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Outcomes of Kidney Transplantation From Donors on Renal Replacement Therapy

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Background. The increasing demand for organs has pushed transplant providers to expand kidney acceptance criteria. The use of kidneys from donors with AKI has been shown to provide good long-term graft survival. We aim to evaluate and compare the outcomes of deceased donor kidney transplantation from donors with acute kidney injury (AKI), either with or without renal replacement therapy (AKI-RRT) before donation. **Methods.** A single-center retrospective review of all patients who underwent deceased donor kidney transplantation from AKI donors between 2009 and 2020 was performed. AKI donors were defined on the basis of donor terminal creatinine ≥ 2.0 mg/dL or use of RRT before donation. We compared the outcomes of recipients receiving a kidney from a donor with AKI versus AKI-RRT. Data are presented as medians (interquartile ranges) and numbers (percentages). **Results.** Four hundred ninety-six patients were identified, of whom 300 (60.4%) were men with a median age of 57 y at transplantation. Thirty-nine patients received an AKI-RRT, whereas 457 received an AKI kidney. Donors in the AKI-RRT group were younger (28 versus 40), had less incidence of hypertension (15.3% versus 31.9%), and were more likely to be imported (94.9% versus 76.8%). There was a higher incidence of delayed graft function (72% versus 44%, $P < 0.001$) in the AKI-RRT group. Recipients in both groups had similar 90-d (100% versus 95.2%) and 1-y (100% versus 91.9%) graft survival. With a median follow-up of 5 y, there was no difference in death-censored graft survival in both groups ($P = 0.83$). **Conclusions.** Careful selection of kidneys from donors with AKI on RRT can be safely used for kidney transplantation with favorable clinical outcomes.

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Organ shortage is an ongoing problem as there are more patients added annually to the kidney transplant waitlist compared with the number of available organs.¹ To address this ever-expanding gap between supply and demand, Organ

Procurement and Transplantation Network has launched an expeditious task force to increase organ donation and efficiency of organ placement and transplant centers on their end have been expanding donor acceptance criteria and increasing utilization of kidneys from “marginal donors.”² One scenario is using kidneys from donors with acute kidney injury (AKI).^{3,4} However, expanding donor acceptance criteria might be associated with inferior outcomes and accepting transplant physicians must always balance the benefit of accepting renal allografts from “marginal donors” with the risk of graft loss.

Due to concerns for higher rates of primary nonfunction (PNF) and inferior long-term graft function, kidneys from donors with severe AKI are widely underused and have a high discard rate, reaching up to 44%.⁵⁻⁷ This is likely due to the paucity of data reporting on outcomes of kidney transplantation from donors with severe AKI, particularly those requiring renal replacement therapy (RRT).

Here, we report on a single-center experience in using kidneys from donors with severe AKI requiring RRT. We compared short- and long-term outcomes in these donors compared with those of AKI without RRT. We hypothesized that outcomes of kidney transplantation from donors with AKI on RRT are equivalent to donors with AKI without RRT.

MATERIALS AND METHODS

After an institutional review board approval was obtained, we performed a retrospective review of all patients who

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underwent deceased donor kidney transplantation between January 2009 and December 2020 at a single high-volume kidney transplantation center. Patients who received multivisceral, dual organ or en bloc transplantation were excluded. Our cohort included recipients who received a kidney from a donor with AKI, defined as a donor with a terminal creatinine (Cr) ≥ 2 mg/dL or a donor requiring acute RRT. We compared outcomes and donor and recipient characteristics between patients receiving a renal graft from a donor with AKI requiring RRT (AKI-RRT group) and patients receiving a renal graft from a donor with AKI not requiring RRT (AKI group).

The following donor characteristics were obtained from the United Network for Organ Sharing Donor Net: donor age, sex, race, cause of death, body mass index (BMI), kidney donor profile index (KDPI), urine output before donation (milliliter per hour), duration of dialysis in days, donation after circulatory death status, cold ischemia time, warm ischemia time, and share status (local versus imported). Imported was defined as organs from outside our center's donation service area. Cold ischemia time was defined as the time from donor cross-clamp to reperfusion in the recipient. Warm ischemia time was defined as the time from extubation to initiation of flush in the donor. Donor urine output of <0.3 mL/kg/h was used to define oligoanuric donors. The severity of AKI was defined on the basis of the Acute Kidney Injury Network (AKIN) criteria.⁸

Hypothermic machine perfusion (HMP) utilization, duration of pumping, terminal pumping parameters (flow and resistive index), and whether pumping was performed in the organ procurement organization (OPO) or our institution were examined. Our center's practice relies heavily on HMP, and we have the capability to place kidneys on a pump in our institution.

Results of procurement frozen section biopsies performed and read by the OPO were analyzed, looking at percentage of glomerulosclerosis, degree of interstitial fibrosis tubular atrophy, degree of vascular changes, degree of acute tubular necrosis (ATN), presence of cortical necrosis, and glomerular fibrin thrombi. Our institution does not routinely rebiopsy or re-read biopsies obtained by the OPO. As previously reported, we tend to decline kidneys that show evidence of chronicity ($>20\%$ glomerulosclerosis, $>25\%$ interstitial fibrosis tubular atrophy, and/or evidence of moderate to severe vascular disease) or presence of $>10\%$ cortical necrosis on a biopsy.

Recipient characteristics including age, sex, race, BMI, calculated panel-reactive antibodies (cPRAs), estimated posttransplant survival (EPTS), history of diabetes, prior transplantation, preemptive, and duration of dialysis before transplantation were obtained. Recipients with a cPRA of $>40\%$ were regarded as sensitized on the basis of our institution policy.

Recipient outcomes including delayed graft function (DGF), duration of DGF, hospital length of stay, PNF, graft and patient survival, and serial renal function during a span of 5 y were obtained. DGF was defined as a need for dialysis within 7 d from transplantation. PNF was defined as dialysis dependence or failure to achieve adequate graft function (glomerular filtration rate [GFR] >20 mL/min/m²) 90 d posttransplant. GFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration 2021 formula.

To compare 2 groups with similar baseline donor characteristics, a subgroup analysis was performed in the propensity score-matched cohort. Donor age, BMI, donation after circulatory death (DCD) status, history of hypertension (HTN) and diabetes, cause of death (cerebrovascular accident [CVA] versus non-CVA), cold ischemic time (CIT), pump use, and KDPI were matched for 1 AKI-RRT patient to 5 patients with AKI.

All patients received induction immunosuppression at the time of transplantation using rabbit antithymocyte globulin. Tacrolimus and mycophenolate mofetil were used for maintenance immunosuppression starting on postoperative day 1. All patients except for sensitized patients (cPRA $>40\%$) received a rapid steroid withdrawal.

Statistical Analysis

Descriptive statistics for donor and recipient characteristics and outcomes are presented as medians with interquartile ranges for continuous variables and numbers with frequencies for categorical variables. Differences between the 2 groups were assessed using the *t* test for continuous variables and the chi-square test for categorical variables. Statistical significance was defined as a *P* value of ≤ 0.05 . Kaplan-Meier estimates were performed for patient survival and death-censored graft survival. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC).

RESULTS

Recipient Characteristics

During the study period, our center performed 2667 deceased donor kidney transplants, of which 496 (18.6%) were from donors with AKI. The median age at transplantation was 57 (46–65) y and 300 (60.4%) were men. Thirty-nine patients (7.9%) underwent deceased donor kidney transplantation from donors on RRT (AKI-RRT group), whereas the remaining received a kidney from a donor with AKI without RRT (AKI group). There was no statistical difference between both groups in regard to recipient demographics. Patients in the AKI-RRT group had a lower EPTS score than those in the AKI group (36% versus 52%, *P* = 0.03; Table 1).

Donor Characteristics

Donors in the AKI-RRT group were younger (28 versus 40, *P* = 0.005), less likely to have a history of HTN (15.3% versus 31.9%, *P* = 0.03), more likely to have anoxia as the cause of death (79.5% versus 44.9%, *P* < 0.001), and more likely to be imported (94.9% versus 76.8%, *P* = 0.007; Table 2). All the donors in the AKI-RRT group were on RRT due to severe AKI. Based on the AKIN criteria, all the donors in the AKI-RRT group were AKIN 3; in the AKI group, 290 (63.5%) were AKIN 3, 106 (23.2%) were AKIN 2, and 61 (13.3%) were AKIN 1. There were more oligoanuric patients in the AKI-RRT group (92.3% versus 21.0%, *P* < 0.001), likely a reflection of being on RRT before procurement. The median duration of dialysis in the AKI-RRT group before procurement was 2 d (range, 1–20 d). There was no statistical difference in the KDPI and DCD status between groups. The CIT was longer in the AKI-RRT group (30.3 versus 27.6 h, *P* = 0.31), but it did not reach statistical significance.

TABLE 1.
Recipient characteristics

	AKI-RRT group (N = 39)	AKI group (N = 457)	P
Age, y	52 (40–62)	58 (47–66)	0.06
Sex (male)	23 (59.0%)	277 (60.6%)	0.84
Race			0.16
White	12 (30.7%)	131 (28.7%)	
Black	5 (12.8%)	65 (13.1%)	
Hispanic	11 (28.2%)	124 (27.1%)	
Other	11 (28.2%)	137 (29.9%)	
BMI	25.7 (22–30)	27.4 (24–31)	0.38
cPRA	3 (0–26)	0 (0–44)	0.32
cPRA >40%	8 (20.5%)	118 (25.8%)	0.46
EPTS	36 (16–65)	52 (27–79)	0.03
EPTS >80%	5 (12.8%)	110 (24.1%)	0.11
DM	9 (23%)	172 (37.6%)	0.08
Preemptive	5 (12.8%)	76 (16.6%)	0.66
Duration of dialysis, y	4.3 (2.4–6.5)	3.7 (1.8–5.6)	0.06
Prior kidney transplant	2 (5.1%)	31 (6.8%)	1.0

Data are presented as numbers (percentages) and medians (interquartile ranges).
BMI, body mass index; cPRA, calculated panel-reactive antibody; DM, diabetes mellitus; EPTS, estimated posttransplant survival.

TABLE 2.
Donor characteristics

	AKI-RRT (N = 39)	AKI (N = 457)	P
Age, y	28 (22–42)	40 (29–50)	0.005
Sex (male)	26 (66.7%)	310 (67.8%)	0.88
BMI	28.1 (23.1–32.1)	28.4 (24.7–33.5)	0.11
History of hypertension	6 (15.3%)	146 (31.9%)	0.03
History of DM	3 (7.7%)	45 (9.8%)	1
Cause of death			<0.001
Anoxia	31 (79.5%)	205 (44.9%)	
CVA	5 (12.8%)	111 (24.3%)	
Head trauma	1 (2.6%)	125 (27.4%)	
Other	2 (5.1%)	16 (3.5%)	
Oligoanuric	36 (92.3%)	96 (21.0%)	<0.001
Admission Cr, mg/dL	1.2 (1.0–1.6)	1.3 (1.0–1.6)	0.009
Terminal Cr, mg/dL	2.6 (2.0–4.2)	3.1 (2.5–4.4)	0.09
Peak Cr, mg/dL	4.5 (2.8–5.7)	3.5 (2.7–4.7)	0.004
Nadir Cr, mg/dL	1.2 (0.8–1.6)	1.2 (0.9–1.5)	0.71
Duration of dialysis, d	2 (1–2)		
KDPI	48 (28–65)	51 (32–66)	0.18
KDPI >85%	0 (0.0%)	37 (8.1%)	0.10
DCD	7 (17.9%)	44 (9.6%)	0.10
Warm ischemic time, min	24 (16–51)	22.5 (19–28)	0.35
Uncontrolled	2 (28.5%)	4 (9.0%)	0.19
Cold ischemic time, h	30.3 (26.0–36.7)	27.6 (21.3–35.6)	0.31
Share status (imported)	37 (94.9%)	351 (76.8%)	0.007

Data are presented as numbers (percentages) and medians (interquartile ranges).
BMI, body mass index; Cr, creatinine; CVA, cerebrovascular accident; DCD, donation after circulatory death; DM, diabetes mellitus; KDPI, kidney donor profile index.

HMP Parameters

The majority of the kidneys in our cohort (89.3%) were preserved partially on HMP either at the OPO or at our institution (Table 3). There was no significant difference in the duration of pumping (10.3 versus 10.6 h, $P = 0.61$), terminal flow (89 versus 92 mL/min, $P = 0.58$), or terminal resistive index (0.31 versus 0.29 mmHg/mL/min, $P = 0.43$) between the AKI-RRT group and the AKI group.

Biopsy Findings

Procurement fresh frozen section biopsies were performed on 406 kidneys (81.9%) from our cohort (Table 4). Biopsy results from both groups showed the absence of chronic changes in the glomeruli, tubules, interstitium, and blood vessels as evidenced by the low percentage of glomerulosclerosis, absence to minimal interstitial fibrosis and tubular atrophy, and absence of minimal vascular disease. However,

TABLE 3.
Hypothermic machine perfusion utilization and parameters

	AKI-RRT group (N = 39)	AKI group (N = 457)	P
Pumped	37 (94.9%)	406 (88.8%)	0.41
Duration of pumping, h	10.3 (7.0–15.3)	10.6 (6.2–16.3)	0.61
Pumped in the OPO	13 (33.3%)	93 (20.4%)	0.07
Pumped in UCD	36 (92.3%)	384 (84.0%)	0.24
Duration of pumping in UCD, h	8.9 (4.6–14.5)	10.0 (5.6–14.5)	0.47
Terminal flow, mL/min	89 (78–104)	92 (79–109)	0.58
Terminal RI, mm Hg/mL/min	0.31 (0.25–0.36)	0.29 (0.23–0.38)	0.43

Data are presented as numbers (percentages) and medians (interquartile ranges).

AKI, acute kidney injury; OPO, organ procurement organization; RI, resistive index; RRT, renal replacement therapy; UCD, University of California Davis.

TABLE 4.
Biopsy findings

	AKI-RRT group (N = 39)	AKI group (N = 457)	P
Biopsy performed	34 (87.2%)	372 (81.4%)	0.52
Glomerulosclerosis, %	0 (0–5)	2 (0–7)	0.18
Interstitial fibrosis and tubular atrophy			0.62
None/mild	34 (100.0%)	354 (95.1%)	
Moderate/severe	0 (0.0%)	15 (4.0%)	
Vascular changes			0.09
None/mild	34 (100.0%)	339 (91.1%)	
Moderate/severe	0 (0.0%)	30 (8.1%)	
Acute tubular necrosis			<0.001
None/mild	23 (67.6%)	335 (90.0%)	
Moderate/severe	11 (32.4%)	34 (9.1%)	
Cortical necrosis (focal)	0 (0.0%)	6 (2.0%)	1.0
Fibrin thrombi	1 (3.0%)	37 (10.0%)	0.35

Data are presented as numbers (percentages) and medians (interquartile ranges).

AKI, acute kidney injury; RRT, renal replacement therapy.

TABLE 5.
Outcomes

	AKI-RRT group (N = 39)	AKI group (N = 457)	P
DGF	28 (71.8%)	190 (41.6%)	<0.001
Duration of DGF, d	17.0 (11.8–22.5)	16.0 (9.0–22.0)	0.89
Hospital length of stay	5.0 (4.0–7.5)	5.0 (4.0–6.0)	0.94
90-d graft loss	0 (0.0%)	19 (4.2%)	0.39
1-y graft loss	0 (0.0%)	37 (8.1%)	0.10

Data are presented as numbers (percentages) and medians (interquartile ranges).

AKI, acute kidney injury; DGF, delayed graft function; RRT, renal replacement therapy.

the severity of ATN was observed to be more severe as evidenced by the higher percentage of moderate to severe ATN changes in the AKI-RRT group (32.4% versus 9.1%, $P < 0.001$). Focal cortical necrosis (<10%) was seen in 6 biopsies (2.0%) in the AKI group but none in the AKI-RRT group.

Outcomes

There was a higher incidence of DGF in the AKI-RRT group (71.8% versus 41.6%, $P < 0.001$) than in the AKI group (Table 5). The duration of DGF was equivalent in both groups (17 versus 16 d). No difference in hospital length of stay was observed between both groups (5 versus 5 d). We did not observe any graft loss in the AKI-RRT group at 90 d or 1 y posttransplant. There were 19 grafts that were lost

in the first 90 d posttransplant in the AKI group, 7 of which (36.8%) were due to PNF (Table 6). With a median follow-up of 5 y, there was no difference in death-censored graft survival and patient survival between both groups (Figures 1 and 2). Regarding long-term renal function, there was no difference in mean (SD) values of GFR at 6 mo (60.6 [15.6] versus 58.7 [21.4], $P = 0.59$), 1 y (63.1 [17.2] versus 60 [21.3], $P = 0.39$), 2 y (63.8 [18.4] versus 60.9 [21.8], $P = 0.42$), 3 y (62.3 [19.3]) versus 61.1 [21.8], $P = 0.75$), 4 y (62.7 [21.0] versus 61.5 [22.0], $P = 0.77$), and 5 y (67.3 [20.8] versus 61.8 [22.1], $P = 0.29$) between the AKI-RRT group and the AKI group, respectively (Figure 3). After controlling for the donor factors in the propensity score-matched cohort, there were 39 patients in the AKI-RRT group and 195 in the AKI group (1:5 matching). There was no statistical

TABLE 6.
Cause of graft loss in 90 d

Primary nonfunction	7
Graft thrombosis	3
Acute rejection	2
Acute kidney injury	2
Infection	2
Death with a functioning graft	2
Ureteral complications	1

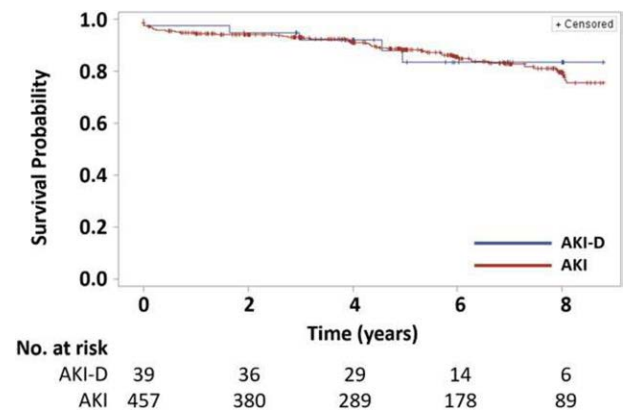


FIGURE 1. Death-censored graft survival for the entire cohort ($P = 0.83$). AKI-D, acute kidney injury donor.

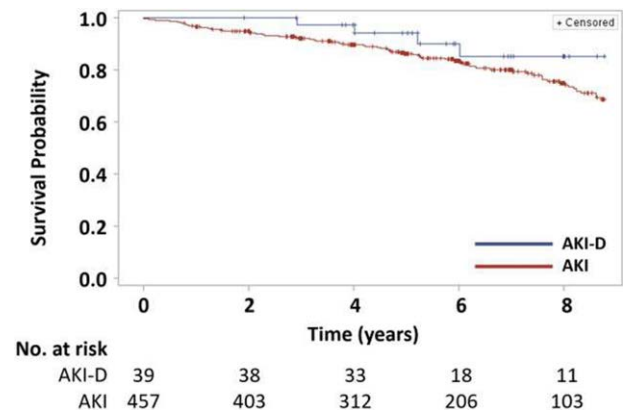


FIGURE 2. Patient survival for the entire cohort ($P = 0.15$). AKI-D, acute kidney injury donor.

difference in donor characteristics except for donor’s cause of death ($P < 0.001$), import status ($P = 0.019$), terminal Cr ($P = 0.0017$), and severity of ATN on biopsy ($P = 0.024$). There was higher incidence of anoxia (but no difference in the incidence of CVA) as a cause of death, higher percentage of imported organs, lower terminal Cr, and higher incidence of moderate to severe ATN on procurement biopsies in the AKI-RRT group. We did not observe any statistical difference in the death-censored graft survival or patient survival (Figures 4 and 5).

DISCUSSION

Several contemporary studies have reported on the utilization and outcomes of kidneys from donors with severe AKI. These studies showed excellent long-term renal allograft

function without compromising graft survival.⁹⁻¹³ Additionally, the use of AKI donors can be expanded to include high KDPI and DCD donors.^{14,15} In comparing kidneys from donors with severe AKI without RRT, single-center and multicenter studies showed that kidneys from donors with severe AKI requiring RRT had similar graft survival without a comprising long-term renal function.¹⁶⁻¹⁸ In all these studies, donor selection was of paramount importance; kidneys that showed no evidence of chronicity and lack of extensive cortical necrosis on biopsy were selected. Short- and long-term outcomes of using these grafts were equivalent to grafts from standard criteria donors.

In the current study, severe AKI kidneys from donors on RRT showed equivalent graft survival and function to non-RRT AKI kidneys. The results of our study are in line with those of prior studies. In our cohort, 39 patients received a renal allograft from donors with severe AKI on RRT. None of the 39 recipients had graft loss within 1 y. We also demonstrated excellent long-term renal function equivalent to the no RRT AKI group without compromising graft or patient survival. After controlling for donor factors in the propensity score-matched analysis, we still observed equivalent outcomes in both groups.

To achieve good outcomes while using kidneys from donors with severe AKI, we think that donor selection is of paramount importance and should be coupled with appropriate recipient selection. Over the last decade, our center’s practice in using kidneys from donors with AKI, particularly severe AKI, has evolved, and we focus on the following criteria. First, as shown in our cohort demographics, we tend to accept younger donors with no significant history of diabetes or HTN. We think that these demographic parameters strongly correlate with the absence of chronic changes in the kidney that negatively affect the kidney’s ability to recover from the AKI insult. Second, we pay particular attention to the gross appearance of the kidneys, with emphasis on the quality of organ flush and the lack of significant vascular disease in the aorta and renal arteries. Third, 88.8% of the kidneys in our cohort were biopsied and the majority showed no evidence of chronic changes or widespread cortical necrosis. We usually avoid kidneys that have evidence of chronicity on the procurement biopsy or the presence of widespread cortical necrosis. We do realize the limitations of procurement biopsies, but coupled with the above-mentioned selection criteria, we think that we can potentially avoid kidneys that have evidence of chronic changes or widespread necrosis. Fourth, 96.9% of the kidneys in our cohort were preserved on HMP for approximately 10h with terminal flows of approximately 90 mL/min and terminal resistive indices around 0.3 mmHg/mL/min. We think that HMP is important in extending the CIT compared with cold storage, and it adds another parameter when evaluating these high-risk grafts. We generally do not decline kidneys solely on perfusion parameters rather we use them as an adjunct when accepting these grafts. Fifth, we generally tend to limit our CIT threshold to 24–30h. Our CIT is significantly longer compared with prior reports.¹⁴⁻¹⁶ Finally, we think recipient selection is as important as donor selection. As these patients are expected to have prolonged DGF (median of 16 d), we tend to select younger patients with good EPTS and good cardiopulmonary reserve for these grafts.

Our study has several limitations; first, the number of recipients in the AKI-RRT group is much smaller compared with those in the AKI group, thus potentially underpowering our

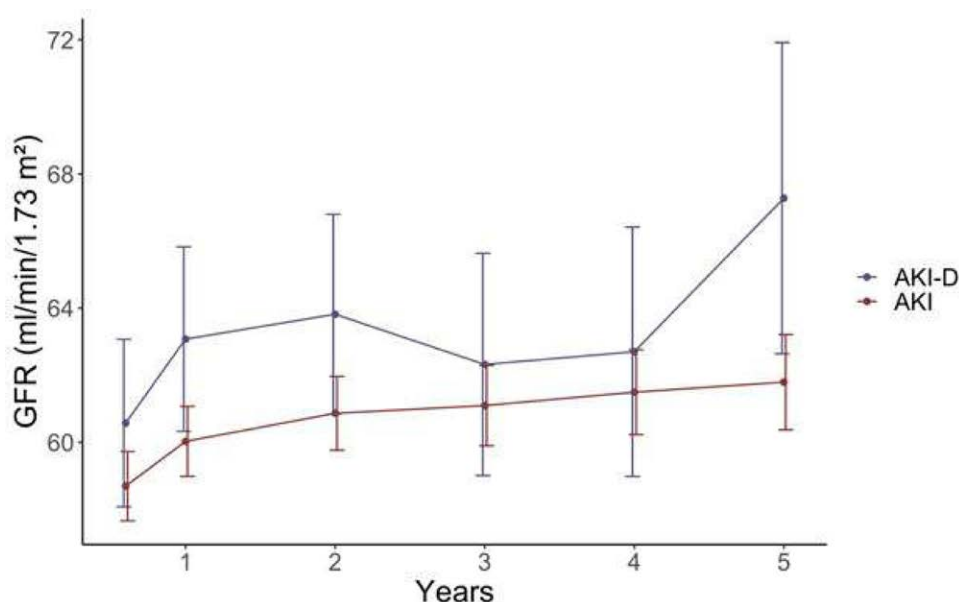


FIGURE 3. Renal function. Data are presented as mean and SE of the mean. AKI-D, acute kidney injury donor; GFR, glomerular filtration rate.

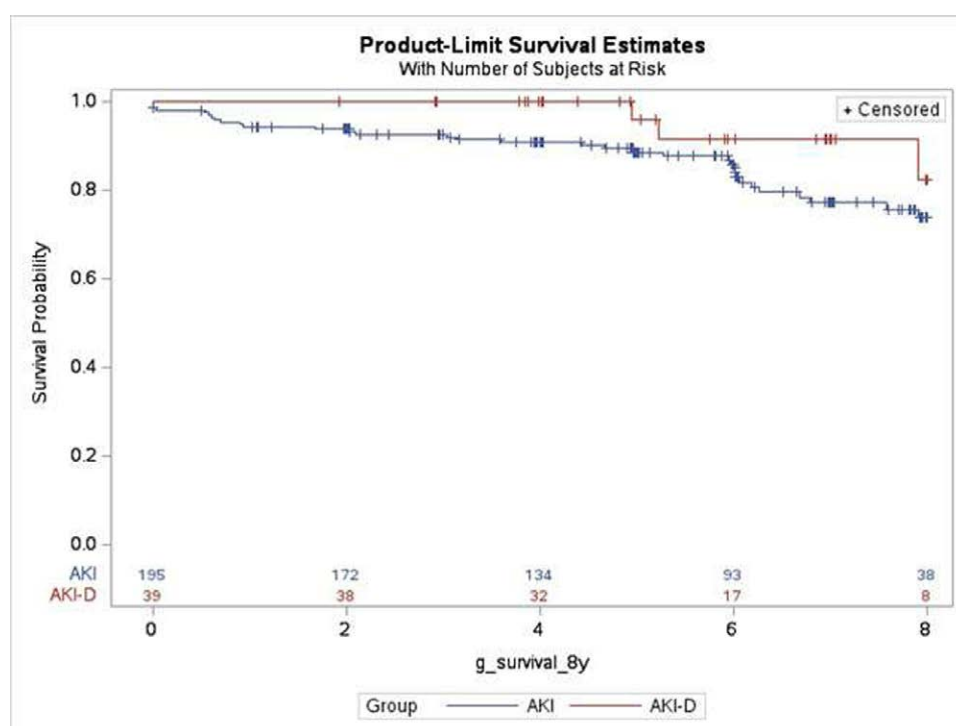


FIGURE 4. Death-censored graft survival for the propensity score-matched cohort ($P = 0.15$). AKI-D, acute kidney injury donor.

study to detect differences between both groups. Second, as we failed to evaluate the characteristics of the kidneys that were rejected, we are unable to fully evaluate the risk factors associated with graft failure. By achieving a 100% 1-y graft survival, we acknowledge that our selection criteria are likely conservative, and we potentially declined some organs that could have been used. Our donor selection in the non-RRT group was more liberal (older donors, higher incidence of HTN, and more chronicity in the biopsy), hence the higher incidence of PNF in that group. Third, because of the low number of patients with PNF ($n = 7$), we did not perform correlation studies between donor

factors and PNF. Fourth, we relied on procurement biopsies that were obtained and reported by the OPO, which are mostly read by a nonspecialized renal pathologist, thus making them less standardized and sometimes misrepresenting the presence and severity of chronic changes on the biopsy. However, we think that there are time and logistical constraints associated with repeating kidney biopsies and re-reading the biopsy with a specialized renal pathologist in our institution. Instead, in this study, we evaluated the results of the procurement biopsies that would have been available to the accepting physician at the time of the offer.

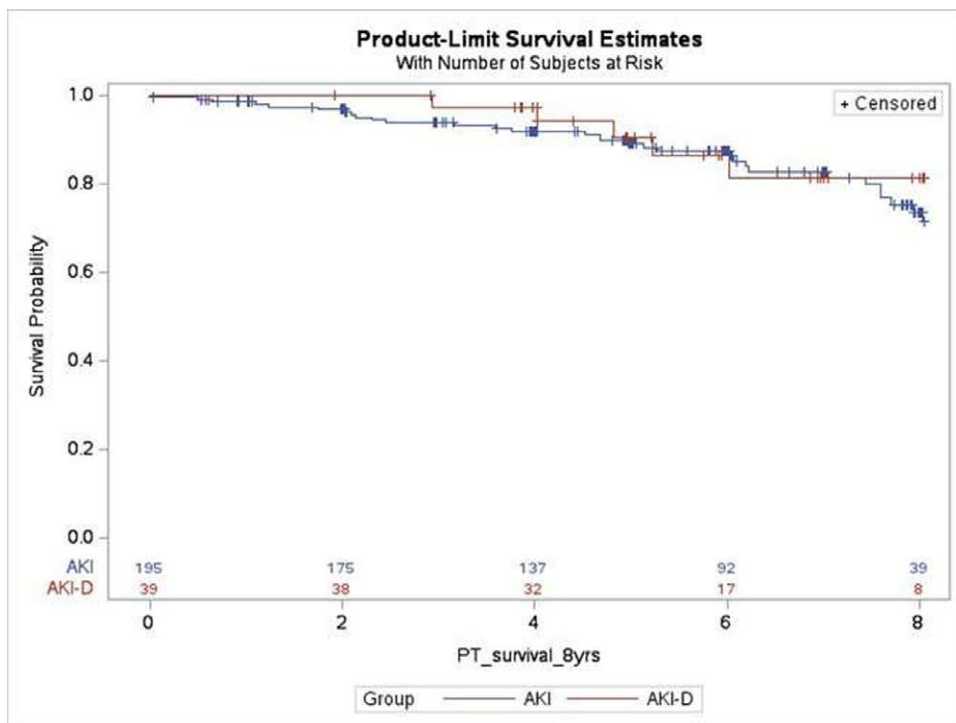


FIGURE 5. Patient survival for the propensity score-matched cohort ($P = 0.56$). AKI-D, acute kidney injury donor.

In conclusion, this study adds to the current literature on the safety of using kidneys from donors with severe AKI. These findings should encourage transplant centers to use kidneys from donors with severe AKI in an effort to expand the donor pool and narrow the gap between supply and demand. We showed that in carefully selected donors, kidneys from donors with severe AKI requiring RRT can achieve excellent long-term outcomes and thus using them can further expand the donor pool. More studies are needed to investigate risk factors associated with graft failure.

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