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Associations of deceased donor kidney injury with kidney discard and function after transplantation

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Abstract

Deceased-donor kidneys with acute kidney injury (AKI) are often discarded due to fear of poor outcomes. We performed a multicenter study to determine associations of AKI (increasing admission-to-terminal serum creatinine by AKI Network stages) with kidney discard, delayed graft function (DGF) and 6-month estimated glomerular filtration rate (eGFR). In 1632 donors, kidney discard risk increased for AKI stages 1, 2 and 3 (compared to no AKI) with adjusted relative risks of 1.28 (1.08–1.52), 1.82 (1.45–2.30) and 2.74 (2.0–3.75), respectively. Adjusted relative risk for DGF also increased by donor AKI stage: 1.27 (1.09–1.49), 1.70 (1.37–2.12) and 2.25 (1.74–2.91), respectively. Six-month eGFR, however, was similar across AKI categories but was lower for recipients with DGF (48 [interquartile range: 31–61] vs. 58 [45–75] ml/min/1.73m^2 for no DGF, P<0.001). There was significant favorable interaction between donor AKI and DGF such that 6-month eGFR was progressively better for DGF kidneys with increasing donor AKI (46 [29–60], 49 [32–64], 52 [36–59] and 58 [39–71] ml/min/1.73m^2 for no AKI, stage 1, 2 and 3, respectively; interaction P=0.05). Donor AKI is associated with kidney discard and DGF, but given acceptable 6-month allograft function, clinicians should consider cautious expansion into this donor pool.

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Disclosure

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Keywords

Kidney transplantation; deceased donor; acute kidney injury; organ discard; delayed graft function; allograft function

Introduction

The growing disparity between organ supply and demand for kidney transplantation necessitates ongoing efforts to both expand the donor pool and maximize the use of good quality organs. While there is an undeniable organ shortage for transplantation, there is also clear regional heterogeneity in deceased-donor organ acceptance and discard patterns (1). Such inconsistencies may be partially explained by differences in organ availability and need due to regional population variation in the number of potential donors and transplant candidates, which may be driven by variations in population density, socioeconomics, race/ethnicity and disease burden (2, 3). In addition to supply and demand differences, however, variance in clinician and/or center-level aggressiveness likely account for some of the regional variability in organ discard rates (4). In particular, acute kidney injury (AKI) in the donor can profoundly complicate an otherwise straightforward organ offer. For these cases, on-call clinicians often scrutinize donor renal function beyond the single "terminal" serum creatinine (SCr) value and consider changes in SCr throughout the hospitalization relative to light-microscopic biopsy findings and urine output (UOP) at the time of procurement.

Donor AKI could plausibly lead to adverse outcomes in the transplant recipient. Severe ischemic AKI often results in the need for renal replacement therapy in the recipient until the kidney can repair itself. These “delays” in functional recovery of injured allografts lead to prolonged hospital stays and increased costs due to dialysis, or even primary non-function of the allograft in the most severe cases. With regard to longer-term function, preclinical studies have linked episodes of AKI with progressive renal fibrosis and the development of chronic kidney disease (5). Human studies have also shown associations between clinically-defined AKI and poor long-term renal outcomes (6).

Our group recently reported a lack of association between pre-implant (procurement) biopsy-reported acute tubular necrosis (ATN) and the development of delayed graft function (DGF) or early graft failure (7). Given evidence of the limited value of pre-implant biopsy reported ATN, we performed the current multicenter cohort study to evaluate potential associations between clinically-defined donor AKI (categorized by changes in SCr from admission to the terminal value) and important transplant outcomes, namely kidney discard, DGF and 6-month allograft function. We hypothesized that the severity of donor AKI would be independently associated with increasing rates of organ discard and DGF as well as worse 6-month allograft function.

Materials and Methods

This is a prospective, multicenter, observational cohort study involving clinical data from deceased kidney donors from five organ procurement organizations (OPOs) between May 2010 and December 2013. Donor characteristics and clinical variables were abstracted from

OPO donor charts. Clinical data for all recipients of the kidneys from these donors were obtained from the United Network for Organ Sharing (UNOS) database. Personnel at each OPO followed institutional protocols for managing deceased donors and obtaining consent for research from donor surrogates. The scientific review committees for participating OPOs as well as the institutional review boards for the participating investigators approved the study. Donors aged 16 years or older were included if at least one kidney was procured for potential transplantation, resulting transplants were for separate recipients (i.e., dual kidney transplants into the same recipient were excluded), and both admission and terminal SCr values were available for analysis.

As the primary exposure variable, donor AKI was defined according to AKI Network criteria based on admission to terminal SCr (irrespective of time between measurements and UOP 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) (8). We calculated the kidney donor risk index (KDRI) as described by Rao et al. (9, 10). We converted the KDRI score for each donor, as per convention (9), to obtain the kidney donor profile index (KDPI). We also reviewed available pathology reports from procurement kidney biopsies with regard to both glomerulosclerosis and ATN, which we defined as present if any histologic evidence of acute tubular injury was mentioned in the report (without regard to severity). Reports that specified the absence of ATN or had no mention of tubular injury were categorized as no ATN. The following outcomes were analyzed as recorded in the UNOS database: discard (kidney procured for transplant but not transplanted), DGF (any dialysis in the first week of transplantation), 6-month estimated glomerular filtration rate (eGFR, calculated from 6-month SCr via the Chronic Kidney Disease Epidemiology Collaboration equation) (11) and death-censored graft failure (return to chronic dialysis or retransplantation).

We evaluated 6-month eGFR as the primary outcome of interest and considered kidney discard and DGF as secondary outcomes. Understanding there would be relatively low event rates and an unavoidable delay in UNOS reporting at this point, we evaluated available 12-month eGFR and death-censored graft failure as currently recorded for study transparency and to explore possible trends for the cohort. We used exclusion to accommodate for missing data, with the notable exception for missing 6-month eGFR values related to graft failure or recipient death before 6 months. For the few recipients with UNOS-reported death-censored graft failure prior to 6 months, eGFR was imputed as 10 ml/min/1.73m^2. We carried forward the last available SCr value to calculate 6-month eGFR in the rare event of recipient death before 6 months.

Descriptive statistics were reported as mean (standard deviation) or median [interquartile range] for continuous variables and as frequency (percentage) for categorical variables. Donor and recipient characteristics and outcomes as well as procurement kidney biopsy reports for ATN and glomerulosclerosis ≥20% were compared between donor AKI stages using the Kruskall-Wallis test for continuous variables and Pearson's Chi-Square test for categorical variables. We also compared the rates of biopsy-reported ATN with donor AKI in the subset of donors that had at least one procurement kidney biopsy. We then compared donor characteristics and biopsy results between donors for which neither, one, or both

kidneys were discarded. Using modified Poisson regression as described by Zou (12), we modeled the relative risks (RRs) of kidney discard and DGF as a function of donor AKI. Donor AKI was operationalized as a dichotomous exposure (any AKI compared with no AKI) as well as a multilevel categorical exposure according to stage (no AKI as reference), adjusting for all donor characteristics that comprise the KDRI except for terminal SCr (already considered for the AKI covariate). We performed further adjustment of the kidney discard model with the addition of procurement kidney biopsy performed (dichotomous) and machine pump perfusion used (dichotomous) as well as both of these covariates plus cold ischemia time in hours for the DGF model. We accounted for the cluster effect of paired kidneys from the same donor via generalized estimating equations for the Poisson models (13).

Similarly, we utilized multivariable linear regression to test for associations between donor AKI and 6-month eGFR. Given its well-described effect on subsequent outcomes, we performed *a priori* stratified analyses according to DGF status and formally tested for interaction between DGF and donor AKI stage on 6-month eGFR. We fit Cox proportional hazards models to evaluate the effect of donor AKI on death-censored graft failure. We used SAS 9.3 statistical software for Windows (SAS Institute, Cary, NC), and all statistical tests and confidence intervals were two-sided with a significance level of 0.05.

Results

After exclusions, a total of 1632 deceased donors were available for analysis, of which 443 (27%) had some degree of AKI. A flowchart for donor enrollment, exclusions and AKI stages along with the numbers of kidney transplants and discards is shown in Figure 1. There were 697 kidney discards (21% of all potential transplants), and 800 (31%) recipients experienced DGF. Median follow-up time for the entire cohort was 625 [345, 856] days, and 185 (7%) death-censored graft failures and 180 (7%) recipient deaths have been reported.

Donor and recipient characteristics by donor AKI stage are shown in Table 1. Donors with higher AKI stages were less likely to have both kidneys transplanted, and more procurement kidney biopsies were performed for donors with higher AKI stages. Compared to donors without AKI, donors with stage 3 AKI tended to be younger but had similar mean KDRI and higher mean admission eGFR. The kidneys from donors with AKI were more often transported via machine pump perfusion, had longer cold ischemia times and were transplanted into older recipients.

As shown in Table 1, the proportion of donors with biopsy-reported ATN significantly increased according to AKI stage. However, within the subset of 909 donors that had at least one procurement biopsy report (which included donors resulting in kidney discards), there was disagreement between ATN and AKI (Table S1). The majority (59%) of the donors with biopsy-reported ATN did not have clinically-defined AKI based on changes in SCr values.

A total of 171 (10%) donors had a single kidney discard, and both kidneys were discarded from 263 (16%) donors (Table 2). The proportion of donors with AKI differed significantly

by kidney discard status (23%, 36% and 38% for none, one or both kidneys discarded, respectively; P<0.001), as did nearly all other donor characteristics. Table 2 also shows the reported reasons for discard, of which 'biopsy' was most common. From the individual kidney perspective, the rate of discard was higher for kidneys from donors with AKI (30% vs. 18% for kidneys from donors without AKI, P<0.001) (Table 3). Donor AKI was independently associated with kidney discard with an adjusted RR of 1.55 (95% confidence interval 1.34–1.79). In addition, a dose-response relationship was apparent for increasing donor AKI stage on the risk of discard with adjusted RRs of 1.28 (1.08–1.52), 1.82 (1.45–2.30) and 2.74 (2.0–3.75), respectively.

Results for DGF are shown in Table 4. The DGF rate progressively increased from 28% for kidneys from donors without AKI to 34%, 52% and 57% for donor AKI stage 1, 2 and 3, respectively (trend test P<0.001). The adjusted RR of DGF for any donor AKI was 1.48 (1.30–1.68), and a dose response was again noted for increasing AKI stage with adjusted RRs for the development of DGF of 1.27 (1.09–1.49), 1.70 (1.37–2.12) and 2.25 (1.74–2.91), respectively.

Allograft function at 6 months was not statistically different by donor AKI on its own (Table 5). Median 6-month eGFR for all recipients was 55 [40, 71] ml/min/1.73m^2. Following stratification by DGF status, however, some differences were observed between donor AKI stages. For recipients that did not experience DGF, allograft function at 6 months was well-preserved and did not vary significantly by donor AKI stage with an overall 6-month eGFR of 58 [45, 75] ml/min/1.73m^2. Overall 6-month eGFR for recipients with DGF was lower than those without DGF at 48 [31, 61] ml/min/1.73m^2 (P<0.001), but allograft function was progressively better for the recipients with DGF that received kidneys from donors with increasing stages of AKI (Table 5 and Figure 2). Formal interaction testing via linear regression demonstrated a statistically significant 5 ml/min/1.73m^2 average increase in 6-month eGFR for the combination of any donor AKI and the development of DGF (P=0.05 for the interaction term).

While follow-up data beyond 6 months are not yet complete for the cohort, an interaction was again observed between donor AKI and DGF on subsequent allograft function for recipients with available 12-month eGFR values (Table S2). Compared with no donor AKI, the risk of death-censored graft failure as currently reported was not significantly different for any donor AKI [adjusted hazard ratio (HR) of 1.23 (0.89–1.71)], nor by donor AKI stage [adjusted HRs of 1.28 (0.88–1.87), 0.98 (0.48–2.0) and 1.35 (0.66–2.77), respectively for AKI stage 1, 2 and 3]. Furthermore, no associations between donor AKI and death-censored graft failure were noted after stratifying by DGF status (not shown); however, DGF itself had an adjusted HR for death-censored graft failure of 3.09 (2.30–4.17).

Discussion

The expanding organ transplant shortage has naturally led to more aggressive organ procurement considerations; however, transplanting clinically injured kidneys raises logical concerns about poorer outcomes and increasing healthcare costs. To critically examine the issue of AKI in deceased donors, we performed the largest multicenter observational study

of its kind to date in order to assess additional donor information that is not available in the UNOS database (i.e., changes in SCr). We found that clinically-defined AKI is common in deceased kidney donors and that the severity of AKI is, as expected, associated with increasing rates of kidney discard as well as DGF. Accounting for additional donor and transplant characteristics, the risk of discard as well as the risk of DGF was over 2-fold higher for kidneys from donors with stage 3 AKI compared with no AKI. However, our primary hypothesis about a relationship between donor AKI and poorer 6-month allograft function was not substantiated by these data. Furthermore, we found evidence for a favorable interaction between donor AKI and DGF on subsequent 6-month eGFR.

In native kidneys, the severity of AKI tends to associate with poorer clinical outcomes including the development of chronic kidney disease and end-stage renal disease (6). In kidney transplantation, DGF is the traditional surrogate exposure for severe AKI at the time of transplant and is a known risk factor for poorer allograft function and survival (14–16). Based on this prior evidence, it seemed reasonable to suppose that even earlier episodes of renal injury in the donor immediately leading up to the period of complete ischemia during organ transport would have detrimental effects. While there is credence to the argument that organ discard and dialysis decisions immediately post-transplant are subjective outcomes (i.e., influenced by the accepting clinician's knowledge about the donor), the fact that we observed no detrimental effect of donor AKI on an objective measure of allograft function at 6 months post-transplant provides reasonably solid evidence in support of the current clinical practice for utilizing these kidneys. One can only speculate, however, about potential transplant outcomes for discarded kidneys in the current cohort, which is an unavoidable limitation of the observational study design. It is quite possible that the discarded AKI kidneys would have had worse outcomes than those that were selected for transplantation.

Data from trials that effectively reduce donor AKI at procurement and include 'protocolized' organ acceptance algorithms with prospective recipient follow-up would advance our understanding of the true impact of donor AKI. Such research protocols are logistically quite difficult, however, considering the level of cooperation needed between multiple stakeholders, including informed consent for donor surrogates as well as potential recipients. Nonetheless, a growing body of literature from observational studies does address the relative importance of deceased-donor AKI. Using specific cutoffs for the single terminal SCr value (rather than changes in SCr) to define donor AKI severity within the Scientific Registry of Transplant Recipients database, Kayler *et al.* described progressively worse long-term allograft survival for recipients of expanded-criteria donor (ECD) kidneys with increasing "AKI" severity but not for standard-criteria donor (SCD) kidneys (17). The authors also determined that the risks for kidney discard and DGF were greater for these "AKI" kidneys regardless of ECD/SCD status. More recently, Klein *et al.* also used the single terminal SCr value to define AKI (>1.5 mg/dl) in a single-center cohort of 1235 deceased donors and noted higher rates of DGF but no differences in 1-year patient, allograft or rejection-free survival (18). The handful of other studies conducted to address this issue appropriately utilized changes in SCr values to define donor AKI but were all single-center and had relatively small numbers (19–26). All but one of these prior studies reported higher

rates of DGF and no discernable differences in intermediate or longer-term allograft function or survival. While our results corroborate these prior studies, our multicenter data also help to explain these somewhat counterintuitive findings considering the evidence for AKI's detrimental effect on subsequent function in native kidney (non-transplant) settings.

We found that while kidneys from donors with AKI (which have been selected for transplant) are at increased risk for DGF, they appear to provide similar 6-month allograft function compared with kidneys from donors without AKI. The lack of association with this continuous outcome cannot be dismissed as a power issue, though such an argument could have been considered had we specified a dichotomous, low-event outcome like graft failure within a period for which we had complete follow-up data (i.e., 6 months). Finding a significant *favorable* interaction between donor AKI and DGF on 6-month eGFR was unexpected, however, and suggests that current AKI kidney utilization practices are quite reasonable for selected kidney-recipient matches. In their report of a protocol to utilize AKI kidneys, Farney *et al.* noted a similar interaction between donor AKI and DGF on subsequent allograft outcomes (21). They found that donor AKI nullified the deleterious effect of DGF on allograft survival. This does not mean that donor AKI directly improves long-term allograft function. Rather, it appears to modify the effects of DGF. The clinical interpretation could be that DGF resulting from donor AKI is less worrisome (in terms of long-term function) than DGF from other causes.

An epidemiological explanation for this apparent effect modification is that AKI kidneys selected for transplant predominantly come from otherwise high-quality donors. This also likely explains the association we observed between donor AKI and organ discard. Donors for which both kidneys were discarded had the highest AKI burden, but they were also biopsied more frequently and had more significant glomerulosclerosis than biopsied donors that resulted in transplants. High rates of biopsy likely reveal underlying concerns about donor quality, which may or may not be related to increasing SCr values. Thus, one could argue that clinical gestalt drives discard decisions, with histopathologic findings sealing the fate of the unrealized transplant. Nonetheless, our data indicate that among the kidneys selected for transplant, those with AKI tended to come from younger donors that were less likely to die from stroke (i.e., were likely otherwise higher quality) than the non-AKI kidneys.

Besides the obvious donor selection issue, however, other potential mechanistic explanations for the interaction between donor AKI and DGF on 6-month allograft function are worthy of further investigation. Ischemic preconditioning is a particularly intriguing possibility. The inflammatory/repair pathways initiated in kidneys from donors with AKI prior to procurement may make them more prone to reperfusion injury and the development of DGF. Those previously activated pathways, however, could potentially make AKI kidneys more capable of subsequent successful repair with better intermediate and long-term function than kidneys from donors without AKI that develop DGF from other causes.

Limitations of the current study predominantly stem from its observational design. We adjusted for multiple donor factors using the variables that comprise the KDRI, but residual confounding is still possible given transplant centers accept or reject organ offers based on

center-specific protocols and clinical judgement. While we consider the multicenter design a strength with regard to generalizability, study outcomes were limited to available UNOS database information. In addition, we do not have complete follow-up data beyond 6 months; however, we specifically chose 6-month eGFR as the primary outcome for several reasons. First, 6 months is early enough post-transplant to be considered representative of baseline allograft function and reflective of kidney (donor) quality at the time of transplant. Second, the 6-month time-point is sufficiently beyond the period of rapid fluid shifts, variable allograft recovery phases and frequent adjustments to immunosuppression. Third, prior data demonstrate the relative stability in allograft function beyond 6 months in the current transplant era (27). Lastly, we reasoned that if any donor-level characteristic were to have a large effect on long-term allograft survival, we should begin to see a trend for that effect by 6 months (28). Notwithstanding, the fact that results were relatively unchanged using available 12-month, rather than complete 6-month, eGFR data indicates the overall robustness of these findings.

In conclusion, clinical situations that involve patient death in the hospital and considerations for organ donation can be quite variable, and as the current study shows, AKI is a common occurrence in these scenarios. While organ allocation is a regimented process by design, organ acceptance or decline is a decision based on clinical judgment, which can vary in complexity depending on the situation and a large number of factors. Donor AKI is an influential factor, but as has been shown with other donor risk factors like DCD status (29, 30), our data also indicate that current acceptance practices for AKI kidneys yield (eventually) acceptable allograft function despite higher DGF rates. A separate but related question that deserves proper investigation is whether novel AKI biomarkers provide added decision-making value in this context, as limited data from our group and others would suggest (31–34). Better understanding of the relative importance of and interaction between certain traditional risk factors, like donor AKI and DGF, will likely facilitate the optimization of organ allocation, acceptance and transplantation moving forward. Nonetheless, our current findings suggest that there is room for cautious expansion of the deceased-donor kidney pool by considering more aggressive utilization of these kidneys for transplantation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

AKI	acute kidney injury
AKIN	Acute Kidney Injury Network
ATN	acute tubular necrosis
DCD	donation after cardiac death
DGF	delayed graft function
ECD	expanded-criteria donor
eGFR	estimated glomerular filtration rate
HR	hazard ratio
KDRI	kidney donor risk index
KDPI	kidney donor profile index
OPO	organ procurement organization
OPTN	Organ Procurement and Transplantation Network
RR	relative risk
SCD	standard criteria donor
SCr	serum creatinine
UNOS	United Network for Organ Sharing

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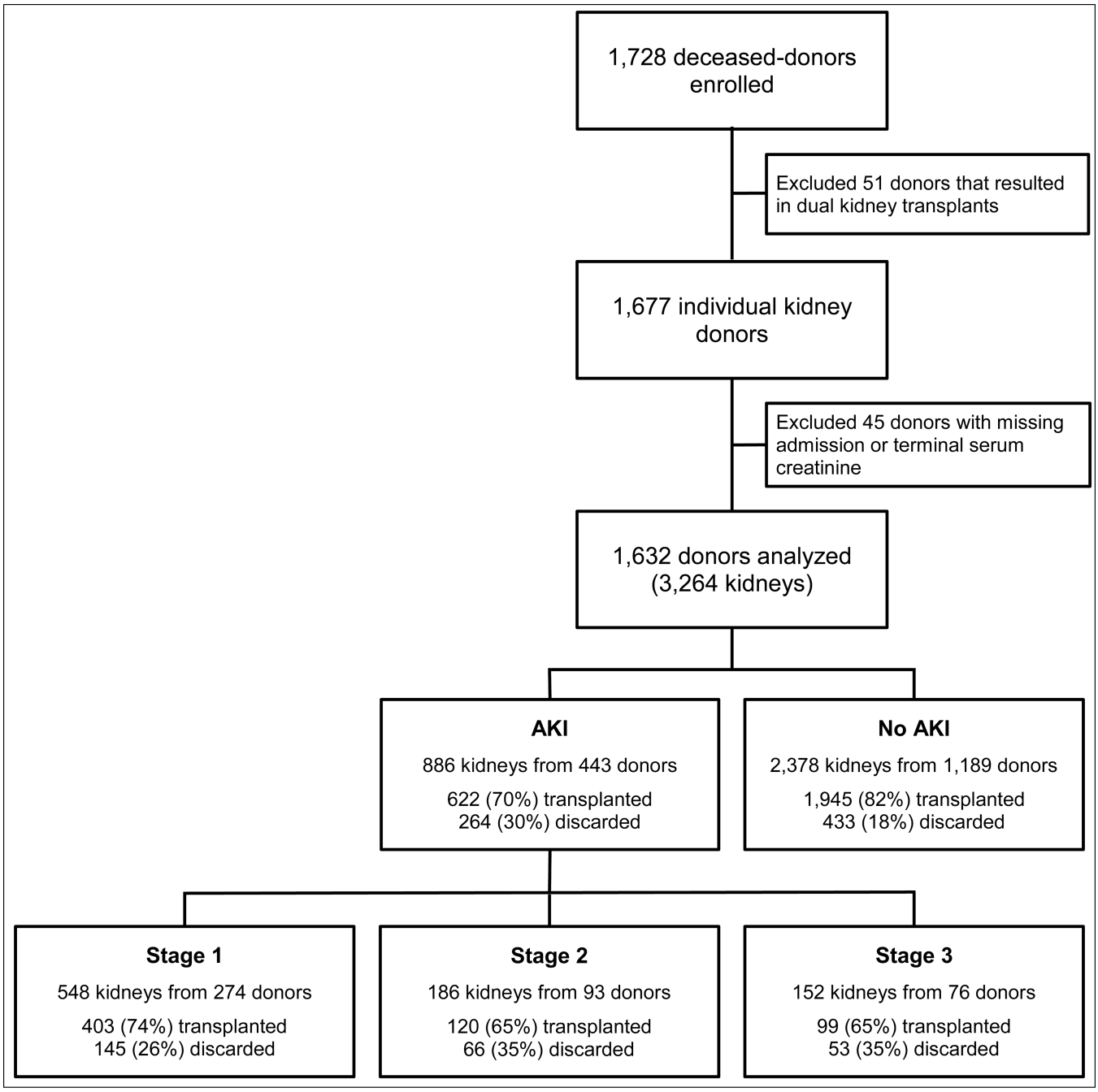

Figure 1.
Flowchart showing distribution of acute kidney injury (AKI) among deceased organ donors

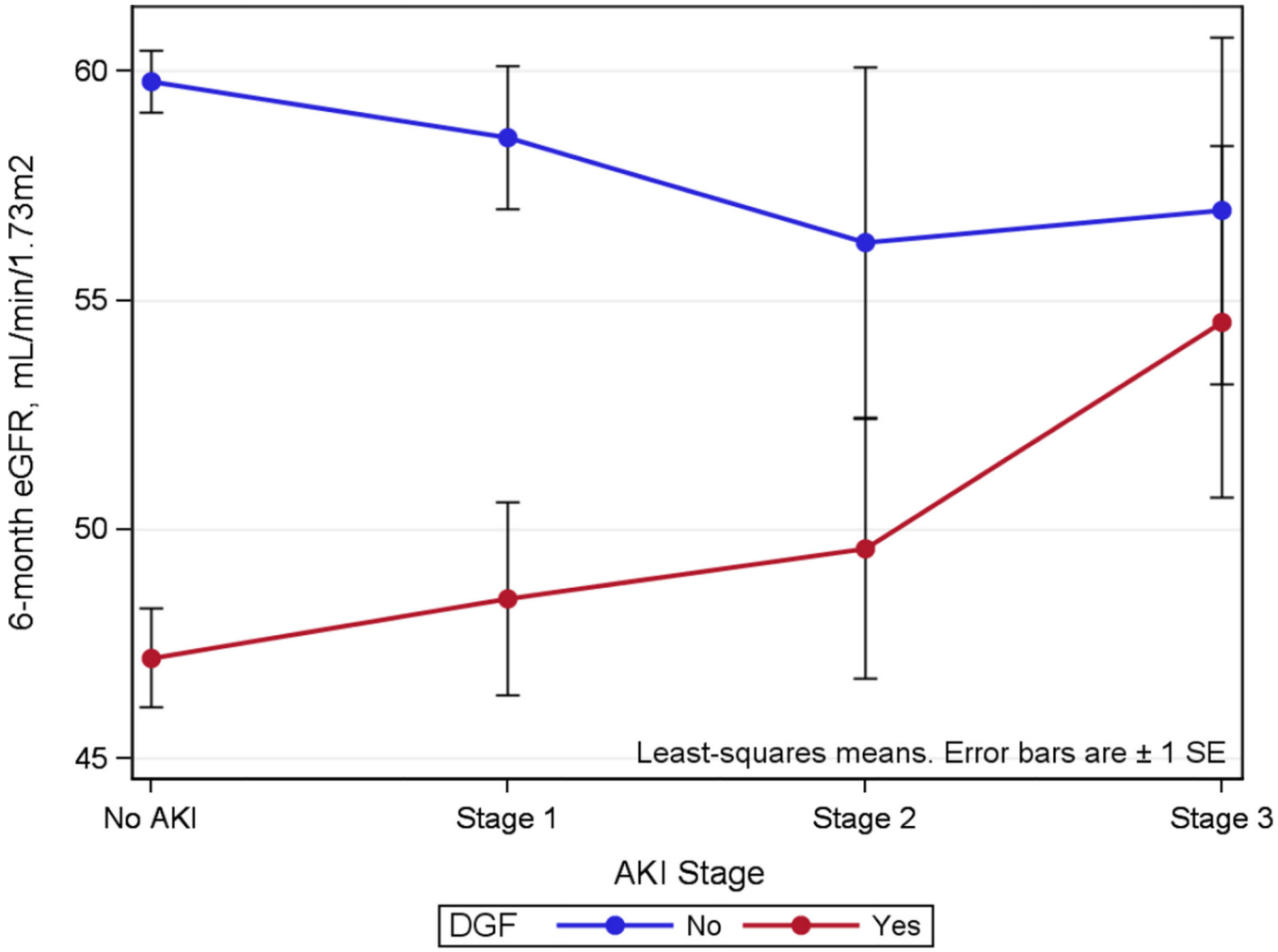

Figure 2.

Linear regression interaction plot for donor acute kidney injury (AKI) and delayed graft function (DGF) on predicted 6-month estimated glomerular filtration rate (eGFR). P=0.05 for the interaction term (any AKI*DGF).

Table 1

A: Donor characteristics by donor AKI stage							
Variable		**ALL (N=1369)**	**No AKI (N=1027)**	**Stage 1 (N=218)**	**Stage 2 (N=68)**	**Stage 3 (N=56)**	**P-value** [1]
Age, years		41 (15)	41 (16)	41 (14)	40 (14)	35 (13)	**0.040**
Male		829 (61%)	613 (60%)	139 (64%)	39 (57%)	38 (68%)	0.423
Black race		220 (16%)	138 (13%)	58 (27%)	13 (19%)	11 (20%)	**<.001**
Weight, kg		82 (23)	81 (22)	88 (24)	87 (32)	84 (23)	**0.001**
Hypertension		406 (30%)	287 (28%)	83 (38%)	24 (35%)	12 (21%)	**0.008**
Diabetes		136 (10%)	95 (9%)	30 (14%)	6 (9%)	5 (9%)	0.234
Cause of death	Head trauma	412 (31%)	314 (31%)	67 (31%)	16 (24%)	15 (27%)	**0.030**
	Anoxia	467 (35%)	342 (34%)	69 (32%)	24 (36%)	32 (58%)	
	Stroke	436 (33%)	329 (33%)	74 (34%)	25 (38%)	8 (15%)	
	Other	21 (2%)	15 (2%)	5 (2%)	1 (2%)		
Hepatitis C seropositive		48 (4%)	37 (4%)	6 (3%)	3 (4%)	2 (4%)	0.906
ECD		250 (18%)	180 (18%)	50 (23%)	13 (19%)	7 (13%)	0.184
DCD		228 (17%)	184 (18%)	27 (12%)	12 (18%)	5 (9%)	0.090
KDRI		1.28 (0.41)	1.25 (0.41)	1.4 (0.41)	1.4 (0.34)	1.26 (0.37)	**<.001**
KDPI, %		66 (24)	64 (24)	73 (21)	76 (16)	67 (19)	**<.001**
Admission to procurement, days		4 (7)	4 (8)	3 (3)	4 (5)	2 (2)	0.097
Admission SCr, mg/dL		1.09 (0.6)	1.1 (0.64)	1.05 (0.35)	0.89 (0.32)	1.2 (0.84)	**0.008**
Admission eGFR, ml/min/1.73m^2		85 (29)	84 (28)	87 (27)	99 (33)	90 (43)	**0.004**
Terminal SCr, mg/dL		1.17 (0.88)	0.87 (0.35)	1.58 (0.52)	2.08 (0.81)	4.05 (1.81)	**<.001**
Admission SCr > Terminal SCr		655 (48%)	655 (64%)				**<.001**
Terminal urine output, ml/hr		187 (148)	190 (150)	204 (147)	156 (116)	116 (126)	**<.001**
Machine perfusion used [2]		554 (40%)	387 (38%)	90 (41%)	41 (60%)	36 (64%)	**<.001**
Procurement biopsy performed [2]		672 (49%)	452 (44%)	121 (56%)	50 (74%)	49 (88%)	**<.001**
Biopsy report describing acute tubular necrosis in at least 1 kidney		108 (8%)	62 (6%)	22 (10%)	11 (16%)	13 (23%)	**<.001**
Biopsy report describing ≥20% glomerulosclersosis in at least 1 kidney		39 (3%)	26 (3%)	8 (4%)	3 (4%)	2 (4%)	0.657
Kidneys transplanted	1	171 (12%)	109 (11%)	33 (15%)	16 (24%)	13 (23%)	**<.001**

A: Donor characteristics by donor AKI stage							
Variable		**ALL (N=1369)**	**No AKI (N=1027)**	**Stage 1 (N=218)**	**Stage 2 (N=68)**	**Stage 3 (N=56)**	**P-value** [1]
	2	1198 (88%)	918 (89%)	185 (85%)	52 (76%)	43 (77%)	

B: Recipient and transplant characteristics by donor AKI stage							
Variable		**ALL (N=2567)**	**No AKI (N=1945)**	**Stage 1 (N=403)**	**Stage 2 (N=120)**	**Stage 3 (N=99)**	**P-value** [1]
Age, years		53 (15)	52 (15)	55 (14)	52 (13)	55 (14)	**0.008**
Male		1576 (61%)	1180 (61%)	249 (62%)	75 (63%)	72 (73%)	0.117
Black race		1012 (39%)	759 (39%)	156 (39%)	57 (48%)	40 (40%)	0.316
Hispanic ethnicity		289 (11%)	221 (11%)	40 (10%)	20 (17%)	8 (8%)	0.154
Cause of ESRD	Diabetes	750 (29%)	564 (29%)	125 (31%)	28 (23%)	33 (33%)	0.680
	Hypertension	695 (27%)	515 (26%)	111 (28%)	42 (35%)	27 (27%)	
	Glomerulonephritis	422 (16%)	324 (17%)	65 (16%)	18 (15%)	15 (15%)	
	Graft failure	162 (6%)	129 (7%)	18 (4%)	9 (8%)	6 (6%)	
	Other or unknown	538 (21%)	413 (21%)	84 (21%)	23 (19%)	18 (18%)	
Dialysis duration, months		52 (36)	51 (36)	52 (37)	56 (37)	48 (35)	0.256
Preemptive transplant		290 (11%)	228 (12%)	44 (11%)	13 (11%)	5 (5%)	0.227
Pre-transplant blood transfusion		443 (17%)	335 (17%)	67 (17%)	22 (18%)	19 (19%)	0.925
Kidney pumped		1019 (40%)	718 (37%)	165 (41%)	72 (60%)	64 (65%)	**<.001**
Cold ischemia time, hours		15.4 (7.2)	15 (7)	15.5 (7.5)	18.6 (7.2)	18.8 (8.7)	**<.001**
HLA mismatch level	0	160 (6%)	130 (7%)	20 (5%)	6 (5%)	4 (4%)	0.599
	1	20 (1%)	18 (1%)	2 (0%)			
	2	87 (3%)	66 (3%)	14 (3%)	2 (2%)	5 (5%)	
	3	312 (12%)	232 (12%)	52 (13%)	15 (13%)	13 (13%)	
	4	676 (26%)	520 (27%)	101 (25%)	33 (28%)	22 (22%)	
	5	876 (34%)	670 (35%)	135 (34%)	35 (29%)	36 (37%)	
	6	430 (17%)	306 (16%)	78 (19%)	28 (24%)	18 (18%)	

Values are mean (SD) or n (%). AKI, acute kidney injury; ECD, expanded-criteria donor; DCD, donation after cardiac death; KDRI, kidney donor risk index; KDPI, kidney donor profile index; SCr serum creatinine; eGFR, estimated glomerular filtration rate.

[1] Kruskal-Wallis test for continuous variables and Chi-Square test for categorical variables

[2]Variable considered at the level of the donor (i.e., information available for at least one of the kidneys from a particular donor)

Values are mean (SD) or n (%). AKI, acute kidney injury; ESRD, end-stage renal disease; HLA, human leukocyte antigen.

[1]Kruskal-Wallis test for continuous variables and Chi-Square test for categorical variables

Table 2

Donor characteristics by number of kidneys discarded

Variable		ALL (N=1632)	None Discarded (N=1198)	One Discarded (N=171)	Both Discarded (N=263)	P-value [1]
AKI stage	Any AKI	443 (27%)	280 (23%)	63 (36%)	101 (38%)	**<.001**
	Stage 1	274 (17%)	185 (15%)	33 (19%)	56 (21%)	
	Stage 2	93 (6%)	52 (4%)	16 (9%)	25 (10%)	
	Stage 3	76 (5%)	43 (4%)	13 (8%)	20 (8%)	
Age, years		43 (16)	39 (15)	50 (12)	57 (15)	**<.001**
Male		974 (60%)	737 (62%)	92 (54%)	145 (55%)	**0.041**
Black race		269 (16%)	195 (16%)	25 (15%)	49 (19%)	0.509
Weight, kg		83 (24)	82 (23)	88 (26)	86 (27)	**0.004**
Hypertension		587 (36%)	317 (26%)	89 (52%)	181 (69%)	**<.001**
Diabetes		136 (8%)	102 (9%)	34 (20%)		**<.001**
Cause of death	Head trauma	446 (28%)	385 (33%)	27 (16%)	34 (13%)	**<.001**
	Anoxia	538 (34%)	401 (34%)	66 (40%)	71 (27%)	
	Stroke	589 (37%)	365 (31%)	71 (43%)	153 (59%)	
	Other	23 (1%)	18 (2%)	3 (2%)	2 (1%)	
Hepatitis C seropositive		69 (4%)	26 (2%)	22 (13%)	21 (8%)	**<.001**
ECD		418 (26%)	186 (16%)	64 (37%)	168 (64%)	**<.001**
DCD		255 (16%)	198 (17%)	30 (18%)	27 (10%)	**0.031**
KDRI		1.38 (0.49)	1.24 (0.39)	1.59 (0.42)	1.91 (0.52)	**<.001**
KDPI, %		70 (24)	63 (24)	83 (16)	91 (13)	**<.001**
Admission SCr, mg/dL		1.11 (0.67)	1.08 (0.56)	1.12 (0.84)	1.25 (0.93)	**0.002**
Admission eGFR, ml/min/1.73m^2		83 (30)	86 (29)	81 (30)	70 (26)	**<.001**
Terminal SCr, mg/dL		1.24 (0.95)	1.14 (0.85)	1.4 (1.03)	1.57 (1.2)	**<.001**
Admission SCr > Terminal SCr		745 (46%)	593 (49%)	62 (36%)	90 (34%)	**<.001**
Terminal urine output, ml/hr		184 (147)	189 (145)	174 (172)	165 (141)	**<.001**
Machine perfusion used [2]		665 (41%)	476 (40%)	78 (46%)	111 (43%)	0.217

Variable		ALL (N=1632)	None Discarded (N=1198)	One Discarded (N=171)	Both Discarded (N=263)	P-value [1]
Procurement biopsy performed [2]		909 (56%)	540 (45%)	137 (80%)	232 (88%)	**<.001**
Biopsy report describing acute tubular necrosis in at least 1 kidney		155 (17%)	81 (15%)	27 (20%)	47 (20%)	0.137
Biopsy report describing ≥20% glomerulosclersosis in at least 1 kidney		136 (15%)	18 (3%)	21 (15%)	97 (42%)	**<.001**
Discard reason[3]	Biopsy	154 (35%)		38 (22%)	116 (44%)	**<.001**
	Poor quality	128 (29%)		53 (31%)	75 (29%)	0.063
	Anatomical abnormalities	75 (17%)		45 (26%)	30 (11%)	0.105
	Vascular damage	17 (4%)		15 (9%)	2 (1%)	**0.002**
	Other	29 (7%)		14 (8%)	15 (6%)	1.00
	Not reported	15 (3%)		6 (4%)	9 (3%)	1.00
	Discordant reasons	16 (4%)			16 (6%)	

Values are mean (SD) or n (%). AKI, acute kidney injury; ECD, expanded-criteria donor; DCD, donation after cardiac death; KDRI, kidney donor risk index; KDPI, kidney donor profile index; SCr serum creatinine; eGFR, estimated glomerular filtration rate.

[1] Kruskal-Wallis test for continuous variables and Chi-Square test for categorical variables

[2] Variable considered at the level of the donor (i.e., information available for at least one of the kidneys from a particular donor)

[3] The same reason was reported for both discarded kidneys in all but 16 donors as shown. For these discordant reasons, 'biopsy' was most common–reported for one but not the other discarded kidney in 12 of these donors.

Table 3

Risk of kidney discard by donor AKI status

AKI Status	Number of Discards (%)	Relative Risk (95% Confidence Interval)		
		Unadjusted	Adjusted [1]	Adjusted [2]
No AKI	433 (18%)	1.0 (referent)	1.0 (referent)	1.0 (referent)
Any AKI	264 (30%)	1.64 (1.38–1.94)	1.60 (1.38–1.85)	1.55 (1.34–1.79)
No AKI	433 (18%)	1.0 (referent)	1.0 (referent)	1.0 (referent)
Stage 1 AKI	145 (26%)	1.45 (1.17–1.80)	1.28 (1.07–1.52)	1.28 (1.08–1.52)
Stage 2 AKI	66 (35%)	1.95 (1.49–2.55)	1.95 (1.54–2.46)	1.82 (1.45–2.30)
Stage 3 AKI	53 (35%)	1.91 (1.42–2.58)	3.03 (2.23–4.13)	2.74 (2.00–3.75)

AKI, acute kidney injury.

[1] Adjusted for donor variables that comprise the kidney donor risk index (KDRI), with the exception of terminal serum creatinine (i.e., age, height, weight, Black race, death from stroke, donation after cardiac death, and history of hypertension, diabetes, and hepatitis C seropositivity)

[2] Includes donor variables listed above plus procurement biopsy performed and use of machine pump perfusion

Table 4

Risk of delayed graft function by donor AKI status

AKI Status	Number with DGF (%)	Relative Risk (95% Confidence Interval)		
		Unadjusted	Adjusted [1]	Adjusted [2]
No AKI	543 (28%)	1.0 (referent)	1.0 (referent)	1.0 (referent)
Any AKI	257 (41%)	1.50 (1.31–1.70)	1.56 (1.37–1.77)	1.48 (1.30–1.68)
No AKI	543 (28%)	1.0 (referent)	1.0 (referent)	1.0 (referent)
Stage 1 AKI	139 (34%)	1.25 (1.06–1.47)	1.28 (1.09–1.49)	1.27 (1.09–1.49)
Stage 2 AKI	62 (52%)	1.88 (1.53–2.30)	1.82 (1.47–2.25)	1.70 (1.37–2.12)
Stage 3 AKI	56 (57%)	2.03 (1.65–2.48)	2.55 (2.04–3.21)	2.25 (1.74–2.91)

AKI, acute kidney injury; DGF, delayed graft function.

[1] Adjusted for donor variables that comprise the kidney donor risk index (KDRI), with the exception of terminal serum creatinine (i.e., age, height, weight, Black race, death from stroke, donation after cardiac death, and history of hypertension, diabetes, and hepatitis C seropositivity)

[2] Includes donor variables listed above plus procurement biopsy performed, use of machine pump perfusion, and cold ischemia time in hours

Table 5

Allograft function at 6 months by donor AKI and stratified by DGF status

	6-month SCr, mg/dl			6-month eGFR, ml/min/1.73m^2		
	All recipients (n=2567)	**Recipients with DGF (n=800)**	**Recipients without DGF (n=1767)**	**All recipients (n=2567)**	**Recipients with DGF (n=800)**	**Recipients without DGF (n=1767)**
No Donor AKI (N=1945)	1.34 [1.07, 1.7]	1.52 [1.27, 2.1]	1.3 [1.0, 1.6]	55 [41, 72]	46 [29, 60]	59 [45, 75]
Stage 1 AKI (N=403)	1.35 [1.1, 1.8]	1.5 [1.2, 1.95]	1.3 [1.1, 1.6]	54 [40, 68]	49 [32, 64]	56 [46, 72]
Stage 2 AKI (N=120)	1.5 [1.15, 1.75]	1.54 [1.3, 1.85]	1.3 [1.0, 1.65]	53 [38, 67]	52 [36, 59]	55 [40, 74]
Stage 3 AKI (N=99)	1.3 [1.1, 1.68]	1.3 [1.1, 1.75]	1.3 [0.97, 1.6]	59 [40, 73]	58 [39, 71]	59 [41, 78]
P-value [1]	0.276	0.049	0.497	0.377	0.060	0.537

Values are median [interquartile range]. AKI, acute kidney injury; DGF, delayed graft function; eGFR, estimated glomerular filtration rate; SCr, serum creatinine

[1] Kruskal-Wallis test.