Utility of applying quality assessment tools for kidneys with KDPI 80

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Abstract

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Background—Kidneys with "high" kidney donor profile index (KDPI) are often biopsied and pumped, yet frequently discarded.

Methods—In this multicenter study, we describe the characteristics and outcomes of kidneys with KDPI 80 that were procured from 338 deceased donors. We excluded donors with anatomical kidney abnormalities.

Results—Donors were categorized by the number of kidneys discarded: 1) none (n=154, 46%), 2) 1 discarded and 1 transplanted (n=48, 14%), 3) both discarded (n=136, 40%). Donors in group 3 were older, more often white, and had higher terminal creatinine and KDPI than group 1 (all p<0.05). Biopsy was performed in 92% of all kidneys, and 47% were pumped. Discard was associated with biopsy findings and 1st hour renal resistance. Kidney injury biomarker levels (NGAL, IL-18, and KIM-1 measured from donor urine at procurement and from perfusate soon after pump perfusion) were not different between groups. There was no significant difference in 1-year estimated glomerular filtration rate (eGFR) or graft failure between groups 1 and 2 (41.5±18 vs. 41.4±22 mL/min/1.73m^2; p=0.97 and 9% vs. 10%; p=0.76).

Conclusions—Kidneys with KDPI 80 comprise the most resource consuming fraction of our donor kidney pool and have the highest rates of discard. Our data suggest that some discarded kidneys with KDPI 80 are viable; however, current tools and urine- and perfusate-biomarkers to identify these viable kidneys are not satisfactory. We need better methods to assess viability of kidneys with high KDPI.

Introduction

The ever-growing disparity between demand for kidneys and their availability is a motivation to expand the pool of deceased kidney donors and reduce organ discard. As a move towards more effective organ utilization, the Organ Procurement and Transplantation Network (OPTN) modified the organ allocation system in 2014 to better match allograft and recipient longevity and to expand the offer of marginal kidneys regionally to minimize cold ischemia time and improve their viability (1). As part of this system, all kidneys from deceased donors are now given a Kidney Donor Risk Index (KDRI), which is calculated from 14 donor and transplant characteristics and represents the risk (hazard ratio, HR) of allograft failure compared with a kidney from an "average" deceased donor between 1995 and 2005 (2). The Kidney Donor Profile Index (KDPI) ranks the quality of those kidneys deemed transplantable (as a percentile from 1 to 100). KDPI is derived from a simplified KDRI (using 10 donor-only characteristics) that has been rank-ordered and normalized to the median donor-only KDRI value from the prior year. While KDPI can be considered a prognostic score, some clinicians may use it as a discriminatory tool to accept or reject kidney offers. Among the organs retrieved between 2002 and 2012, discard rates for kidneys with KDPI 80-90 and KDPI >90 are reported to be 36% and 63%, respectively (3). The discard of high-KDPI kidneys should be reevaluated, given the increase in the number of patients on the waiting list and the steady rise in the number of elderly transplant candidates who may not survive on dialysis long enough to get a kidney with lower KDPI (4). Massie et al reported that the benefit of receiving a kidney with KDPI 80 was far superior to the conservative approach of waiting and perhaps receiving a lower KDPI kidney transplant,

especially in candidates older than 50 years and those with an expected wait time in excess of 33 months (5).

Currently, preimplant biopsy and pump parameters are also used to determine kidney quality from less desirable donors. Preimplant biopsy is obtained in over half of all deceased donors, and these biopsy results are the most commonly cited reason for discard of the kidney (6). Several studies have evaluated the correlation of biopsy findings with graft outcomes and have reported varying results. While Kasiske et al (6) reported a lack of association between procurement biopsy results and graft outcomes, a recent study by Gandolfini et al (7) showed that standardized preimplant biopsy scoring (used to allocate marginal kidneys as dual versus single kidney transplants) increased organ utilization without compromising 3-year graft survival.

Similarly, hypothermic machine perfusion has been recommended to improve graft outcomes for marginal-quality kidneys (8). While the pump parameters and their trends are often used to discern kidney quality, this practice was challenged by Guarrera et al, who demonstrated reasonably good outcomes for kidneys with sub-optimal pump parameter values (9). Measuring protein biomarker levels in urine and pump perfusion solution is yet another emerging tool to assess kidney injury and quality. We and others have shown that certain biomarkers are associated with delayed graft function and even 1-year graft outcomes (8, 10-13).

The predictive power of traditional tools to evaluate organ quality over and above clinical donor characteristics remains questionable, but findings from these tools contribute to the most common reasons for discard. Some of these tools have been assessed individually in small, single-center studies, but high-quality evidence is lacking (14, 15). Thus, we conducted a sub-study within our large multicenter cohort to describe and evaluate the performance of traditional (biopsy reports and perfusion parameters) and newer (urine and perfusate protein biomarkers) organ quality assessment tools with regard to predicting early graft and patient outcomes in recipients of kidneys with KDPI 80.

Materials and Methods

Study design

The study cohort was selected from a prospective, multicenter, observational cohort study conducted via collaboration between 5 organ procurement organizations (OPO) and 5 academic centers. Yale University served as the sample and data coordinating center. The study was approved by the scientific review committee at each OPO and the institutional review board at each academic center. Protocols for managing deceased donors and obtaining consent for research were followed according to individual OPO guidelines. This study used data from the Organ Procurement and Transplantation Network (OPTN). The OPTN data system includes data on all donor, waitlisted candidates, and transplant recipients in the U.S. submitted by the members of the OPTN. The Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services provides oversight to the activities of the OPTN contractor.

Study population

Participating OPOs enrolled deceased kidney donors between May 2010 and December 2013. KDRI was calculated based on the following donor characteristics: age, race, height, weight, stroke as the cause of death, donation after cardiovascular determination of death (DCD) status, terminal serum creatinine (SCr), hepatitis C serostatus, and history of hypertension and diabetes. The KDRI for each donor was converted, as per convention, to obtain the KDPI based on the 2010 scaling factor (2). The revised allocation system for kidneys with KDPI 85 went into effect after our study enrollment had ended, and therefore, did not impact distribution of kidneys included in the study cohort. Donors with KDPI 80 were included in this study based on previously published discard data (3). Since this sub-study was designed to evaluate tools used to assess organ quality and their associations with graft outcomes, kidneys discarded due to anatomical/technical issues as reported by UNOS were excluded, ie, kidneys with vascular damage, diseased appearance, anatomical abnormalities, surgical damage, or not flushed properly. There were no dual kidney transplants in the current cohort. Donors were categorized into 3 groups based on the number of discarded kidneys: Group 1) none discarded, Group 2) 1 discarded and 1 transplanted, and Group 3) both discarded.

Donor management and sample collection

Donor management, kidney biopsy decisions, and machine perfusion were carried out based on individual OPO protocols. Ten mL of fresh urine was collected from all donors in the operating room just prior to organ procurement and was transported on ice to the individual OPOs. Wedge biopsies were performed in a subset of donors immediately after kidney procurement, and pathology services associated with these OPOs generated biopsy reports for review by potential transplant centers. The Life-Port Kidney Transporter (Organ Recovery Systems, Itasca, IL) and RM3 Renal Preservation System were used for individually- and en-bloc-perfused kidneys, respectively. All kidneys were pumped using pulsatile flow with 1L of Kidney Preservation Solution-1. Perfusate samples were collected immediately after placing on pump and then just before leaving the OPO, referred to as 'base' and 'post' samples, respectively. Both the urine and perfusate samples were temporarily stored at the OPO and shipped at least monthly to the sample coordinating center, where they were stored at −80°C until biomarker measurement. Additional details regarding collection of biopsy and perfusate samples can be obtained from our previous publications (10, 16).

Data collection

Donor characteristics and transplant details were abstracted by study staff from OPO donor charts and from the United Network for Organ Sharing (UNOS, the current OPTN contractor) database. Donor acute kidney injury (AKI) was defined according to AKI Network criteria based on admission to terminal SCr (irrespective of time between measurements and urine output cut offs) as follows: Stage 1, increase in SCr by 0.3 mg/dL or 1.5 to <2-fold increase; Stage 2, 2 to <3-fold increase; and Stage 3, 3-fold increase, or terminal SCr 4.0 mg/dL after a rise of at least 0.5 mg/dL (no donors were dialyzed) (17). OPO biopsy reports were retrospectively categorized via standardized adjudication for the

presence of acute tubular necrosis (ATN), arteriosclerosis, and interstitial fibrosis. The data on glomerulosclerosis for each biopsied kidney was retrieved from the OPTN/UNOS database. Each finding was graded as 'mild', 'moderate', or 'severe' if tissue involvement was noted to be <25%, 26-50% or >50%, respectively. The histological finding was considered absent only if the report specifically indicated it as absent or indeterminate. Perfusion parameters (pump duration, resistance, and flow) were abstracted from OPO perfusion records that were sent to the data coordinating center.

Measurements of biomarkers in urine and perfusate samples

Neutrophil gelatinase-associated lipocalin (NGAL) measurement was performed with the Architect platform (Abbott Diagnostics). Kidney injury molecule-1 (KIM-1) and Interleukin-18 (IL-18) were measured using the Meso Scale Discovery platform (Meso Scale diagnostics, Gaithersburg, MD, USA), which employs electrochemiluminescence detection combined with patterned arrays. Liver-type fatty acid binding protein (L-FABP) was measured using latex-enhanced immunoturbidimetry with anti-human L-FABP mouse monoclonal antibodies (Sekisui Medial Co. Ltd).

Supplemental Digital Content (SDC), Materials and Methods provides further information about assays for biomarker measurement.

Recipient Outcomes

Recipient outcomes up to 2 years were ascertained from the OPTN/UNOS database and were compared between study donor groups. Delayed graft function (DGF) was defined as any dialysis in the first week after transplantation. Graft failure was defined as return to chronic dialysis or a repeat transplant and was censored for patient death. Primary nonfunction (PNF) was defined as the need for continued/permanent dialysis beyond 90 days posttransplant and was considered a graft failure event. Estimated glomerular filtration rate (eGFR) was calculated from SCr reported in UNOS follow-up forms at 1- and 2-years using the Chronic Kidney Disease Epidemiology Collaboration equation (18). For recipients with graft failure, we imputed eGFR as 10 ml/min/1.73m^2. For recipients who died with a functioning graft, we carried forward the last available SCr to calculate eGFR. Due to incomplete reporting on acute rejection rates beyond 6 months and SCr at 2 years in the OPTN/UNOS database, analyses were not performed for these individual outcomes.

Effect of transplant center volume on utilization and outcomes of these kidneys was also studied. The 235 adult kidney transplant centers in United States were classified as high, medium, and low volume based on quartile of transplants performed during the study duration (>75%, 75-25% & <25% respectively).

Statistical analyses

Descriptive statistics were reported as mean (standard deviation) or median [interquartile range] for continuous variables and as frequency (percentage) for categorical variables. Donor characteristics, kidney biopsy findings, pump parameters, and urine and perfusate biomarkers were compared among the 3 donor study groups. We compared recipient outcomes between Group 1 (ie, the sister kidney was transplanted) and Group 2 (ie, the

sister kidney was discarded). Pairwise comparisons were made using Wilcoxon rank sum tests for continuous variables and Pearson's chi-square test for categorical variables. Generalized Estimating Equations for continuous outcomes; logistic model with Firth adjustment for rare events for categorical outcomes were used for adjusted analyses, accounting for both recipient factors (age, gender, race, duration of dialysis) and transplant center volume. Kaplan-Meier survival curves were constructed to compare composite outcomes of death or graft loss censored for death between the 2 groups. Cox proportional hazards models of time to death or graft loss censored for death were constructed and adjusted for differences in recipient age, gender, race, and duration of dialysis.

We generated a forest plot to compare 1-year eGFR between recipient groups categorized by the different quality assessment tools such as acceptance of the mate kidney for transplant, clinical AKI in the donor, biopsy findings, pump parameters, and KDPI. SAS 9.3 statistical software for Windows (SAS Institute, Cary, NC) was used for statistical testing, and all statistical tests and confidence intervals were 2-sided with a significance level of 0.05.

Results

Description of study cohort

Figure 1 shows the flowchart for deceased kidney donor inclusion into the present study. The characteristics of deceased donors included in our study were similar to that in UNOS during the same period (Table 1). Of the 676 kidneys included in the study cohort, 320 (47%) kidneys were discarded. Reasons for discard reported to UNOS were biopsy findings (59%), no recipient located (18%), poor organ function (8%), long cold time/warm time (4%), and unclear reasons (11%). The donors were grouped based on number of kidneys that were discarded: Group 1 (none discarded) consisted of 154 (46%) donors, Group 2 (1 kidney discarded and the other transplanted) had 48 (14%) donors, and Group 3 (both kidneys discarded) had 136 (40%) donors. Donor characteristics by study group are shown in Table 2. KDPI increased across the groups. Compared with donors in Group 1, those in Group 3 were older, frequently white, less likely to be diabetic, and had higher terminal SCr (all p-values <0.001). The presence of clinical AKI in the donor was not statistically different between groups.

Biopsy was performed in 619 (92%) of all kidneys, and the proportion biopsied did not significantly vary between study groups (Table 3). Kidneys from donor Group 3 had the highest proportion with moderate/severe arteriosclerosis, fibrosis, and glomerulosclerosis (Table 3). Of the kidneys that were biopsied and then discarded (292/619, 47%), 131 (45%) had absent or mild biopsy findings, and 161 (55%) had moderate/severe biopsy findings across any of the compartments. Sixty-four (40%) of the latter had isolated findings of glomerulosclerosis >20%, 34 (21%) had isolated moderate/severe arteriosclerosis, 6 (4%) had isolated moderate/severe fibrosis, and 57 (35%) had 2 or more abnormalities.

As shown in Table 3, 320 (47%) kidneys were placed on pump for a median of 8.3 [5.4-11.4] hours. Kidneys from Group 3 donors were less likely to have been placed on pump than kidneys from Group 1 donors (38% versus 56%, p<0.001). Median 1-hour renal resistance was highest and pump flow was lowest in kidneys from Group 3 donors. Of the

kidneys that were placed on pump and then discarded (125/320, 39%), 60 (48%) had 1-hour renal resistance >0.35 mm Hg/mL/min. Of the 320 kidneys that were discarded from the study cohort, 123 (38%) were both biopsied and pumped.

Urine samples were available from 335 donors (99%) for biomarker assays. As shown in Table 4A, there was no significant difference in urinary concentrations between study groups for NGAL, IL-18, KIM-1 and L-FABP. Of the 320 kidneys placed on pump, 28 were pumped en-bloc and were excluded from perfusate biomarker analyses. Perfusate samples were available for 292 kidneys (91% of those placed on pump) for the same biomarker assays. As shown in Table 4B, median base perfusate L-FABP was higher in pumped kidneys from Group 2 than Group 1 (18.7 [10, 35.6] versus 9.75 [2.8, 26.4] ng/ml, p=0.04). Otherwise, perfusate biomarker levels did not differ significantly between study groups.

Recipient Characteristics and Outcomes

Table 5 shows recipient characteristics for study groups 1 and 2. Recipients of kidneys from Group 2 were more frequently black race (p=0.019) and had shorter dialysis vintage (p=0.035). There was a trend in increased utilization of kidneys from Group 2 by high volume transplant centers. The overall incidence of DGF and PNF was 39% and 3%, respectively, and 6-month acute rejection rate was 8%. At 1 year, 33 (9%) patients had graft failure and 26 (7%) died with a functioning graft. Overall mean 1-year eGFR was 41.5 (19) mL/min/1.73m^2. Notably, there were no significant differences between study groups 1 and 2 for any of these early or 1- or 2-year recipient outcomes, even after adjusting for transplant volume and recipient factors.

Figure 2 shows there was no significant difference in the composite outcome of death or graft loss censored for death between the 2 groups (p=0.46). There appears to be an early increased risk of graft loss in the group where 1 kidney is discarded, but thereafter, the graft attrition rates appear similar between the 2 groups. There was no significant difference in time to death-censored graft loss between the groups; unadjusted HR 1.25 (0.69-2.25) and HR adjusted for recipient age, gender, race, and duration of dialysis 1.30 (0.72-2.37).

Figure 3 depicts median 1-year recipient eGFR for recipient groups based on different quality-assessment measures. Only glomerulosclerosis >20% was associated with worse allograft function at 1 year, p=0.046.

Discussion

This is the largest prospective, multicenter cohort study to evaluate simultaneously associations between several allograft quality assessment tools and outcomes (including discard) of deceased-donor kidneys with KDPI 80. Importantly, our overall cohort is reflective of the national kidney pool, with approximately 23% of donors having a KDPI 80 (19). Our results indicate that nearly half of potential kidney transplants with KDPI 80 are discarded. We have also shown that these kidneys almost universally undergo procurement biopsy (over 90%). The most common reason reported to OPTN/UNOS for kidney discard was "biopsy findings" (59% of those discarded), though 45% of the discarded kidneys in the current cohort had no more than minimal biopsy findings with

regard to arteriosclerosis, interstitial fibrosis, and glomerulosclerosis. For kidneys with minimal biopsy findings and yet discarded, common reasons for discard reported to UNOS were 'recipient not located' and 'poor organ function'. While biopsy information clearly plays an important role, our data support the idea that multiple factors likely influence the clinical decision to accept or refuse a kidney offer from a "high-KDPI" donor.

In addition, we found that nearly half of these "high-KDPI" kidneys were placed on pump (likely for therapeutic and quality assessment purposes as supported by long pump duration), yet more than one-third of the pumped kidneys were discarded. Of those kidneys that were pumped and discarded, only half had moderately elevated renal resistance >0.35 mm Hg/mL/min at 1 hour. This observation also provides evidence that clinicians do not predominantly consider pump parameters in isolation. As widely known, accepting or refusing a kidney offer for transplant is a multifactorial decision-making process.

We measured urinary and perfusate biomarkers for ischemic injury in nearly all of the donors and pumped kidneys in the current cohort. Levels of these protein biomarkers were not significantly different between donor groups, indicating that the degree of ischemic kidney injury does not appear to vary based on current organ acceptance patterns.

We demonstrated that kidneys from Group 2 donors (where 1 was transplanted and the other discarded) had higher KDPI values and inferior biopsy findings, yet their 1-year outcomes were similar to kidneys from Group 1 donors (where both were transplanted) (SDC Figure S1). We acknowledge that 1-year graft failure rates and death rates were higher and 1-year eGFRs are lower with use of high-KDPI kidneys (SDC Table S1), but this has to be balanced against the mortality of remaining on dialysis. Massie et al (5) reported that receipt of a high-KDPI kidney was associated with a transient period of increased posttransplant mortality, which was followed by several years of decreased mortality compared with remaining on dialysis awaiting transplant with a lower KDPI kidney. SDC Table S2 shows the biopsy pump findings were similar between kidneys in donors from Group 2 where 1 was transplanted and the mate was discarded. Barring recipient factors, it is likely that the outcome of the discarded mate kidney in Group 2 would be similar to the 1 transplanted.

Comparison of 1-year eGFR between recipient groups stratified by widely used quality-assessment indicators such as acceptance of the mate kidney for transplant, clinical AKI in the donor, biopsy findings, pump parameters, and KDPI suggested that none of the tools (with the possible exception of biopsy findings) are particularly useful on their own. Glomerulosclerosis >20% was associated with lower eGFR at 1-year in this cohort. There was also a trend towards lower 1-year eGFR among kidneys with biopsy findings of moderate to severe arteriosclerosis or fibrosis at organ procurement; however, the groups are too small to draw meaningful conclusions.

Strengths of the current study include detailed data collection from 5 OPOs for donor, biopsy, and pump information that is not available in the OPTN/UNOS database. We also examined a near complete set of donor urine and pump perfusate samples for novel biomarker measurements. As for limitations, despite this being the largest study of its kind to date, our focus on "high-KDPI" kidneys resulted in a relatively modest sample size. There

was lack in uniformity in obtaining, processing, interpreting, and reporting biopsy findings as well as in managing machine perfusion. Each OPO followed their own protocol for these procedures, which could explain their lack of correlation with graft outcomes. While 2 types of pumps were used for perfusion, 1 was exclusively used for en-bloc kidneys which were excluded from analyses on pump parameters and perfusate biomarkers. Biopsy reports were generated by multiple on-call pathologists at the individual donor hospitals, likely introducing some degree of inter-observer variability. While abnormal biopsy findings were reported to be the most common cause of discard, we do not have precise pathological reasons for declining the kidneys. The recipient outcomes are dependent on the accuracy and reliability of the OPTN/UNOS database. While we demonstrate that in Group 2 the mate and discarded kidneys were treated similarly and had similar quality (biopsy and pump parameters), the outcomes of the transplants also rely on recipient characteristics (eg, recipient demographics, medical history and comorbidities, socio-economic issues, compliance, cold ischemia time, antigen mismatch, etc.) and transplant center, which we cannot account for. There may be significant practice heterogeneity between participating transplant centers with regard to organ acceptance/refusal decisions (eg, recipient health status, prior kidney offers, number of recent poor outcomes in high-risk kidneys at a given transplant center) which are challenging to account for.

In summary, kidneys with KDPI 80 comprise the most resource consuming fraction of our donor kidney pool (ie, more often biopsied and/or pumped) and have the highest rates of discard. Consistent with findings of prior studies, our study confirms that current tools for quality indicators, ie, biopsy and pump perfusion, are not reliable in predicting graft outcomes. Biopsies and machine perfusion can prolong the cold ischemia time, which may be detrimental to the quality of kidneys that are already marginal. We need to carefully reconsider the use and interpretation of biopsy and machine perfusion results, especially when they have not been proven to impact graft outcomes. The newer tools to assess organ quality, ie, urinary and perfusate biomarkers, were also not discriminatory. While we show that certain kidneys with KDPI 80 may be used cautiously, we are unable to guide on which 1 to use. Our data suggest that kidneys with moderate to severe glomerulosclerosis (ie, >20%) should be considered cautiously due its association with lower eGFR. We acknowledge that in the current era of strict scrutiny by regulatory agencies, the increased graft failure rates for high-KDPI kidneys may not be permissive for all transplant centers. Nevertheless, given the current organ shortage and growing demand, certain kidneys with KDPI 80 may be beneficial cautiously, some possibly as dual kidney transplants, in order to expand the deceased-donor pool. The potential benefits of declining a kidney offer with a high KDPI in hopes of a future lower KDPI kidney should be balanced against the cumulative risk of dying while waiting for the next offer.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Abbreviations

AKI	acute kidney injury
ATN	acute tubular necrosis
CV	coefficient of variance
DCD	donation after cardiovascular determination of death
DGF	delayed graft function
eGFR	estimated glomerular filtration rate
IL-18	Interleukin-18
KDRI	kidney donor risk index
KDPI	kidney donor profile index
KIM-1	kidney injury molecule-1
L-FABP	liver-type fatty acid binding protein
NGAL	neutrophil gelatinase-associated lipocalin
SCr	serum creatinine
OPO	organ procurement organization
OPTN	Organ Procurement and Transplantation Network

| **PNF** | primary nonfunction |
| **UNOS** | United Network for Organ Sharing |

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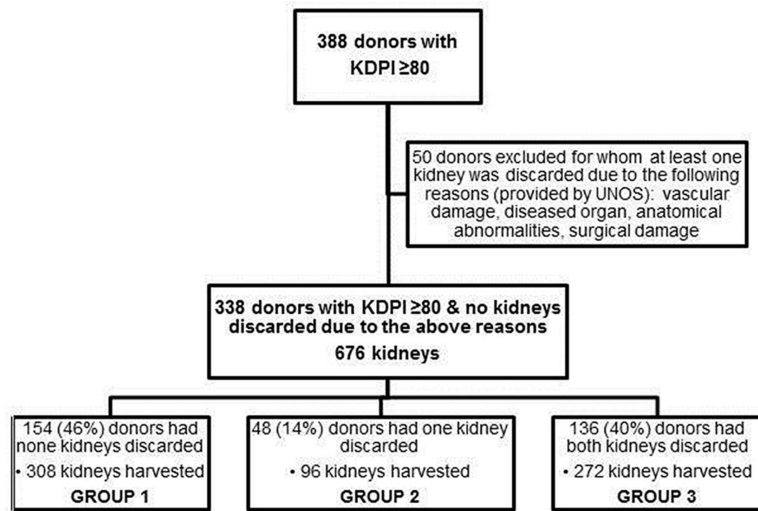
Figure 1. Enrollment of deceased kidney donors into the study cohort
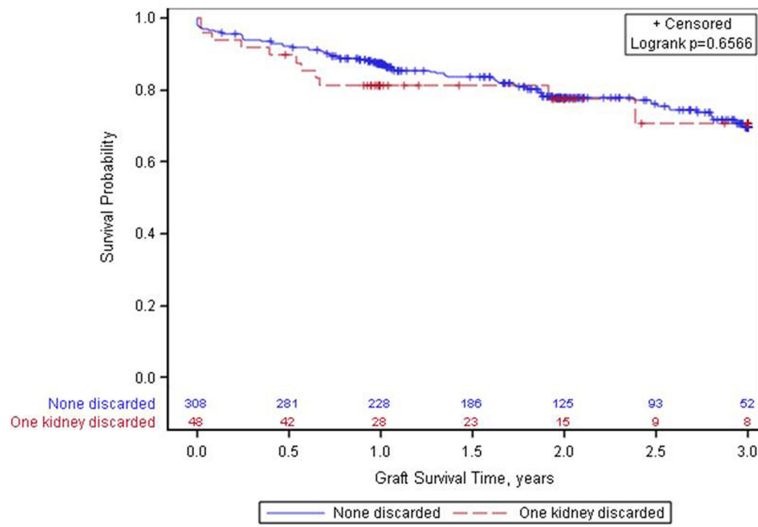
Figure 2. Kaplan-Meier graphs to assess differences in composite outcomes of death and graft loss censored for death

Points and error bars are median and interquartile range for 12-month estimated glomerular filtration rate (eGFR) by subgroups.
Dotted reference line indicates median 12-month eGFR for the cohort. P-values by Wilcoxon rank sum.
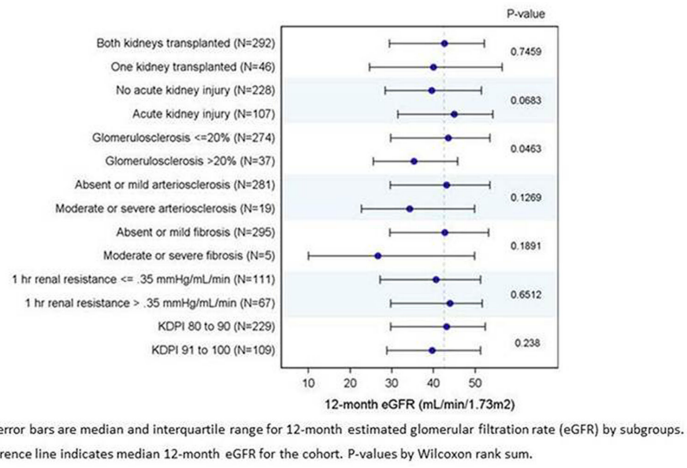
Figure 3. 12-month graft function in subgroups of kidneys with KDPI 80

Table 1

Comparison of donor characteristics between study cohort and all deceased donor kidneys with KDPI 80 reported to UNOS from same study period

		Study Cohort (n_{donor}=338)	UNOS (N_{donor}=6844)
KDPI		90 (6)	91 (6)
Age, years		60.9 (10.32)	57.5 (15.89)
Male		156 (46%)	3304 (48%)
Black race		104 (31%)	2096 (31%)
DCD		21 (6%)	345 (5%)
Hypertension		257 (76%)	5341 (78%)
Diabetes		63 (19%)	2300 (34%)
Height, cm		166 (13)	163 (25)
Weight, kg		81.6 (23)	79.1 (28)
Cause of death	Head trauma	35 (11%)	716 (10%)
	Anoxia	63 (19%)	1419 (21%)
	Stroke	228 (70%)	4608 (67%)
	Other	2 (1%)	101 (1%)
Terminal serum creatinine, mg/dL		1.3 (0.8)	1.8 (1.9)

KDPI, kidney donor profile index; DCD, donation after cardiovascular determination of death Values are mean (SD) or n (%).

Table 2

Donor characteristics by discard groups

		ALL (n_donor=338)	GROUP 1 None discarded (n_donor=154)	GROUP 2 One discarded (n_donor=48)	GROUP 3 Both discarded (n_donor=136)	P (GRP 1 vs. GRP 2)	P (GRP 1 vs. GRP 3)
KDPI		90 (6)	88.1 (6)	89.8 (5)	92.3 (6)	0.052	<.001
Age, years		60.9 (10.32)	58.6 (8.9)	59.3 (6.4)	64.1 (12.1)	0.958	<.001
Male		156 (46%)	66 (43%)	22 (46%)	68 (50%)	0.717	0.223
Black race		104 (31%)	55 (36%)	16 (33%)	33 (24%)	0.763	0.034
DCD		21 (6%)	10 (6%)	4 (8%)	7 (5%)	0.661	0.626
Hypertension		257 (76%)	118 (77%)	33 (69%)	106 (78%)	0.273	0.789
Diabetes		63 (19%)	49 (32%)	14 (29%)	0 (0%)	0.729	<.001
Cause of death	Head Trauma	35 (11%)	12 (8%)	9 (20%)	14 (11%)	0.015	0.573
	Anoxia	63 (19%)	27 (18%)	11 (24%)	25 (19%)		
	Stroke	228 (70%)	112 (74%)	25 (54%)	91 (69%)		
	Other	2 (1%)		1 (2%)	1 (1%)		
Terminal serum creatinine, mg/dL		1.28 (0.82)	1.07 (0.45)	1.27 (0.64)	1.51 (1.1)	0.072	<.001
Acute Kidney Injury	No	219 (66%)	105 (69%)	31 (66%)	83 (63%)	0.731	0.307
	Stage 1 or higher	113 (34%)	48 (31%)	16 (34%)	49 (37%)		

Values are mean (SD) or *n* (%).

P-values were obtained by Wilcoxon rank sum test for continuous variables and Chi-square test for categorical variables.

Table 3

Kidney biopsy findings and pump parameters by discard group

		ALL (N_kidney=676)	GROUP 1 None discarded (N_kidney=308)	GROUP 2 One discarded (N_kidney=96)	GROUP 3 Both discarded (N_kidney=272)	P (GRP 1 vs. GRP 2)	P (GRP 1 vs. GRP 3)
Kidney and Biopsy Characteristics							
Kidney Biopsy Taken		619 (92%)	283 (92%)	88 (92%)	248 (91%)	0.946	0.760
ATN[**]	Absent	308 (78%)	144 (80%)	40 (77%)	124 (75%)	0.013	0.407
	Mild	60 (15%)	27 (15%)	4 (8%)	29 (18%)		
	Moderate/Severe	28 (7%)	8 (4%)	8 (15%)	12 (7%)		
Arteriosclerosis	Absent	220 (37%)	119 (44%)	36 (42%)	65 (27%)	0.537	<.001
	Mild	279 (47%)	138 (51%)	42 (49%)	99 (41%)		
	Moderate/Severe	99 (17%)	16 (6%)	8 (9%)	75 (31%)		
Fibrosis	Absent	252 (42%)	137 (50%)	34 (40%)	81 (34%)	0.004	<.001
	Mild	300 (50%)	133 (49%)	46 (53%)	121 (51%)		
	Moderate/Severe	46 (8%)	3 (1%)	6 (7%)	37 (15%)		
Glomerulosclerosis	Indeterminate or less than 10%	378 (61%)	237 (84%)	63 (72%)	78 (31%)	0.020	<.001
	11%-20%	114 (18%)	38 (13%)	18 (20%)	58 (23%)		
	More than 20%	127 (21%)	8 (3%)	7 (8%)	112 (45%)		
Pump Parameters							
Pumped		320 (47%)	172 (56%)	46 (48%)	102 (38%)	0.174	<.001
Pump duration		9.5 [6.3, 12.9]	10.3 [5.9, 14.2] N=167	9.8 [7.0, 13.5] N=43	8.8 [6.7, 11.3] N=101	0.756	0.098
Renal resistance, mmHg/mL/min (hour 1)		0.3 [0.24, 0.41]	0.3 [0.24, 0.38]	0.29 [0.22, 0.41]	0.36 [0.27, 0.5]	0.932	<.001
Pump flow, mL/min (hour 1)		89 [68, 109]	93 [72, 111]	103 [74, 113]	77.5 [55.5, 102]	0.536	<.001
Perfusate collection time		8.25 [5.43, 11.42]	7.63 [5, 10.72]	9.13 [6.45, 11.92]	8.83 [7.5, 11.42]	0.114	0.011

Values are median [interquartile range] or *n*(%). "Absent" biopsy status also includes indeterminate findings.

[**] ATN reporting was described only in 64% of all biopsies. P-values were obtained by Wilcoxon rank sum test for continuous variables and Chi-square test for categorical variables.

Table 4A
Donor Urine biomarkers by discard group

	ALL (N_donor=338)	GROUP 1 None discarded (N_donor=154)	GROUP 2 One discarded (N_donor=48)	GROUP 3 Both discarded (N_donor=136)	P (GRP 1 vs. GRP 2)	P (GRP 1 vs. GRP 3)
At least 1 urine biomarker sampled	335 (99%)	152 (99%)	47 (98%)	136 (100%)	0.695	0.182
NGAL, ng/mL	60 [17.5, 199.6]	52.1 [17, 164.85]	61.3 [19.1, 123.9]	81.35 [17.45, 239.1]	0.934	0.116
IL-18, pg/mL	53.38 [22.66, 113.37]	49.16 [19.57, 109.39]	45.64 [21.26, 99.25]	62.61 [28.83, 125]	0.575	0.166
KIM-1, pg/mL	1411.28 [635.59, 3315.15]	1312.83 [644.57, 3305.89]	1374.13 [591.21, 3110.94]	1499.7 [635.36, 3472.53]	0.825	0.634
L-FABP, ng/mL	15.4 [5.2, 60]	12.8 [4.4, 56.4]	11.2 [4.8, 35.6]	19.8 [6.4, 71.2]	0.538	0.122

Values are median [interquartile range].

P-values were obtained by Wilcoxon rank sum.

Table 4B

Perfusate biomarkers by discard group

	ALL (N_kidney=320)	GROUP 1 None discarded (N_kidney=172)	GROUP 2 One kidney discarded (N_kidney=46)	GROUP 3 Both discarded (N_kidneyr=102)	P (GRP 1 vs. GRP 2)	P (GRP 1 vs. GRP 3)
At least 1 base perfusate biomarker sampled	274 (86%)	144 (84%)	23 (50%)	93 (91%)	0.005	0.081
At least 1 post perfusate biomarker sampled	215 (67%)	124 (72%)	23 (50%)	68 (67%)	0.868	0.343
Base NGAL, ng/mL	3.65 [0.3, 9.2]	4.15 [1.3, 9.15]	7.8 [4.4, 17.9]	3 [0, 8.4]	0.868	0.160
Post NGAL, ng/mL	9 [5, 16.6]	9 [4.6, 17.6]	3.38 [2.58, 7.44]	9.6 [6.65, 14.4]	0.969	0.497
Base IL-18, pg/mL	4.08 [2.58, 8.13]	4.34 [2.58, 8.24]	10.76 [7.65, 30.07]	4.27 [2.58, 7.75]	0.513	0.666
Post IL-18, pg/mL	12.18 [7.4, 18.85]	12.1 [6.22, 18.75]	58.96 [58.96, 58.96]	12.85 [8.47, 18.45]	0.717	0.367
Base KIM-1, ng/mL	58.96 [58.96, 58.96]	58.96 [58.96, 58.96]	61.53 [58.96, 96.69]	58.96 [58.96, 58.96]	0.102	0.285
Post KIM-1, ng/mL	58.96 [58.96, 110.76]	58.96 [58.96, 119.78]	6.6 [1.3, 12.4]	58.96 [58.96, 103.74]	0.710	0.923
Base L-FABP, ng/mL	8.4 [2.5, 23.5]	9.75 [2.8, 26.4]	18.7 [10, 35.6]	7.6 [1.4, 21.5]	0.042	0.123
Post L-FABP, ng/mL	3.65 [0.3, 9.2]	4.15 [1.3, 9.15]	7.8 [4.4, 17.9]	3 [0, 8.4]	0.203	0.578

Values are median [interquartile range].

P-values were obtained by Wilcoxon rank sum test for continuous variables.

Table 5
Recipient characteristics and outcomes by discard group

		ALL (N_kidney=356)	GROUP 1 None discarded (N_kidney=308)	GROUP 2 One kidney discarded (N_kidney=48)	P*	P – adjusted #1	P – adjusted #2
Age		62.54 (9.57)	62.35 (9.64)	63.77 (9.12)	0.556		…
Male		236 (66%)	208 (68%)	28 (58%)	0.210		…
Black race		145 (41%)	118 (38%)	27 (56%)	0.019		…
Duration of dialysis, months		50.65 (28.67)	52.02 (28.93)	42.11 (25.68)	0.035		…
Cause of ESRD	Diabetes	120 (34%)	102 (33%)	18 (38%)	0.787		
	Hypertension	126 (35%)	109 (35%)	17 (35%)			
	Other/unknown	30 (8%)	28 (9%)	2 (4%)			
	Glomerulonephritis	19 (5%)	16 (5%)	3 (6%)			
	Graft failure	61 (17%)	53 (17%)	8 (17%)			
Transplant center volume	Low	23 (6%)	21 (7%)	2 (4%)	0.079		
	Medium	104 (29%)	96 (31%)	8 (17%)			
	High	229 (64%)	191 (62%)	38 (79%)			
DGF		139 (39%)	118 (38%)	21 (44%)	0.477	0.471	0.463
PNF		12 (3%)	11 (4%)	1 (2%)	0.605	0.657	0.764
6-month acute rejection		28 (8%)	25 (8%)	3 (7%)	0.686	0.734	0.838
1-year death censored graft failure		33 (9%)	28 (9%)	5 (10%)	0.769	0.788	0.598
1-year recipient death		26 (7%)	21 (7%)	5 (10%)	0.382	0.343	0.313
1-year composite outcome (death or graft failure)		47 (7%)	38 (12%)	9 (9%)	0.194	0.211	
2-year death-censored graft failure		47 (15%)	41 (13%)	6 (13%)	0.877	0.924	0.938
2-year recipient death		36 (11%)	30 (10%)	6 (13%)	0.560	0.531	0.388
2-year composite outcome (death or graft failure)		69 (24%)	59 (19%)	10 (21%)	0.786	0.746	0.613
1-year eGFR, mL/min/1.73m^2		41.5 (19)	41.5 (18)	41.4 (22)	0.977	0.981	0.978

ESRD: end stage kidney disease, DGF: delayed graft function, PNF: primary non-function; Values are mean (SD) or n (%).

adjusted #1 – adjusted for transplant center volume (low/medium/high)

adjusted #2 – adjusted for recipient factors (age, male, race, duration of dialysis) and recipient transplant center volume (low/med/high)

*GEE model for continuous outcomes; logistic model with Firth adjustment for rare events for categorical outcomes