

Good Outcomes in Kidney Transplantation With Deceased Donor With Acute Kidney Injury: Donor's Age and Not Acute Kidney Injury Predicts Graft Function

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ABSTRACT

Background. With the increased demand for kidney transplants and the short supply of organs, it is necessary to have a better strategy to evaluate the available organs, especially from donors with acute kidney injury (AKI), because these organs are often rejected for transplantation.

Methods. We evaluated patients undergoing transplantation with kidneys from deceased donors with AKI. The cases were divided into AKI stages according to the Acute Kidney Injury Network (AKIN) criteria. The outcomes examined were delayed graft function (DGF), creatinine (Cr), and creatinine clearance (CrCl) at 6 months after transplantation.

Results. We evaluated 101 patients and included 53 in the final model. There was no statistical difference in the demographic characteristics, comorbidities, and immunosuppression according to each AKIN stage, showing a population of homogeneous transplant recipients. Recipients in AKIN stages I, II, and III, respectively had DGF in 72.7%, 61.9%, and 71.4% of cases; Cr of 1.6 ± 0.5 , 1.7 ± 0.7 , and 1.6 ± 0.2 mg/dL at 6 months; and CrCl of 60.6 ± 22.4 , 52.4 ± 27.4 , and 52.03 ± 12.1 mL/min at 6 months. Each additional year in donor age increased the relative risk of DGF by 1.08 (1.0–1.13) ($P = .01$), and organs from older donors were associated with worse renal function at 6 months.

Conclusion. Kidney transplantation of organs from deceased donors with AKI showed greater DGF but good outcomes. Donor age was the only characteristic that correlated with outcome.

WITH the increasing number of patients waiting for kidney transplantation, there is a greater demand for organs. There is an imbalance in offers of organs to transplant, and a need to expand the deceased donor pool [1]. Organs from donors with acute kidney injury (AKI) are usually discarded because of the possibility of adverse outcomes. Use of these organs may result in more delayed graft function (DGF) and worse renal function, because AKI is an independent risk factor for chronic kidney disease (CKD) [2,3]. Nevertheless, it is assumed that AKI in deceased donors is commonly caused by hypoxic-ischemic and/or nephrotoxic lesions, which are potentially reversible [4]. In addition, we do not know what terminal creatinine (Cr) value in a deceased donor would determine the discarding of the organ [4,5]. Most studies show favorable results in donors

with AKI [6–9]. Siedlecki et al showed favorable outcomes of creatinine clearance (CrCl) at 6 months despite the higher rate of DGF [6], and other studies confirm these findings in regard to long-term renal function [7,8]. It has also been noted that there are good outcomes for organs of donors with AKI who had only a slight injury on biopsy [9].

The aim of this study was to describe the results of patients undergoing transplantation of kidneys from deceased donors with AKI, and the impact on renal function at 6 months after transplantation.

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PATIENTS AND METHODS

This was an observational retrospective study of all patients who underwent renal transplantation with deceased donor kidneys at the Universidade Estadual Paulista (UNESP), from January 2010 to September 2014. We selected all cases in which the donor had AKI. The AKI patients were divided into stages according to the Acute Kidney Injury Network (AKIN) criteria [10] based on initial and terminal creatinine values.

We excluded patients whose stage of AKI could not be determined because of a lack of baseline Cr or initial Cr data, and patients with <6 months of follow-up.

The recipient baseline characteristics examined were age, sex, race/ethnicity, underlying disease, induction therapy, immunosuppression, and panel reactive antibody. The donor baseline characteristics were age, creatinine, cause of death, and presence of hypertension or diabetes.

We evaluated as outcomes the number of days of hospitalization (length of stay), DGF, Cr, and CrCl at 6 months after transplantation and compared these outcomes according to each AKI stage by AKIN criteria. The CrCl was estimated by the Modification of Diet in Renal Disease (MDRD) equation [11].

Statistical Analysis

Analysis of variance for parametric variables was used for the statistical analysis of continuous variables, and the Kruskal-Wallis test was used for nonparametric variables. For categorical variables, the χ^2 test was used. Binary logistic regression was used for the multivariate analysis, considering the DGF risk, and adjusting

for donor age, AKIN stage, and panel reactive antibody. Multivariate linear regression analysis was also performed with CrCl at 6 months as the dependent variable and adjusted to AKIN stages, donor age, cause of death, panel reactive antibody, and DGF. We constructed a classification tree model having as the dependent variable the CrCl at 6 months and tested as variables donor age, cause of death, panel reactive antibody, and DGF with the CHAID growing method. The significance level was set at $P < .05$. SPSS version 20 software was used.

RESULTS

We evaluated 101 patients undergoing transplantation with kidneys from deceased donors with AKI. We excluded 48 patients, 27 because we could not determine AKIN stage and 11 because they had less than 6 months of follow-up; in addition, 8 patients died before 6 months, 1 graft was lost (surgical cause) in less than 6 months, and 1 patient were transferred. A total of 53 patients were included in the final model.

The recipient characteristics showed a predominantly male population of white ethnicity, in the fifth decade of life; systemic arterial hypertension and diabetes mellitus were the main causes of CKD. Induction therapy was performed mostly with basiliximab and the standard immunosuppression consisting of tacrolimus, mycophenolate, and prednisone. Regarding the donor characteristics,

Table 1. Characteristics of Transplant Patients With Kidneys From Deceased Donors With Acute Kidney Injury

Characteristic	AKIN I (n = 23)	AKIN II (n = 21)	AKIN III (n = 9)	P Value
Male sex	17 (73.9%)	13 (61.9%)	6 (66.7%)	NS
White race	17 (73.9%)	14 (66.7%)	7 (77.8%)	NS
Age (y)	50 ± 14	52 ± 13	56 ± 11	NS
Underlying disease				NS
Hypertension	8 (34.8%)	8 (38.1%)	3 (33.3%)	
Diabetes	8 (34.8%)	5 (23.8%)	5 (55.6%)	
Glomerulonephritis	4 (17.4%)	3 (14.3%)	0	
Unknown	2 (8.7%)	3 (14.3%)	1 (11.1%)	
Other	1 (4.3%)	2 (9.5%)	0	
Induction therapy				NS
Basiliximab	20 (87%)	14 (66.7%)	7 (77.7%)	
Thymoglobulin	3 (13%)	7 (33.3%)	2 (22.2%)	
Immunosuppression				NS
Tacrolimus	23 (100%)	21 (100%)	9 (100%)	
Mycophenolate	20 (87%)	18 (85.7%)	9 (100%)	
Prednisone	23 (100%)	21 (100%)	9 (100%)	
Azathioprine	2 (8.7%)	1 (4.8%)	0	
SRL/EVR	1 (4.3%)	2 (9.5%)	0	
Panel reactive antibody (%)	7 ± 19	17 ± 31	23 ± 34	NS
Donor age (y)	40 ± 13	46 ± 12	39 ± 12	NS
Donor creatinine (mg/dL)	1.94 ± 0.26	2.38 ± 0.46	3.18 ± 0.54	.05
Cause of donor death				NS
Cranial trauma	13 (56.5%)	7 (33.3%)	3 (33.3%)	
Cerebrovascular	9 (39.1%)	13 (61.9%)	6 (66.7%)	
Others	1 (4.3%)	1 (4.8%)	0	
Donor hypertension	10 (43.5%)	11 (52.4%)	3 (33.3%)	NS
Donor diabetes	1 (4.3%)	2 (9.5%)	0	NS

Data based on univariate analysis.

Abbreviations: NS, not significant; SRL, sirolimus; EVR, everolimus; DGF, delayed graft function; Cr, creatinine; CrCl, creatinine clearance; AKIN, Acute Kidney Injury Network.

Table 2. Outcomes in Transplant Patients With Kidneys From Deceased Donors With Acute Kidney Injury

	AKIN I	AKIN II	AKIN III	P
DGF	16 (72.7%)	13 (61.9%)	7 (71.4%)	NS
Length of stay (days)	16 ± 10	18 ± 9	18 ± 11	NS
Cr at 6 months (mg/dL)	1.6 ± 0.5	1.7 ± 0.7	1.3 ± 0.2	NS
CrCl at 6 months (mL/min)	60.6 ± 22.4	52.4 ± 27.4	62.03 ± 12	NS

Data are number (%), or mean ± standard deviation; based on univariate analysis.

Abbreviations: NS, not significant; DGF, delayed graft function; Cr, creatinine; CrCl, creatinine clearance.

the average age was the fourth decade of life, and the cause of death was predominant cranial trauma or cerebrovascular disease (Table 1).

As for the evolution of the patients, there was no statistical difference for DGF, longer hospital stay, or Cr and CrCl at 6 months in relation to AKIN stages. The DGF rates were 72.7%, 61.9%, and 71.4% respectively for AKIN stages I, II, and III. The Cr values were an average of 1.6 ± 0.5 mg/dL for stage I, 1.7 ± 0.7 mg/dL for stage II, and 1.3 ± 0.2 mg/dL for stage III. The CrCl values at 6 months were 60.6 ± 22.4 mL/min, 52.4 ± 62 mL/min, and 62.03 ± 12 mL/min, respectively, for stages I, II, and III (Table 2). In multivariate linear regression analysis, among the variables related to CrCl at 6 months, only the age of the donor was negatively related to renal function ($\beta = -0.58$, $P = .01$) (Table 3). In addition, multivariate logistic regression showed that donor age was an independent risk factor for DGF, with a relative risk of 1.08 (1.008–1.137, $P = .02$) (Table 4).

By classification tree analysis, we noted that the age of the donor was the main determinant for CrCl at 6 months, with an average of 57.59 ± 23 mL/min. When the donor's age was less than 31 years, the CrCl rose to 77.6 ± 28 mL/min. On the other hand, when the donor's age was more than 54 years, the CrCl dropped to 38 ± 14 mL/min ($P = .01$). The cause of the donor's death determined renal function in the recipient. When the cause was cranial trauma, the CrCl was better (56 ± 10 mL/min), and when cause of death was cerebrovascular disease, the renal function was worse (31.5 ± 8.4 mL/min, $P = .001$) (Fig 1).

Table 3. Creatinine Clearance at 6 Months in Kidney Transplant Recipients

	β	P Value
AKIN stage	0.06	.62
Donor age (y)	−0.58	.01
Cause of donor death	−0.09	.51
Panel reactive antibody	0.07	.62
Delayed graft function	0.18	.18

Data are based on multivariate analysis and linear regression.

Abbreviation: AKIN, Acute Kidney Injury Network.

Table 4. Multivariate Analysis and Logistic Regression of Risk for Delayed Graft Function

Variable	RR (95% CI)	P
Donor age (y)	1.08 (1.008–1.137)	.02
AKIN I	1.02 (0.13–7.8)	.98
AKIN II	0.40 (0.05–3.0)	.38
Panel reactive antibody	0.99 (0.96–1.02)	.68

Abbreviations: RR, relative risk; CI, confidence interval; AKIN, Acute Kidney Injury Network.

DISCUSSION

The majority of recipients with deceased donor kidneys with AKI presented with DGF. The rates are around 70% for all AKIN stages. The DGF rates are similar to those found in this service in patients with deceased donor kidneys without AKI (around 60%) [12]. These rates are also similar to the incidence of DGF in Brazil (70%) [13]. In a study by Hall et al [14], DGF rates were slightly lower for the AKIN stages 1, 2, and 3, which were 34%, 52%, and 57%, respectively. Similar results were found in a study by Jung et al [15], with DGF higher in patients with AKI compared to the group without AKI. Nevertheless, in the present study, the renal function of transplant recipients was good after 6 months posttransplantation at the 3 AKIN stages, with an average creatinine clearance of 60 mL/min. Then, despite the high rates of DGF in patients who received kidneys with AKI, reflecting an increased hospital stay, our patients had favorable outcomes. Hall et al [9] found the glomerular filtration rate (GFR) at 6 months to be 55 mL/min for renal transplant patients with AKI. In native kidneys, the severity of AKI is associated with worse clinical outcomes [16,17]. In transplanted kidney, DGF is traditionally a response to AKI and it is a known risk factor to poor outcome and graft survival [14]. Based on this evidence, it seems reasonable to assume that AKI in the donor can lead to a nonfunctioning graft; however, recent clinical studies [7–9] and the present study failed to demonstrate this association.

Our results indicate that, more important than the severity of AKI, was the age of the donor. Each 1-year increase in age of the donor resulted in an 8% increased risk of DGF and also poorer renal function after 6 months. Classification tree analysis showed a division in 3 age stages (31 years, 31–54 years, and more than 54 years) that predicts renal function at 6 months. For donors older than 54 years, the main determinant of renal function was the cause of death, with better renal function if the donor's cause of death was cranial trauma.

In conclusion, in this study, transplant patients with kidneys with AKI had favorable outcomes at 6 months despite high rates of DGF. The severity of AKI appears to have no impact on renal function; instead, the age of the donor is the main risk factor for DGF and poor renal function after 6 months. The cause of death of the donor is an important determinant of renal function in donors older than 54 years.

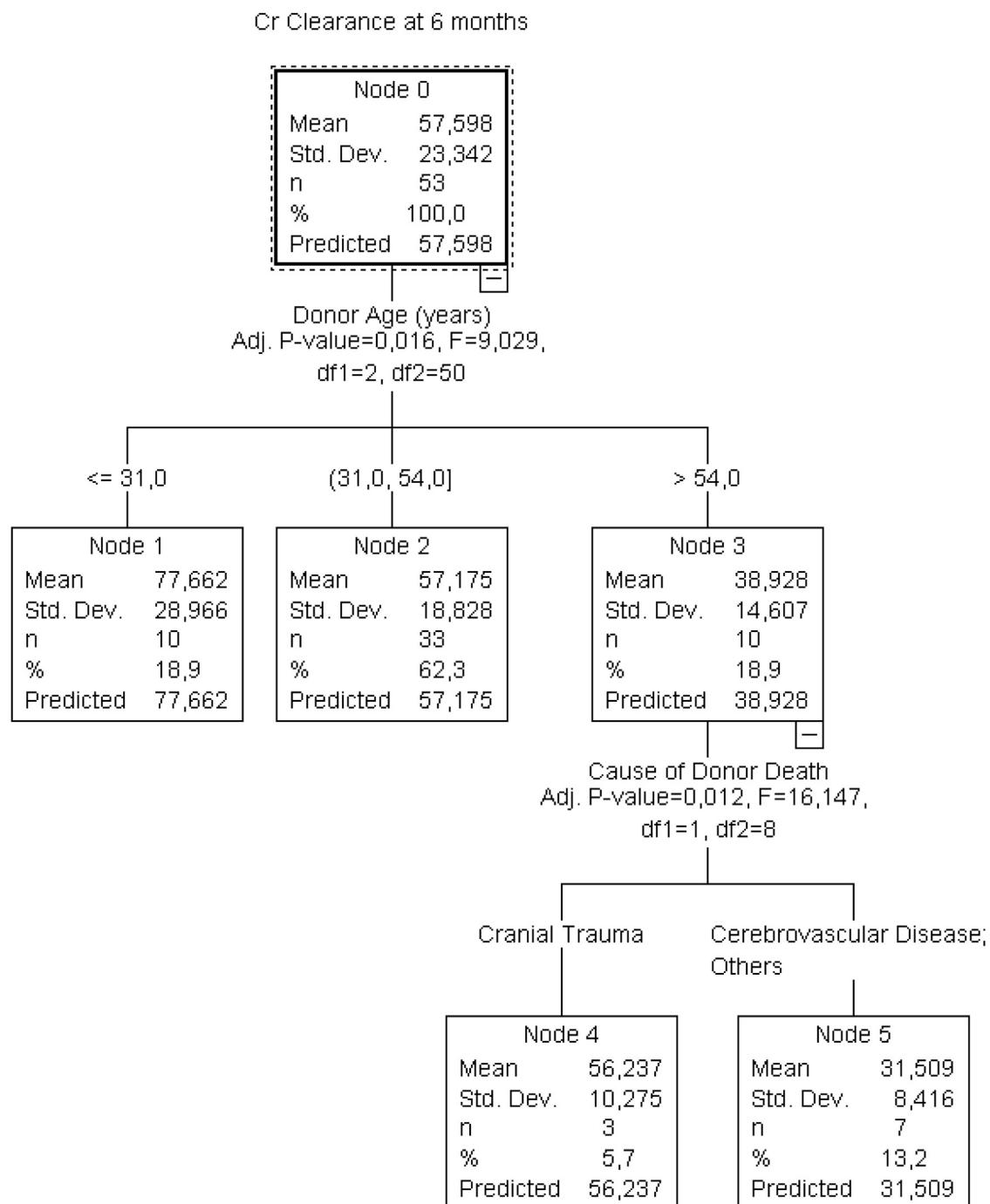


Fig 1. Classification tree model for transplant patients with deceased donor kidney with acute kidney injury (AKI). The model has as dependent variable the creatinine clearance (CrCl) at 6 months and tests for age of donor, cause of donor death, panel reactive antibody, and delayed graft function using CHAID growing method. Std. Dev., standard deviation.

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