Predictors of Acute Kidney Injury in Deceased Kidney Donors After Brain Death

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ABSTRACT

Background. Donors with acute kidney injury (AKI) are generally accepted as a valuable source of kidneys for transplant. The aim of this study was to assess the risk of developing AKI based on deceased kidney donor parameters.

Materials and Methods. The data of 162 kidneys procured from deceased donors after brain death were collected. These included clinical characteristics of donors and histologic assessment in organ biopsy specimens. The donors' kidney terminal function was classified according to the Acute Kidney Injury Network criteria. All biopsies were performed with the use of a 16G automatic needle, and the 20-mm tissue specimen was available in all cases. Biopsy specimens were secured and prepared in a routine way with hematoxylin and eosin. The presence of chronic changes was analyzed according to the Banff 2009 classification by 1 experienced nephropathologist. The logistic regression model was used to assess the risk of AKI regarding donor characteristics and histologic findings.

Results. There were 50 kidneys (30.9%) with AKI identified. The risk of AKI increased with donor age ($P = .002$; odds ratio [OR], 1.02; 95% CI, 1.01–1.03), body mass index ($P = .003$; OR, 1.05; 95% CI, 1.01–1.09), and male sex ($P = .001$; OR, 1.79; 95% CI, 1.31–2.27). Regarding the histologic findings, the interstitial fibrosis presence was a risk factor of AKI ($P = .004$; OR, 1.04; 95% CI, 1.01–1.06).

Conclusions. Older donor age, male sex, higher body mass index, and presence of interstitial fibrosis in kidney graft biopsy specimen are risk factors of AKI.

THERE is no one definition of an ideal kidney donor, but it may be summarized as a young (less than 30 years old) man with no medical history and low body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) who died because of central nervous system trauma with a short hospital stay [1]. As there is a persistent discrepancy between the number of available organs and patients on the waiting list for kidney transplant, the transplant community has to balance between the risk of transplanting a less than ideal organ and the risk of waiting [2]. According to different sources, the annual mortality on the waiting list for kidney transplant fluctuates around 5% to 10% [3,4] but can be higher among older patients. Kidneys procured from expanded criteria donors, donors after circulation death, or donors with acute kidney injury (AKI) present different degrees of damage [5]. There are obvious differences in the severity and reversibility of organ damage between donors. Kidney injury may

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almost completely recover in the post-transplant period when the cause of this injury has been mitigated. [6]

Donors with AKI are generally accepted as a valuable source of kidneys for transplant [7,8]. However, there is no agreement regarding the AKI criteria and principles of management with kidneys from AKI donors, including additional examination such as pretransplant biopsy.

The aim of this study was to assess the risk of developing AKI based on deceased kidney donor parameters.

MATERIAL AND METHODS

The data of 162 kidneys procured from deceased donors after brain death and accepted for transplant in the single center were collected retrospectively. These included clinical characteristics of donors and histologic assessment in organ biopsy specimens. The donor age, sex, BMI, length of stay in the intensive care unit (ICU), history of hypertension, cardiac arrest episodes, usage of vasoactive drugs, episodes of hypotension, as well as serum creatinine concentration at the admission and before retrieval (terminal creatinine) were analyzed.

The donors' kidney terminal function was classified according to the Acute Kidney Injury Network (AKIN) criteria. [9] Kidneys were divided into 4 groups regarding the presence of acute kidney injury. The scoring system of the AKIN was used to classify kidneys to 1 of the groups based on the change of donor serum creatinine concentration (from baseline). The increase of $\geq$ 0.3 mg/dL or 1.5- to 2-fold from baseline was classified as stage 1 (AKIN 1). The increase of more than 2-fold and less than 3-fold from baseline was classified as stage 2 (AKIN 2). The increase of more than 3-fold from baseline was classified as stage 3 (AKIN 3). Kidneys from donors who did not meet the AKIN criteria were classified as non-AKI. The baseline creatinine concentration was defined as the creatinine outcome at the moment of admission to ICU. Because of small numbers, non-AKI kidneys (non-AKI group) were compared with AKI kidneys (AKI group).

Kidney Biopsy

Preimplant kidney biopsies were performed during back-table preparation of the organs. All biopsies were performed with the use of a 16G automatic needle, and the 20-mm tissue specimen was available in all cases. Biopsy specimens were secured and prepared in a routine way with hematoxylin and eosin. The histologic findings in the analyzed series were not available prior to transplant. The presence of chronic changes was analyzed according to the Banff 2009 classification by 1 experienced nephropathologist. The presence of chronic changes as tubular atrophy (TA), interstitial fibrosis (IF), glomerulosclerosis, arteriolar hyalinosis, interstitial inflammation, and vascular intimal sclerosis was evaluated.

Statistical Analysis

Statistical analysis was performed using SAS software (Version 8.2; SAS Institute Inc, Cary, NY, United States). Categorical variables were summarized through the calculation of frequency, and continuous variables were summarized using descriptive statistics. The *t* test or Wilcoxon test was applied for testing differences between means and medians, respectively. Multivariate regression analysis was performed using the logistic regression model. The chronic histologic changes as well as variables characterizing the donor, when the testing differences *P* value was equal or lower than .15, were included into the multivariate analysis. The impact of the donor factors on AKI was reported using odds ratios (ORs), 95% CIs, and statistical significance test results. A critical α level for hypothesis testing was set at 0.05.

RESULTS

A total of 69.1% (n = 112) of kidneys were classified in the non-AKI group. In the AKI group (n = 50), 24 kidneys were included in the AKIN 1 group, 15 were assigned to the AKIN 2 group, and 11 were included in the AKIN 3 group. The AKI kidneys were procured from older donors (53.3 vs 47 years; $P = .03$); there were significantly less men in the non-AKI group compared with the AKI group (50.7% vs 79.3%; $P = .002$). Donors of kidneys from the AKI group presented higher BMI compared with the non-AKI group (27.4 vs 25.2; $P = .04$).

There were no significant differences between groups (non-AKI and AKI) regarding the mean ICU stay, history of hypertension, cardiac arrest episodes, use of vasoactive medications, and episodes of hypotension (Table 1).

In the multivariate analysis, 3 variables characterizing donors were independent risk factors of AKI: donor age ($P = .002$; OR, 1.02; 95% CI, 1.01–1.03), BMI ($P = .003$; OR, 1.05; 95% CI, 1.01–1.09), and male sex ($P = .001$; OR, 1.79; 95% CI, 1.31–2.27). The IF presence was the only independent risk factor of AKI among histologic chronic changes in the kidney biopsy specimen ($P = .004$; OR, 1.04; 95% CI, 1.01–1.06) (Table 2).

DISCUSSION

The analysis of risk factors that determine AKI has not been explored intensively among the deceased donor population. In the current study, donor age, BMI, male sex, and IF were independent risk factors of AKI. The sex issue was discussed in many studies, and recent meta-analysis confirms that female sex is protective for AKI among hospitalized patients [10]. Age was identified as an independent risk factor of AKI in different patient cohorts [11]. The gradual reduction of the glomerular filtration rate and the loss of renal functional reserve are correlated with aging [12]. This explains why older donors are more receptive for the kidney injury during agony. Regarding BMI, the correlation between obesity and AKI seems to be not so evident [13]. The BMI itself is not well accepted as an independent risk factor for AKI, although some studies have emphasized the role of metabolic changes in obese patients and the progress of kidney injury [14]. In our analysis, donor BMI was the one of risk factors of developing AKI.

The unique aspect of this study is the time-zero biopsy evaluation. There is normally no access to the kidney tissue in the nontransplant clinical setting, so histologic chronic changes were not investigated intensively as risk factors for AKI. However, intuitionally kidneys with nephron structural damage should be more prone to develop AKI. In the study published by Heilman et al, there were no significant differences in chronic histologic changes between the AKI and non-AKI groups [15]. However, they did not analyze

Table 1. Donor Characteristics

	Non-AKI (n = 112)	AKIN 1 (n = 24)	AKIN 2 (n = 15)	AKIN 3 (n = 11)	AKI (n = 50)	*P* Value
Age, mean (SD), y	47.0 (15.5)		53.3 (14.7)			.03
Male sex, %	50.7		79.3			.002
BMI, mean (SD)	25.2 (4.0)		27.4 (8.2)			.04
ICU stay, mean (SD), d	4.5 (2.9)		4.7 (2.7)			.85
Hypertension history, %	24.6		28.9			.09
Donor cardiac arrest, %	27.2		19.9			.10
Donor vasoactive medications use, %	81.6		94.9			.15
Hypotension, %	60.3		79.1			.25
Terminal serum creatinine, mean (SD), mg/dL	0.91 (0.32)		3.76 (1.18)			< .001

Abbreviations: AKI, acute kidney injury; AKIN, Acute Kidney Injury Network; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); ICU, intensive care unit; NS, not significant.

histologic chronic changes separately (as we did), and they analyzed post-transplant biopsy specimens at 1, 4, and 12 months. They calculated the sum of Banff IF score and TA score, and they observed progressive increase in time of chronic changes measured by fraction of biopsy specimens with IF/TA greater than 2. The kidneys procured from high risk donors (including AKI) should be evaluated in biopsy examination [16]. Although the biopsy result cannot be the only determinant for the decision-making about an organ's acceptance, but it helps to achieve an opinion about the kidney quality in general [17]. In the study published by Lin et al, the time-zero biopsy histologic evaluation from donors with high terminal serum creatinine concentration allowed the achievement of optimal organ use and helped to optimize results of kidney transplant [18].

This compendious analysis has several limitations. It can be assumed that some bias is presented in the kidney donor selection as this is a single-center, retrospective study. The potential donor acceptance decision is based on the analysis of a combination of different factors. When there is a kidney offer from a deceased donor with AKI, both the nephrologist as well as the transplant surgeon are more precautious in acceptance when other donor risk factors are present.

Table 2. Multivariate Analysis and Logistic Regression of Risk for Acute Kidney Injury in Deceased Donor

Variable	OR (95% CI)	*P* Value
Donor age, y	1.02 (1.01–1.03)	.02
Donor male sex, yes/no	1.79 (1.31–2.27)	.001
Donor BMI	1.05 (1.01–1.09)	.03
Donor hypertension history, yes/no	0.97 (0.43–1.53)	.94
Donor cardiac arrest, yes/no	0.92 (0.54–1.30)	.69
Donor vasoactive drugs use, yes/no	0.93 (0.27–1.58)	.83
Tubular atrophy, yes/no	1.61 (0.05–3.27)	.47
Interstitial fibrosis, yes/no	1.04 (1.01–1.06)	.04
Arteriolar hyalinosis, yes/no	1.07 (0.85–1.29)	.54
Glomerulosclerosis, ≥ 15%/< 15%	1.16 (0.73–1.59)	.46
Interstitial inflammation, yes/no	1.67 (0.81–2.53)	.12
Vascular intimal sclerosis, yes/no	1.18 (0.91–1.46)	.19

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); OR, odds ratio.

Second, the randomly selected kidney biopsy specimen represents only a piece of the organ and may not provide the whole picture of structural changes. Finally, the analyzed cohort consists of 162 records, and the results should be confirmed in further studies. However, we believe that the current study will help to reduce the discard rate of deceased donor kidneys and increase the number of transplants.

CONCLUSIONS

Older donor age, male sex, higher BMI, and the presence of interstitial fibrosis presence in kidney graft biopsy specimen are risk factors of AKI. Kidneys procured from donors with AKI should be assessed in pretransplant renal biopsy. Kidneys with AKI may increase the pool of transplanted organs when careful donor and organ assessment is performed.

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