized reviews of biopsy slides could not be performed, we believe this study provides an innovative analysis of the pathology reports that are currently used during organ allocation. By definition, only transplanted kidneys have posttransplant outcomes, which make selection bias possible and underscores our decision to analyze discard as a primary outcome.

In conclusion, our data highlight some of the “real-world” clinical shortcomings of procurement biopsy reports and reveal their limited predictive utility. Given sufficient equipoise and the fact that deceased-donor organs are a national resource, we believe a properly designed donor trial is needed to collect procurement biopsy data to determine how to appropriately obtain and use this information. An example could be a large cluster trial for organ utilization and allograft outcomes in which OPOs are randomized to current biopsy practice versus standardized biopsies from prespecified donors (eg, KDPI >50%) with rapid fixation,^{35,36} whole-slide imaging,³⁷ and centralized pathology evaluation in real-time.

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