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Deceased-Donor Acute Kidney Injury is Not Associated with Kidney Allograft Failure

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Abstract

Deceased-donor acute kidney injury (AKI) is associated with organ discard and delayed graft function, but data on longer-term allograft survival are limited. We performed a multicenter study to determine associations between donor AKI (from none to severe based on AKI Network stages) and all-cause graft failure, adjusting for donor, transplant, and recipient factors. We examined whether any of the following factors modified the relationship between donor AKI and graft survival: kidney donor profile index, cold ischemia time, donation after cardiac death, expanded-criteria donation, kidney machine perfusion, donor-recipient gender combinations, or delayed graft function. We also evaluated the association between donor AKI and a 3-year composite outcome of all-cause graft failure or estimated glomerular filtration rate ≥ 20 mL/min/1.73m² in a subcohort of 30% of recipients. Among 2,430 kidneys transplanted from 1,298 deceased donors, 585 (24%) were from donors with AKI. Over a median follow-up of 3.7 years, there were no significant differences in graft survival by donor AKI stage. We found no evidence that pre-specified variables modified the effect of donor AKI on graft survival. In the subcohort, donor AKI was not associated with the 3-year composite outcome. Donor AKI was not associated with graft failure in this well-phenotyped cohort. Given the organ shortage, the transplant community should consider measures to increase utilization of kidneys from deceased donors with AKI.

Graphical Abstract

Keywords

Acute kidney injury; delayed graft function; chronic allograft nephropathy

Introduction

The need for kidney transplantation drives efforts to expand organ donation. In deceased donors, acute kidney injury (AKI) is a common complication that has received increasing attention. Centers in the United States (U.S.) are often hesitant about accepting kidneys from donors with elevated serum creatinine, even with reversible AKI.¹ Consequently, the discard rate is 30% for AKI kidneys, compared with 18% for kidneys procured from donors without AKI.² Concerns about donor AKI often focus on the potential for early graft failure as well as reduced long-term allograft survival. Poor outcomes may be particularly worrisome to U.S. centers given the current regulatory environment in conjunction with uncertainty about donor kidney quality assessment scores.^{3,4} While several studies have demonstrated safe and effective use of these kidneys, especially with regard to 1-year outcomes,⁵⁻⁹ centers and their recipients may encounter these offers more often in the future given increasing hospitalized AKI incidence.¹⁰

We previously found elevated risk for organ discard and the development of delayed graft function (DGF, temporary dialysis in the first week post-transplant) with increasing donor AKI stages but no association between donor AKI and 6-month allograft function.² We also noted higher resource utilization for AKI kidneys in the same analysis – over two-thirds of procured kidneys from donors with AKI stage 3 underwent machine perfusion, and 88% underwent procurement biopsy to evaluate kidney quality histologically.

Notwithstanding increased resource utilization, most prior studies point to acceptable early post-transplant outcomes when utilizing donor AKI kidneys.^{2,5-9,11-22} One possible exception was a Transplant Registry study from the United Kingdom that found slightly

inferior 1-year allograft survival and function for donor AKI kidneys compared to kidneys from donors without AKI,²³ though the study did not determine whether AKI kidneys provided benefit compared to staying on dialysis. An earlier study found significant survival benefit for older patients (>50 years) who accept even the highest-risk kidneys in centers with median waiting times of ~3 years.²⁴ It is unclear whether donor AKI is associated with allograft function and survival beyond the first post-transplant year. Thus, we performed the current analysis in a highly phenotyped, multicenter cohort. The aims were to determine associations between donor AKI and long-term transplant outcomes and to evaluate several risk factors as potential effect modifiers. We performed additional 3-year chart reviews in a subset of recipients for longitudinal allograft function.

Results

Of 1679 enrolled donors, 1298 were included. Prior to exclusions, 713 (21%) of procured kidneys were discarded from 445 donors. Figure 1 shows donor exclusions and AKI stages. Table S1 provides the donor characteristics for the kidneys that were transplanted compared with those that were discarded (and excluded from the current analysis). A total of 2430 kidney transplants were analyzed, out of which 585 (24%) were from donors with AKI. None of the donors required dialysis. Table 1 shows donor and recipient characteristics. Compared to donors without AKI, donors with AKI were more often black, more likely to have underlying hypertension, and had higher mean kidney donor profile index (KDPI). Recipients of kidneys from donors with AKI tended to be older, and donor AKI kidney transplants had longer mean cold ischemia time, were more likely to undergo machine perfusion, and had slightly more human leukocyte antigen (HLA) mismatches.

Allograft Survival

The total combined follow-up of the cohort was 9479 patient-years with a median follow-up of 3.7 (3.5-4.9) years. There were 623 (26%) all-cause graft failures, which included 402 deaths and 313 death-censored graft failures. All-cause graft failure was not statistically different by donor AKI, occurring in 475 (26%) recipients of kidneys without donor AKI and 148 (25%) recipients of kidneys with donor AKI ($p=0.94$). As shown in Figure 2, cumulative incidence curves by donor AKI stage suggested increased graft failure risk in the first year for kidneys from donors with stage 3 AKI, though confidence intervals were wide with only 85 kidneys (rates provided in Table S2). There were no statistical differences in all-cause graft failure within the first year between donor AKI stages [150 (8%) events without donor AKI, 55 (9%) with any donor AKI, 37 (9%) with stage 1, 8 (7%) with stage 2, 10 (12%) with stage 3; $p=0.54$]. There were no significant associations between donor AKI stages and all-cause graft failure via proportional hazards analyses (Table 2), and proportional hazards assumptions were not violated.

There was no evidence for effect modification between donor AKI and graft failure based on any donor/transplant characteristic or donor-recipient gender combination evaluated (Figure 3, all interaction p -values >0.1). As shown in Table 2 and Figures 2 and 3, results were unchanged for death-censored graft failure.

Detailed Recipient Sub-Cohort

A total of 739 kidneys from 601 enrolled donors were transplanted at 12 participating centers. Chart abstractions provided granular 3-year longitudinal allograft function data. Clinical variables for the sub-cohort were comparable to the entire cohort (Table S3). The composite outcome occurred in 143 (19%) recipients, consisting of 44 deaths with functional allografts, 65 death-censored graft failures, and 34 patients progressing to estimated glomerular filtration rate (eGFR) < 20 mL/min/1.73m². Unadjusted cumulative incidence for the composite outcome was not statistically different by donor AKI status (Figure 4, log-rank $p=0.79$). There was no independent association between donor AKI and the composite outcome via proportional hazards analysis (Table 2, all covariates provided in Table S4).

Discussion

The need for transplantation exceeds the supply of donated kidneys. Waiting times continue to increase. Over 25% of the 30,000 patients added to the waiting list each year in the U.S. are subsequently removed due to death or frailty. While the number of living-donor kidney transplants has remained flat in the U.S. at 6000 per year since 2011, deceased-donor kidney transplantation has recently accelerated, surpassing 14,000 in 2017.²⁵ Despite these modest gains in deceased donation, over 18% of the kidneys recovered for transplant are discarded, and donor AKI more than doubles the discard risk.²

In this study involving the largest multicenter deceased-donor kidney transplant cohort in the U.S., we have shown that the current practice of utilizing donor AKI kidneys is not associated with reduced allograft survival. We found no evidence for effect modification between donor AKI and other known risk factors with regard to allograft survival. Furthermore, we found no evidence of a donor AKI effect on a 3-year composite outcome of all-cause graft failure or eGFR < 20 mL/min/1.73m² in our detailed sub-cohort of recipients with rigorous chart reviews.

It is important to consider these longer-term results in relation to the short-term outcomes we previously reported from this cohort.² We demonstrated that increasing donor AKI stage was independently associated with kidney discard as well as DGF. However, we found no direct relationship between donor AKI and 6-month allograft function. Our preliminary 1-year results were in agreement with other reports and were subsequently confirmed by two smaller studies.^{21,22} Our current results with complete follow-up beyond the first year are consistent with the U.K. kidney transplant report by Boffa et al regarding long-term outcomes.²³ While the Standard Transplant Analysis and Research file from the Organ Procurement and Transplantation Network (OPTN) does not provide serial serum creatinines, the U.K. Transplant Registry allowed Boffa et al. to characterize AKI stages within the U.K. population of 11,649 donors. They did find, however, that donor AKI was weakly but independently associated with 1-year all-cause graft failure with an adjusted odds ratio of 1.2 (95% confidence interval: 1.03-1.41). Compared with no AKI, they also noted that donor AKI stage 3 was associated with 3-fold increased risk for primary non-function. In our current study, confidence intervals were wide for the hazard ratios for graft failure in adjusted analyses for the 85 kidneys from donors with AKI stage 3. Associations

were not significant but extended from 49% decreased risk to 94% increased risk for death-censored graft failure. This degree of potential decreased or increased risk could be viewed as clinically important and suggests that our study had insufficient power to rule out poorer outcomes for stage 3 donor AKI.

Besides power, there are other differences between the present study and the recent U.K. report.²³ While the U.K. sample size was larger, cohort characteristics were also different. For example, only 1% of the U.K. donors were black compared with 16% in our donor cohort and 24% of our donors with AKI. Just as importantly, however, all observational transplant studies must contend with possible selection bias. Because they are more often discarded, donor AKI kidneys that are selected for transplant may have other favorable characteristics that offset graft failure risk. While we attempted to address confounding by adjusting for other donor factors (i.e., KDPI) as well as prognostic recipient factors (e.g., pre-emptive transplant status), it is typically not possible to address selection bias in observational studies using statistical techniques. It is interesting to note, however, that our overall 21% kidney discard rate was lower than that of the U.K. cohort at 28%.

Our objective was to investigate donor AKI kidneys currently transplanted in the U.S., which is likely related to but nonetheless distinct from organ utilization and access to transplant. Alternative study designs are needed to evaluate potential causal effects for donor AKI with regard to transplant outcomes. In the native kidney (non-transplant) setting, AKI is a risk factor for chronic kidney disease over several years.^{26,27} While causation has not been established clinically,²⁸ a number of mechanisms (e.g., hypoxia, profibrotic signaling, inflammation, microvascular rarefaction) may be involved.²⁹⁻³¹ Reasons for the lack of definitive evidence for AKI leading to chronic kidney disease in transplantation may be related to the younger median age of deceased donors compared with typical adult native kidney injury cohorts as well as shortened timeframes for kidney transplants. It may take >20 years for acutely injured native kidneys to develop chronic disease, but over half of all deceased-donor allografts are lost within 10 years of transplant. Additional complicating factors in transplantation might involve time-dependent effects related to immunosuppression and certain post-transplant complications (e.g. BK virus or other infections).

Another interesting concept in AKI research is protection with ischemic preconditioning.³² A small kidney transplant trial of ischemic preconditioning noted reduced post-transplant AKI biomarker secretion and improvements in eGFR,³³ whereas more recent trials in recipients of deceased-donor³⁴ or living-donor³⁵ kidneys have not. While deceased-donor trials of ischemic preconditioning may provide additional insights, the lack of deleterious associations between clinically-defined donor AKI and long-term outcomes in our cohort suggests that current utilization practices for these kidneys are appropriate and should be encouraged. We believe it is possible to expand the use of these kidneys, especially with improved donor risk phenotyping for recipients that may not tolerate prolonged DGF (e.g., frail recipients sensitive to volume overload).

Our study has limitations. Deceased-donor kidneys are clinically selected for transplantation, and we cannot be certain about outcomes for discarded kidneys if they were

instead transplanted. It is plausible that donor AKI kidneys selected for transplant have a more favorable risk factor distribution than is the case for donor kidneys without AKI. Such an imbalance in non-AKI risk factors might be expected because of collider bias, which is another form of selection bias. That is, donor AKI kidneys may be less likely to be selected for transplant unless they have other more favorable characteristics that induce utilization. Lastly, while we controlled for several important donor and recipient characteristics, residual confounding is still possible.

Some cases of donor AKI on admission that subsequently improved may not have been captured given our use of admission serum creatinine to define baseline donor kidney function. Such nondifferential misclassification of donor AKI could have biased results toward the null. Some donors may also have chronic kidney disease, which may be a risk factor for AKI;^{36,37} however, chronic kidney disease can be challenging to diagnose in this setting without a biopsy given that donor admission serum creatinine may not be at steady state.³⁸ We performed multivariable adjustment for donor factors via the KDPI.^{39,40} This score incorporates 10 donor characteristics associated with allograft survival and includes terminal serum creatinine, which was also used to define donor AKI based on the change from admission to terminal values. Because increasing KDPI is associated with discard,⁴¹ there is the potential for overlap/interaction between KDPI and donor AKI with regard to kidney discard and selection for transplant. In addition, change in serum creatinine does not fully characterize all aspects of donor AKI but was chosen for consistency and comparisons with prior literature.^{2,5-9,11-23} We previously noted that structural markers of kidney injury like donor urine neutrophil gelatinase-associated lipocalin (NGAL) were associated with clinical AKI but only modestly associated with 6-month allograft function.⁴² However, future research may help determine the clinical consequences, in terms of both organ allocation and allograft longevity, of utilizing biomarkers like NGAL and many other potential measures of donor AKI in addition to changes in serum creatinine concentrations.⁴³⁻⁴⁵

The decision to accept a deceased-donor kidney offer is often complex and may depend on multiple donor, kidney and recipient factors as well as many logistical considerations. Our findings indicate that the current practice of utilizing kidneys from donors with AKI does not adversely affect post-transplant outcomes beyond the first year. Additional research is likely needed, however, to determine outcomes for recipients of kidneys from donors with the most severe forms of AKI. Such research could lead to innovative donor management and kidney preservation trials in hopes of further expanding the donor pool.

Methods

Cohort Generation

This is a multicenter, observational cohort study of deceased donors and their kidney recipients. Five organ procurement organizations (OPOs) enrolled donors between May 2010 and December 2013 and followed their own protocols for research authorization and donor management. We excluded donors that did not yield kidney transplants, provided no urine samples,⁴² had missing admission or terminal serum creatinine, or were younger than 16 years. Clinical variables were abstracted from OPO charts. Data for all kidney recipients

from these donors were obtained from the OPTN. The OPTN data system includes data on all donors, wait-listed candidates, and transplant recipients in the U.S., submitted by the members of the OPTN, and is more fully described elsewhere.⁴⁶ The Health Resources and Services Administration, U.S. Department of Health and Human Services provides oversight to the activities of the OPTN. The current analyses are based on OPTN data as of July 31, 2017. The OPO scientific review committees and the institutional review boards for participating investigators approved the study.

We performed chart reviews for the subset of recipients at participating transplant centers in our study network who received kidneys from enrolled donors. Trained site coordinators reviewed medical records and recorded detailed recipient characteristics, treatments and outcomes. Yale University study staff validated abstractions to confirm data quality and accuracy (see Supplemental Material Appendix A).

Risk Factors

We defined donor AKI according to AKI Network criteria (irrespective of time between admission and terminal serum creatinine, and not including urine output) as follows: stage 1, increase in serum creatinine from admission to the terminal value by ≥ 0.3 mg/dl or 1.5- <2 -fold; stage 2, 2- <3 -fold; and stage 3, ≥ 3 -fold, or terminal serum creatinine ≥ 4.0 mg/dl after a rise of ≥ 0.5 mg/dl from admission, or dialysis support.⁴⁷ We calculated the kidney donor risk index and KDPI relative to all deceased donors in the OPTN database in 2010.^{39,40} Historically, expanded-criteria donors are defined by age ≥ 60 years or age 50-59 years with 2 of the following: death via cerebrovascular accident, history of hypertension, or terminal serum creatinine >1.5 mg/dl. We assessed eGFR using the Chronic Kidney Disease Epidemiology equation.⁴⁸

Outcomes

Co-primary outcomes were all-cause graft failure (all-cause mortality, return to dialysis, or retransplantation) and death-censored graft failure. We also examined longitudinal outcomes for 3 years after transplant in recipients with medical chart reviews. For this detailed recipient sub-cohort, we evaluated time to all-cause graft failure or development of eGFR <20 mL/min/1.73m² – chosen because it is the eGFR threshold to place recipients on the waiting list for kidney re-transplantation in the U.S. (OPTN Policy 8.4).⁴⁹

Statistics

We reported descriptive statistics as means (standard deviation), medians (interquartile range), or frequencies (percentages). Clinical characteristics and outcomes were compared between donor AKI stages using Kruskal-Wallis or Chi-Square tests. We fit Cox proportional hazards models to evaluate the association of donor AKI on the co-primary outcomes. Donor AKI was operationalized as any AKI versus no AKI as well as a multilevel categorical exposure according to stage (reference: no AKI). We used Kolmogorov-type supremum tests to evaluate proportional hazards assumptions. We accounted for the cluster effect of paired kidneys from the same donor using robust sandwich estimates. To account for other covariates that predict graft failure, we utilized variables from prior analyses,^{42,50} which are available at organ offer (KDPI and recipient characteristics), but not post-

transplant factors (e.g., rejection episodes). We performed initial multivariable adjustment for allograft quality via the KDPI. Final adjusted models included the KDPI plus cold ischemia time and the following recipient variables: age, black race, sex, previous kidney transplant, diabetes as the cause of end-stage kidney disease, number of HLA mismatches, percent panel reactive antibody, body mass index, and pre-emptive transplantation.

We assessed whether any of the following variables modified the relationship between donor AKI and all-cause graft failure: KDPI (cut-off: 80%), expanded-criteria donation, donation after cardiovascular determination of death, kidney machine perfusion, cold ischemia time (using the median value of 14 hours as the cut-off), recipient DGF, or donor-recipient gender combinations. We excluded participants with missing covariate data (<5%) and used SAS 9.4 for Windows (SAS Institute, Cary, NC). All statistical tests and confidence intervals were two-sided with a significance level of 0.05.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Disclosure

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Figure 1.
Flowchart for donor enrollment and distribution of acute kidney injury (AKI). OPO, organ procurement organization.

Figure 2.

Cumulative incidence curves for (A) all-cause graft failure (log-rank $p=0.68$) and (B) death-censored graft failure (log-rank $p=0.93$) by donor acute kidney injury stage. 95% confidence intervals shown at approximately 1, 3 and 5 years post-transplant (time-points staggered for clarity).

Figure 3.

Tests for effect modification between donor acute kidney injury (AKI) and (A) all-cause graft failure or (B) death-censored graft failure based on donor, transplant, and recipient characteristics. All p-values for interaction >0.1. GF, graft failure; HR, hazard ratio; KDPI, kidney donor profile index; ECD, expanded-criteria donor; DCD, donation after cardiovascular determination of death; CIT, cold ischemia time; DGF, delayed graft function in the recipient.

Figure 4. Cumulative incidence curve for the composite outcome of all-cause graft failure or development of eGFR < 20 ml/min/1.73m² without subsequent improvement in allograft function within 3 years for the detailed recipient sub-cohort by donor AKI. Log-rank $p=0.79$. 95% confidence intervals shown at 6-month intervals post-transplant.

Table 1:

Donor, recipient and transplant characteristics by donor AKI

		ALL	No AKI	AKI	P-value [†]
<i>Donor Characteristics</i>		(N=1298)	(N=976)	(N=322)	
Age, years		41 ± 15	42 ± 15	41 ± 14	0.416
Male		784 (60%)	583 (60%)	201 (62%)	0.392
Black race		205 (16%)	128 (13%)	77 (24%)	<0.001
Hispanic ethnicity		171 (13%)	133 (14%)	38 (12%)	0.401
BMI, kg/m ²		28 ± 7	28 ± 7	30 ± 8	0.028
Hypertension		399 (31%)	282 (29%)	117 (36%)	0.012
Diabetes		130 (10%)	90 (9%)	40 (12%)	0.097
Cause of death	Head trauma	396 (31%)	302 (32%)	94 (30%)	0.797
	Anoxia	425 (34%)	312 (33%)	113 (36%)	
	Stroke	427 (34%)	322 (34%)	105 (33%)	
	Other	18 (1%)	13 (1%)	5 (2%)	
Hepatitis C seropositive		48 (4%)	37 (4%)	11 (3%)	0.757
ECD		246 (19%)	177 (18%)	69 (21%)	0.191
DCD		206 (16%)	168 (17%)	38 (12%)	0.021
KDRI		1.29 ± 0.41	1.26 ± 0.41	1.39 ± 0.4	<0.001
KDPI, %		48 ± 27	46 ± 28	56 ± 24	<0.001
Admission to procurement, days		5 ± 7	5 ± 7	4 ± 4	0.005
Admission SCr, mg/dL		1.10 ± 0.61	1.12 ± 0.65	1.04 ± 0.47	0.107
Terminal SCr, mg/dL		1.17 ± 0.85	0.88 ± 0.34	2.04 ± 1.25	<0.001
Number of individual kidneys transplanted	1	166 (13%)	107 (11%)	59 (18%)	<0.001
	2	1132 (87%)	869 (89%)	263 (82%)	
Donor AKI stage	No AKI	976 (75%)	976 (100%)		<0.001
	Stage 1	211 (16%)		211 (66%)	
	Stage 2	62 (5%)		62 (19%)	
	Stage 3	49 (4%)		49 (15%)	
<i>Recipient and transplant characteristics</i>		(N=2430)	(N=1845)	(N=585)	
Age, years		53 ± 15	52 ± 15	55 14	0.006
Male		1492 (61%)	1123 (61%)	369 (63%)	0.339
Black race		956 (39%)	719 (39%)	237 (41%)	0.506
Hispanic ethnicity		279 (11%)	214 (12%)	65 (11%)	0.747
BMI, kg/m ²		28.0 ± 5.8	28.0 ± 5.8	28.1 ± 5.6	0.928
Cause of ESRD	Diabetes	726 (30%)	549 (30%)	177 (30%)	0.515
	Hypertension	643 (26%)	475 (26%)	168 (29%)	
	Glomerulonephritis	391 (16%)	303 (16%)	88 (15%)	
	Graft failure	174 (7%)	138 (7%)	36 (6%)	

		ALL	No AKI	AKI	P-value [†]
	Other or unknown	496 (20%)	380 (21%)	116 (20%)	
Preemptive transplant		274 (11%)	214 (12%)	60 (10%)	0.371
Dialysis duration, months		46 ± 38	45 ± 38	47 ± 39	0.199
Previous kidney transplant		315 (13%)	245 (13%)	70 (12%)	0.410
Pre-transplant blood transfusion		438 (18%)	329 (18%)	109 (19%)	0.724
Induction Immunosuppression	rATG	625 (85%)	445 (83%)	180 (88%)	0.098
	Basiliximab	114 (15%)	91 (17%)	23 (11%)	0.055
	Alemtuzumab	13 (2%)	12 (2%)	1 (0%)	0.105
	Rituximab	7 (1%)	5 (1%)	2 (1%)	0.954
	Other or unknown	13 (2%)	10 (2%)	3 (1%)	0.713
Maintenance Immunosuppression at Discharge	Steroid free	512 (21%)	366 (20%)	146 (25%)	0.008
	Tacrolimus	2260 (93%)	1707 (93%)	553 (95%)	0.097
	Cyclosporine	44 (2%)	36 (2%)	8 (1%)	0.356
	Mycophenolate	2293 (94%)	1739 (94%)	554 (95%)	0.684
	CNI + Mycophenolate + prednisone	1743 (72%)	1341 (73%)	402 (69%)	0.064
	mTOR inhibitor	16 (1%)	12 (1%)	4 (1%)	0.931
	Belatacept	8 (0%)	6 (0%)	2 (0%)	0.951
	Other or unknown	24 (1%)	21 (1%)	3 (0%)	0.708
PRA	Continuous, %	21 ± 35	22 ± 36	19 ± 34	0.082
	0%	1545 (64%)	1157 (63%)	388 (66%)	0.330
	1-20%	178 (7%)	134 (7%)	44 (8%)	
	21-80%	326 (13%)	253 (14%)	73 (12%)	
	>80%	381 (16%)	301 (16%)	80 (14%)	
Kidney biopsied		1117 (46%)	768 (42%)	349 (60%)	<0.001
Kidney pumped		952 (39%)	680 (37%)	272 (46%)	<0.001
Cold ischemia time, hours		15.3 ± 7.1	14.9 ± 6.9	16.4 ± 7.7	<0.001
HLA mismatch level	Continuous	4.2 ± 1.5	4.2 ± 1.5	4.3 ± 1.5	0.044
	0	153 (6%)	124 (7%)	29 (5%)	0.089
	1	21 (1%)	19 (1%)	2 (0%)	
	2	82 (3%)	62 (3%)	20 (3%)	
	3	292 (12%)	217 (12%)	75 (13%)	
	4	642 (26%)	497 (27%)	145 (25%)	
	5	820 (34%)	628 (34%)	192 (33%)	
	6	414 (17%)	295 (16%)	119 (20%)	
Donor kidney AKI stage	No AKI	1845 (76%)	1845 (100%)		<0.001
	Stage 1	391 (16%)		391 (67%)	
	Stage 2	109 (4%)		109 (19%)	
	Stage 3	85 (3%)		85 (15%)	

Values are mean (SD) or n (%). AKI, acute kidney injury; ECD, expanded-criteria donor; DCD, donation after cardiovascular determination of death; KDRI, kidney donor risk index; KDPI, kidney donor profile index; SCr serum creatinine; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; PRA; panel reactive antibody; HLA, human leukocyte antigen.

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

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Table 2a:

Long-term graft failure risk by donor AKI stage

AKI Stages	Event rate per 1000 patient-years (95% CI)	Hazard Ratio (95% CI)		
		Unadjusted	Adjusted 1	Adjusted 2
All-Cause Graft Failure				
No AKI (n=1845)	66.0 (60.2, 72.3)	Reference	Reference	Reference
AKI Stage 1 (n=391)	70.3 (57.8, 85.4)	1.06 (0.86, 1.32)	0.93 (0.75, 1.2)	0.92 (0.73, 1.14)
AKI Stage 2 (n=109)	55.5 (36.9, 83.5)	0.83 (0.54, 1.25)	0.69 (0.45, 1.05)	0.73 (0.48, 1.11)
AKI Stage 3 (n=85)	63.6 (40.6, 99.7)	0.98 (0.62, 1.55)	0.98 (0.62, 1.55)	0.92 (0.58, 1.47)
Death-Censored Graft Failure				
No AKI (n=1845)	32.7 (28.8, 37.2)	Reference	Reference	Reference
AKI Stage 1 (n=391)	35.6 (27.2, 46.4)	1.08 (0.80, 1.46)	0.93 (0.69, 1.26)	0.92 (0.68, 1.25)
AKI Stage 2 (n=109)	32.4 (19.2, 54.6)	0.97 (0.58, 1.69)	0.81 (0.47, 1.40)	0.77 (0.44, 1.33)
AKI Stage 3 (n=85)	28.9 (15.0, 55.5)	0.88 (0.45, 1.72)	0.89 (0.46, 1.72)	0.99 (0.51, 1.94)

AKI, acute kidney injury; CI, confidence interval.

Model 1 adjusted for kidney donor profile index (KDPI)

Model 2: adjusted for donor KDPI, cold ischemia time and the following recipient variables: age (years), black race, sex, previous kidney transplant, diabetes as the cause of end-stage kidney disease, number of human leukocyte antigen mismatches, panel reactive antibody (%), body mass index (kg/m^2), and pre-emptive transplant.

Table 2b:

Risk of the composite outcome within 3 years for the detailed recipient sub-cohort by donor AKI stage

Risk Factor	Event Rate, n (%)	Hazard Ratio (95% CI)		
		Unadjusted	Adjusted 1	Adjusted 2
No AKI (n=535)	54 (10.1%)	1.0 (referent)	1.0 (referent)	1.0 (referent)
AKI (n=204)	23 (11.3%)	1.05 (0.73, 1.51)	0.92(0.63, 1.32)	0.96 (0.65, 1.39)

The composite outcome was death, death-censored graft failure or last follow-up eGFR <20 ml/min/1.73m²

Model 1 adjusted for donor KDPI (3 observations excluded due to missing KDPI)

Model 2: adjusted for donor KDPI, cold ischemia time and the following recipient variables: age (years), black race, sex, previous kidney transplant, diabetes as the cause of end-stage kidney disease, number of human leukocyte antigen mismatches, panel reactive antibody (%), body mass index (kg/m², and pre-emptive transplant (6 observations excluded due to missing covariates).