Investigating Serum Uric Acid as a Risk Factor in the Development of Delayed Renal Recovery in Living Kidney Donors

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ABSTRACT

Background. Hyperuricemia has been associated with kidney disease and remains controversial with regard to its gender-specific differences and impact in living kidney donation.

Methods. Between 2006 and 2015, charts of live kidney donors who underwent nephrectomy and had a minimum follow-up of 1 year were reviewed. A total of 291 donors were included and divided based on gender-specific pre-donation serum uric acid (SUA) tertiles. Renal functional outcomes included were estimated glomerular filtration rate (eGFR) at 6-month and 1-year follow-up and percentage of donors with a 1-year eGFR <60 mL/min/1.72 m^2. Logistic regression analysis was done.

Results. Mean SUA tertiles were 5.8 ± 1.1 mg/dL in males and 4.1 ± 1 mg/dL in females. Females in the highest tertile (SUA >4.5 mg/dL) had lower 6-month (59.9 ± 10.3 vs 66.9 ± 14.1 vs 67.3 ± 12.1; $P = .018$) and 1-year (60.8 ± 10.6 vs 67.6 ± 10.8 vs 67.8 ± 11.8; $P = .021$) eGFR and a higher percentage of donors with 1-year eGFR <60 mL/min/1.73 m^2 (59.5% vs 31.6% vs 23%; $P = .002$) compared with donors in the lower SUA tertiles (≤4.5 mg/dL). In males, there were similar eGFRs among SUA tertiles at 6-month and 1-year follow-up. In multivariate analysis, SUA was shown to be a significant predictor of developing stage 3 CKD (eGFR <60 mL/min/1.72 m^2), 1 year after donation in females but not in males.

Conclusions. Predonation SUA level is associated with the development of delayed renal recovery (GFR <60 mL/min/1.72 m^2) 1 year after donation in females but not in males.

KIDNEY transplantation has become a treatment of choice among patients with end-stage renal disease (ESRD). Aside from reducing treatment morbidity, it has been shown to provide additional survival benefit, increase quality of life, and be a more cost-effective option relative to chronic dialysis [1–4]. The preferred option for transplantation has been toward live kidney donation because it has been shown to have a superior graft outcome compared with deceased donor transplantation [5]. In addition, there is already a shortage of deceased donor organs [6]. Therefore, efforts have been made to expand the eligibility criteria, while maintaining the safety of donors, for live kidney donation [7].

Donor risk factors such as older age, obesity, and hypertension were previously considered absolute contraindications for donation [7] but evidence continues to surface regarding the comparable safety of donors and nondonors alike [8], leading to shifts in the criteria for relative and absolute contraindications for live kidney donation [9].

Increased serum uric acid (SUA) has been linked to the development of renal dysfunction. Aside from evidence associating it with increased risk of development of hypertension and cardiovascular disease [10], it has been shown as a strong independent risk factor in type 2 diabetes mellitus [11] and diabetic nephropathy [12]. In addition, several studies have already associated increased SUA with the

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Table 1. Baseline Characteristics of Donors Included in the Study

	N = 291		
	Males N = 135	Females N = 156	*P*
Age	38.5 ± 12.4	44.4 ± 10.9	.000
BMI	24 ± 2.3	23 ± 2.9	.002
Systolic BP	123.8 ± 10.6	119.3 ± 12.8	.001
Diastolic BP	75.5 ± 9.1	75.5 ± 10.6	.977
SUA	5.8 ± 1.1	4.1 ± 0.8	.000
Serum glucose	93.2 ± 9.1	92.8 ± 8.4	.700
Baseline MDRD GFR	92.9 ± 16.9	98.1 ± 21.3	.024

Note: Data expressed as mean ± standard deviation.
Abbreviations: BMI, body mass index; BP, blood pressure.

elevation of serum creatinine and increased incidence of chronic kidney disease (CKD) in a span of 2–10 years [13–19]. However, some studies were not able to show this same association with renal dysfunction [20–22].

Apart from its association with the development of CKD, there is evidence that women are more predisposed to urate-induced decrease in glomerular filtration rate (GFR) [23]. Studies supporting this increased susceptibility showed findings wherein the risk of gout and microalbuminuria in pre-hypertensives were elevated by a lower level of SUA in women than in men [24,25].

Several clinical studies have demonstrated that donor age and pre-donation GFR are strong predictors of developing CKD after kidney donation, but only a few studies have investigated the potential impact of pre-donation SUA in the residual renal function of a live kidney donor. Therefore, our aim was to investigate the possible association of pre-donation SUA with delayed renal recovery in living kidney donors, while keeping in mind potential gender-specific differences.

METHODS

Charts of living kidney donors who underwent nephrectomy in our institution from August 2006 to January 2015 were retrospectively reviewed. Recruited for the study were donors having a minimum follow-up of 1 year, in which there were 291 in total. Three surgeons performed all of the donor nephrectomies via video-assisted mini-incision surgery. Data on pre-donation SUA, age, body mass index, blood pressure, and serum fasting glucose were extracted from each donor. Preoperative and postoperative glomerular renal function (estimated GFR [eGFR]) was estimated using the Modification of Diet in Renal Disease (MDRD) formula [26]. Donor candidates with baseline MDRD eGFR of <80 mL/min/1.73 m^2 along with diabetes or hypertension uncontrolled by a single medication were evaluated as unfit for donation.

Donors were grouped based on gender-specific pre-donation SUA tertiles and were followed up at 6 months and 1 year post-donation. The difference of eGFR among tertiles at pre-donation, 6 months, and 1 year and the percentage of donors with eGFR <60 mL/min/1.72 m^2 at 1 year post-donation were the main outcomes of the study.

Male and female donors were analyzed separately. Data were shown as mean ± standard deviation for continuous variables, and as percentiles for categorical variables. Cut-off points to create SUA tertiles were based on the SUA values <25th percentile, 25th–75th percentile, and >75th percentile. The resulting SUA tertiles and eGFR at baseline and follow-up were analyzed. Variables between male and female groups were analyzed using independent sample *t* test, whereas Kruskal-Wallis and chi-square test were used to compare the variables among tertiles. Multivariate logistic regression was performed to determine the independent contribution of pre-donation SUA to the development of eGFR <60 mL/min/1.72 m^2 1 year after donation. Statistical analysis was done using SPSS software SPSS software version 23.0, IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA).

RESULTS

Of the 291 total donors, 135 (46.4%) were males and 156 (53.6%) were females. Mean age of donors were 38.5 ± 12.4 years and 44.4 ± 10.9 years for males and females, respectively. The mean pre-donation SUA was 5.8 ± 1.1 mg/dL for males and 4.1 ± 0.8 mg/dL for females. Other donor variables, expressed as mean ± standard deviation, are shown in Table 1.

SUA tertiles were set as follows: males: SUA ≤5.1 mg/dL, 5.2–6.4 mg/dL, and >6.4 mg/dL; females: SUA ≤3.6 mg/dL, 3.7–4.5 mg/dL, and >4.5 mg/dL. Table 2 compares the baseline, 6-month, and 1-year post-donation MDRD eGFR, and the percentage of subjects with eGFR <60 mL/min/1.73 m^2 1 year post-donation, among the tertiles of both genders. Females in the highest tertile (SUA >4.5 mg/dL) had a significantly lower 6-month (59.9 ± 10.3 vs 66.9 ± 14.1 vs 67.3 ± 12.1; $P = .018$) and 1-year (60.8 ± 10.6 vs 67.6 ± 10.8 vs 67.8 ± 11.8; $P = .021$) eGFR compared with those in the lower tertiles. In males, there were similar eGFR values among tertiles at baseline, 6-month, and 1-year post-

Table 2. MDRD eGFR and Percentage of Donors With 1-Year eGFR <60 mL/min/1.73 m^2 According to Gender-Specific Tertiles of SUA Concentration

	Males				Females			
	SUA ≤5.1 mg/dL	SUA 5.2–6.4 mg/dL	SUA >6.4 mg/dL	*P*	SUA ≤3.6 mg/dL	SUA 3.7–4.5 mg/dL	SUA >4.5 mg/dL	*P*
Baseline eGFR	96.3 ± 18.3	94 ± 16.3	86.6 ± 14.6	.081	101.2 ± 19.8	99.8 ± 21.9	90.9 ± 20.8	.066
6-mo eGFR	62.8 ± 12.7	62.4 ± 12.7	58.7 ± 7.7	.323	67.3 ± 12.1	66.9 ± 14.1	59.9 ± 10.3	.018
1-y eGFR	64.1 ± 13	62.6 ± 11.5	60.1 ± 8.4	.197	67.8 ± 11.8	67.6 ± 60.8	60.8 ± 10.6	.021
1-y eGFR N (%)								
eGFR <60	14 (33.3)	23 (38)	18 (54.5)	0.460	10 (23.3)	24 (31.6)	22 (59.5)	.002
eGFR ≥60	28	37	15		33	52	15	

Note: Data expressed as mean ± standard deviation.