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Association of Pre- and Post-Donation Renal Function with Midterm Estimated Glomerular Filtration Rate in Living Kidney Donors: A Retrospective Study

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Purpose: The estimated glomerular filtration rate (eGFR) at 6 months after donation ($eGFR_{6m}$) is strongly associated with the risk of end-stage renal disease in living kidney donors. This study aimed to investigate the incidence of $eGFR_{6m}$ <60 mL/min/1.73 m^2 ($eGFR_{6m}$ <60) and identify the risk factors that can predict the occurrence of $eGFR_{6m}$ <60 in living kidney donors.

Materials and Methods: Living kidney donors who underwent nephrectomy at Severance Hospital between January 2009 and December 2019 were identified. We excluded 94 of 1233 donors whose creatinine values at 6 months after donation were missing. The risk factors for $eGFR_{6m}$ <60 were assessed using multivariate regression analysis. The optimal cutoff points for candidate risk factors for predicting $eGFR_{6m}$ <60 occurrence were determined using the Youden index.

Results: The $eGFR_{6m}$ <60 occurred in 17.3% of the participants. Older age (≥44 years), history of hypertension, lower preoperative eGFR (<101 mL/min/1.73 m^2), and degree of increase in creatinine levels on postoperative day 2 compared to those before surgery (ΔCr2_pre) (≥0.39 mg/dL) increased the risk of $eGFR_{6m}$ <60. The addition of ΔCr2_pre to preoperative eGFR yielded a higher predictive accuracy for predicting $eGFR_{6m}$ <60 than that with preoperative eGFR alone {area under the receiver operating characteristic curve=0.886 [95% confidence interval (CI), 0.863–0.908] vs. 0.862 (95% CI, 0.838–0.887), p<0.001}.

Conclusion: The incidence of $eGFR_{6m}$ <60 was 17.3%. Older age, lower preoperative eGFR, history of hypertension, and greater ΔCr2_pre were associated with the occurrence of $eGFR_{6m}$ <60 after living donor nephrectomy. The combination of preoperative eGFR and ΔCr2_pre showed the highest predictive power for $eGFR_{6m}$ <60.

Key Words: Creatinine, estimated glomerular filtration rate, eGFR at 6 months after donation, living donor nephrectomy, outcome

INTRODUCTION

The increasing organ shortage, long waiting lists, and superior results over deceased donor kidney transplantation have encouraged living donor kidney transplantation.[1] Although kidney donation per se is of no benefit to the donors themselves, postdonation renal function was traditionally thought to be well-preserved.[2,3] However, several recent studies reported that living kidney donors are at a higher risk for end-stage renal disease (ESRD) compared to healthy non-donors.[4,5]

A study that enrolled >70000 kidney donors reported a strong association between the estimated glomerular filtration rate (eGFR) at 6 months after donation ($eGFR_{6m}$) and the subsequent ESRD risk.[6] Its conclusion that ESRD can be predicted by midterm renal function has great clinical significance in donor surveillance; as an increasing number of donors are lost to follow-up over a long time,[7,8] it may delay the timely treatment of donors who have the potential risk of ESRD. Additionally, several studies have documented that the $eGFR_{6m}$ is the lowest or is comparable to the lowest eGFR value[8-10] during the process of adaptive filtration by the remaining kidney that

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gradually increases the eGFR.[5,11,12] Therefore, measurement of $eGFR_{6m}$ is necessary, and risk factors that affect the decline in $eGFR_{6m}$ need to be explored to reduce the burden of ESRD by early intervention.

The existing body of evidence has found that older age, lower preoperative eGFR, preoperative proteinuria, and first-degree relatives to the recipients, all of which are predonation factors, increase the risk of ESRD.[9,13,14] With this limitation in mind, this retrospective study aimed to investigate the incidence of $eGFR_{6m}$ <60 mL/min/1.73 m^2 ($eGFR_{6m}$ <60) and identify the perioperative risk factors that predict the occurrence of $eGFR_{6m}$ <60 in living kidney donors, including changes in renal function immediately after surgery.

MATERIALS AND METHODS

Ethics statements

This study was approved by the Institutional Review Board (IRB) of Severance Hospital (IRB number: 4-2020-0572). The requirement for informed consent was waived owing to the retrospective nature of the study.

Study population

Donors who underwent living donor nephrectomy at Severance Hospital between January 2009 and December 2019 were included. Our institution encourages patients to attend follow-ups at 1, 3, 6, and 12 months after donation, and every 1 year thereafter, while many of them were lost to follow-up or transferred to their hometown hospital.[8] Among 1233 donors, 94 with missing creatinine values at 6 months after donation were excluded from the study. A total of 1139 donors were included in this study (Fig. 1).

Data collection

Patient data were retrospectively retrieved from the electronic medical records up to January 31, 2021. The preoperative data included the patient demographics, such as age, sex, body mass index (BMI), medical history, smoking status, and first-degree relative to the recipient, biomarkers reflecting renal function (levels of serum creatinine, cystatin C, urine creatinine, and protein), renogram findings, eGFR, serum hemoglobin and albumin levels, and hemodynamic data, which are important conditions in the evaluation of kidney donor[15] or important factors associated with the prognosis after kidney donation.[9,14,16,17] The intraoperative data included the anesthesia time, type of anesthesia, amount of crystalloid and colloid infused, urine output, use of vasopressors or transfusion, and hemodynamic data. The lowest systolic blood pressure during surgery were extracted, and the heart rate at that time point was recorded. Postoperative data were categorized as short-term (up to 7 days after donor nephrectomy) and midterm outcomes (up to 6 months after donor nephrectomy). The short-term outcomes included the incidence of acute kidney injury (AKI), changes in biomarkers reflecting renal function and eGFR, and days of admission. The midterm outcomes included changes in biomarkers reflecting renal function and eGFR, and new-onset diseases, such as episodes of proteinuria.

Assessment of eGFR, $eGFR_{6m}$, and $eGFR_{6m}$ <60

eGFR was calculated using the Chronic Kidney Disease-Epidemiology Collaboration equation derived from the creatinine value.[18] $eGFR_{6m}$ was chosen as the endpoint, as a low $eGFR_{6m}$ is an early biomarker for the risk of ESRD.[6] The cutoff point of reduced eGFR (<60 mL/min/1.73 m^2) was determined using the typically used chronic kidney disease criteria.[19,20] For $eGFR_{6m}$, the creatinine value at 6 months after donation was determined as the nearest value between 3 and 9 months postdonation,[6] considering the retrospective study design.

Statistical analysis

Univariate analysis was performed using independent Student's t test or Mann–Whitney U test for continuous variables and chi-square or Fisher's exact test for dichotomous variables. Continuous variables are presented as the mean±standard deviation or the median (interquartile range), while dichotomous

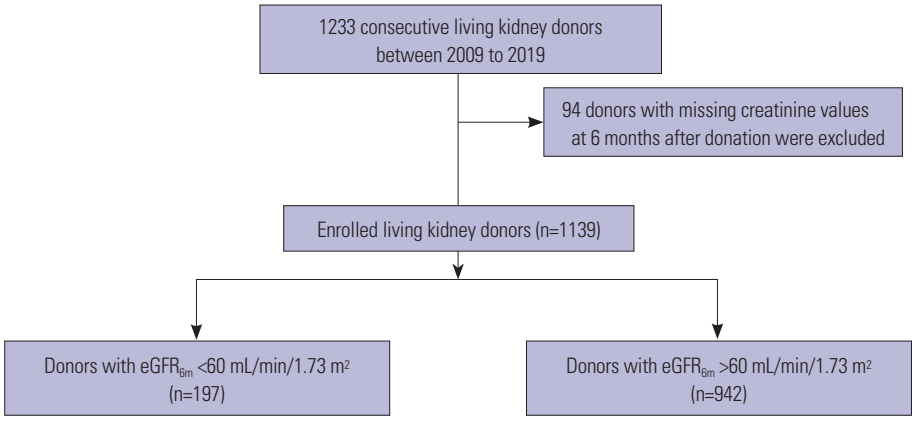

Fig. 1. Flowchart of donors. $eGFR_{6m}$, estimated glomerular filtration rate at 6 months after donation.

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variables are expressed as the percentage.

A logistic regression model was used to assess the risk factors for $eGFR_{6m}$ <60. Variables with a *p*-value <0.05 in the univariate model [age at donation, hypertension, BMI, preoperative eGFR, preoperative cholesterol level, preoperative albumin level, intraoperative packed red blood cells transfusion, intraoperative systolic blood pressure, and degree of increase in creatinine levels on postoperative day (POD) 2 compared to those before surgery (ΔCr2_pre)] and perioperative variables with clinical importance in association with long-term renal outcome after nephrectomy were considered for the risk prediction model (age at donation, hypertension, BMI, preoperative eGFR, female gender, current smoker, and total intravenous anesthesia).[9,14,16,17,21] All potential risk factors were assessed for collinearity before inclusion in the regression analysis. Therefore, the following variables were included in the final multivariate logistic regression model: age at donation, hypertension, BMI, preoperative eGFR, preoperative cholesterol and albumin levels, intraoperative systolic blood pressure, and ΔCr2_pre. ΔCr2_pre was chosen for the following reasons: for 7 days after donation, serum creatinine levels were highest on POD 2 with the greatest intergroup difference, and the area under the receiver operator characteristic curve (AUC) of ΔCr2_pre for $eGFR_{6m}$ <60 was the largest. The optimal cutoff points for candidate risk factors for predicting the occurrence of $eGFR_{6m}$ <60 were determined using the Youden index. The AUC was calculated to investigate the individual diagnostic accuracy of each candidate risk factor. The DeLong test was used to compare the AUCs of the parameters.[22]

Statistical analysis was performed using SPSS 25 (IBM Inc., Armonk, NY, USA) and R package, version 3.6.0 (The R Foundation for Statistical Computing, Vienna, Austria). A *p*-value <0.05 was considered statistically significant. Bonferroni correction was used to adjust for multiple comparisons.

Table 1. Demographic Data

Variables	$eGFR_{6m}$ <60 (n=197)	$eGFR_{6m}$ >60 (n=942)	*p* value
Age (yr)	50±9	41±11	<0.001
Female	102 (52)	555 (59)	0.065
Height (cm)	165±8	165±9	0.833
BDI (kg/m^2)	24±2	23±3	<0.001
First degree relatives	112 (57)	587 (62)	0.152
Current smoker	42 (21)	213 (23)	0.692
Medical history			
Hypertension	22 (11)	50 (5)	0.002
Diabetes	2 (1)	2 (0.2)	0.140
Preoperative renal function			
Serum creatinine (mg/dL)	0.84±0.15	0.72±0.16	<0.001
eGFR (mL/min/1.73 m^2)	93±10	110±12	<0.001
Serum cystatin C (mg/L)	0.86±0.10	0.77±0.10	<0.001
Renogram (Lt/Rt) (mL/min)	44±9/49±10	45±9/51±10	<0.001/<0.001
24-hr urine creatinine (mg/24 hr)	1266±456	1217±455	0.179
24-hr urine creatinine clearance (mL/min/1.73 m^2)	111±92	123±84	0.084
Random urine creatinine (mg/dL)	133±88	138±87	0.439
Random urine protein (mg/dL)	8.4±4.3	8.2±4.9	0.160
Donated kidney			
Lt	179 (91)	840 (89)	0.482
Weight (g)	200±45	196±42	0.255
Preoperative laboratory data			
Hemoglobin (g/dL)	13.9±1.3	13.7±1.5	0.342
Glucose (mg/dL)	98±12	96±14	0.105
Cholesterol (mg/dL)	196±35	186±31	<0.001
Triglyceride (mg/dL)	115±61	112±67	0.536
Albumin (g/dL)	4.4±0.3	4.5±0.3	0.036
Preoperative hemodynamic data			
Heart rate (1/min)	66±9	68±10	0.027
Systolic blood pressure (mm Hg)	123±14	119±12	<0.001

eGFR, estimated glomerular filtration rate; $eGFR_{6m}$, eGFR at 6 months after donation; BDI, body mass index.
Values are presented as the mean±standard deviation or n (%).

RESULTS

The creatinine value was obtained 6 months postoperatively in 1139 (92%) of 1233 donors who underwent living donor nephrectomy between January 2009 and December 2019. The incidence of $eGFR_{6m}$ <60 was 17.3%. Overall, 159 donors were lost to follow-up at 6 months, and 78 donors were further lost to follow-up 12 months after donation. The median follow-up duration was 35 (15–71) months in donors with $eGFR_{6m}$ <60, and 34 (17–69) months in donors with $eGFR_{6m}$ >60. Donors with $eGFR_{6m}$ <60 were older than those with $eGFR_{6m}$ >60 at the time of donation (50 years vs. 41 years). More donors with $eGFR_{6m}$ <60 had higher BMI (24 kg/m^2 vs. 23 kg/m^2), hypertension (11% vs. 5%), higher levels of serum creatinine (0.84 mg/dL vs. 0.72 mg/dL), cystatin C (0.86 mg/dL vs. 0.77 mg/dL), and cholesterol (196 mg/dL vs. 186 mg/dL), lower preoperative eGFR (93 mL/min/1.73 m^2 vs. 110 mL/min/1.73 m^2) and serum albumin level (4.4 g/dL vs 4.5 g/dL) than donors with $eGFR_{6m}$ >60. The renogram showed lower preoperative renal function in donors with $eGFR_{6m}$ <60 than donors with $eGFR_{6m}$ >60 (44 and 49 mL/min vs. 45 and 51 mL/min) (Table 1). The number of donors with missing data is shown in Supplementary Table 1 (only online). None of the donors developed ESRD during the study period. More donors with $eGFR_{6m}$ <60 underwent transfusion (2% vs. 0.1%) and showed a higher systolic blood pressure (Table 2).

The incidence of AKI was higher in donors with $eGFR_{6m}$ <60 (95% vs. 88%). Serum creatinine levels were higher in donors with $eGFR_{6m}$ <60 throughout the study period (all p<0.001). ΔCr2_pre was higher in donors with $eGFR_{6m}$ <60 than that in donors with $eGFR_{6m}$ >60 (0.51 mg/dL vs. 0.40 mg/dL, p<0.001). The maximal decrease in eGFR during the first 7 days was greater in donors with $eGFR_{6m}$ <60 (all, p<0.001) (Table 3). The ratio of reduced eGFR before and 6 months postoperatively was higher in donors with $eGFR_{6m}$ <60 (41% vs. 30%, p<0.001). Hypertensive episodes occurred more in donors with $eGFR_{6m}$ <60 than in those with $eGFR_{6m}$ >60 (4% vs. 1%) (Table 4).

In multivariate analysis, age [odds ratio (OR)=1.043, p<0.001], hypertension (OR=2.024, p=0.036), preoperative eGFR (OR=0.878, p<0.001), and ΔCr2_pre (unit 0.1 mg/dL) (OR=1.655, p<0.001) were associated with the occurrence of $eGFR_{6m}$ <60 (Table 5).

The cutoff values for predicting $eGFR_{6m}$ <60 using the Youden

Table 2. Intraoperative Data

Variables	$eGFR_{6m}$ <60 (n=197)	$eGFR_{6m}$ >60 (n=942)	p value
Operation time (min)	165±41	163±42	0.514
Anesthesia time (min)	214±43	211±50	0.518
TIVA	59 (30)	284 (30)	0.956
Crystalloid (mL)	1750±598	1686±681	0.225
Crystalloid (mL/kg/h)	7.7±2.5	7.8±2.8	0.665
Colloid (mL)	0 [0–0]	0 [0–0]	0.157
Urine output (mL)	330 [230–450]	350 [220–540]	0.361
Bleeding (mL)	30 [0–100]	20 [0–100]	0.291
Input-output fluid balance (mL/kg/h)	5.9±2.7	5.9±3.1	0.792
Mannitol (mL)	62±12	60±12	0.069
pRBC transfusion	6 (2)	1 (0.1)	0.001
Vasopressor	49 (25)	233 (25)	0.967
Hemodynamic data			
Heart rate (1/min)	68±11	70±11	0.069
Systolic blood pressure (mm Hg)	128±14	123±14	<0.001

eGFR, estimated glomerular filtration rate; $eGFR_{6m}$, eGFR at 6 months after donation; TIVA, total intravenous anesthesia; pRBC, packed red blood cells.
Values are presented as the mean±standard deviation, median [interquartile range], or n (%).

Table 3. Short-Term Outcomes

Variables	$eGFR_{6m}$ <60 (n=197)	$eGFR_{6m}$ >60 (n=942)	p value
AKI	187 (95)	827 (88)	0.004
AKI grade (0/1/2)	10/173/14	114/768/59	0.014
ΔCr 2_pre	0.51±0.17	0.40±0.17	<0.001
Serum creatinine (mg/dL)*			
POD 0	1.00±0.87	0.87±0.20	<0.001
POD 1	1.31±0.25	1.10±0.26	<0.001
POD 2	1.34±0.27	1.11±0.28	<0.001
POD 3	1.27±0.26	1.04±0.26	<0.001
POD 5	1.25±0.24	1.02±0.23	<0.001
POD 7	1.34±0.23	1.12±0.23	<0.001
eGFR (mL/min/1.73 m^2)*			
POD 0	77±10	95±13	<0.001
POD 1	67±14	82±16	<0.001
POD 2	55±8	73±15	<0.001
POD 3	58±9	79±16	<0.001
POD 5	59±9	80±15	<0.001
POD 7	54±7	71±13	<0.001
Serum cystatin C (mg/L)*			
POD 3	1.13±0.15	0.99±0.15	<0.001
POD 7	1.24±1.16	1.09±0.15	<0.001
Maximal decrease in eGFR during 7d (%)	45±6	38±9	<0.001
>40%	154 (78)	420 (45)	<0.001
>25%	196 (100)	873 (93)	<0.001
Laboratory data			
POD 5 24-hr urine creatinine (mg/24 hr)	1259±420	1208±430	0.132
POD 5 24-hr urine creatinine clearance (mL/min/1.73 m^2)	80±111	86±86	0.388
POD 7 random urine creatinine (mg/dL)	134±80	124±78	0.200
Admission days (day)	9±2	9±1	0.228

eGFR, estimated glomerular filtration rate; $eGFR_{6m}$, eGFR at 6 months after donation; AKI, acute kidney injury; ΔCr2_pre, the degree of increase in creatinine levels on postoperative day 2 compared to those before surgery; POD, postoperative day.
Values are presented as the mean±standard deviation or n (%).
*p value was corrected with Bonferroni method for multiple comparisons.

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index were as follows: age, ≥44 years; preoperative eGFR, <101 mL/min/1.73 m^2; and ΔCr2_pre ≥0.39 mg/dL. The addition of ΔCr2_pre to preoperative eGFR yielded a higher accuracy for predicting $eGFR_{6m}$ <60 than that with preoperative eGFR alone {AUC=0.886 [95% confidence interval (CI), 0.863-0.908] vs. 0.862 (95% CI, 0.838-0.887), p<0.001} (Fig. 2).

DISCUSSION

In this retrospective study, $eGFR_{6m}$ <60 occurred in 17.3% of donors after living donor nephrectomy, which were associated with older age, lower preoperative eGFR, history of hypertension, and greater ΔCr2_pre. The combination of the preoperative eGFR and ΔCr2_pre demonstrated the highest power for predicting $eGFR_{6m}$ <60 [AUC=0.886 (95% CI, 0.863–0.908)].

Despite the beneficial effects of living donor kidney transplantation to the recipient, the long-term risks of donation itself, such as ESRD and cardiovascular and all-cause mortality, remain unknown in healthy living donors. Although several studies have compared the long-term risks of living kidney donors to a control group of healthy non-donor or general populations, they have been encumbered by limitations such as the selection of a control group and loss to follow-up. Additionally, there is an emerging awareness of the increased risk of mortality and morbidity for living kidney donors compared to matched healthy non-donors or the general population.[4,5,23] Therefore,

Table 4. Midterm Outcomes

Variables	$eGFR_{6m}$ <60 (n=197)	$eGFR_{6m}$ >60 (n=942)	*p* value
Serum creatinine (mg/dL)			
1 month	1.32±0.22	1.08±0.22	<0.001
6 months	1.33±0.20	1.05±0.19	<0.001
eGFR (mL/min/1.73 m^2)			
1 month	55±6	74±13	<0.001
6 months	54±5	78±12	<0.001
Decrease in eGFR (%)	41±7	30±9	<0.001
New onset disease			
Proteinuria episode	12 (6)	66 (7)	0.644
Hypertensive episode	7 (4)	11 (1)	0.024
Glomerulonephritis	1 (0.5)	1 (0.1)	0.316
Renal stone	3 (2)	4 (0.4)	0.368

eGFR, estimated glomerular filtration rate; $eGFR_{6m}$, eGFR at 6 months after donation.
Values are presented as the mean±standard deviation or n (%).

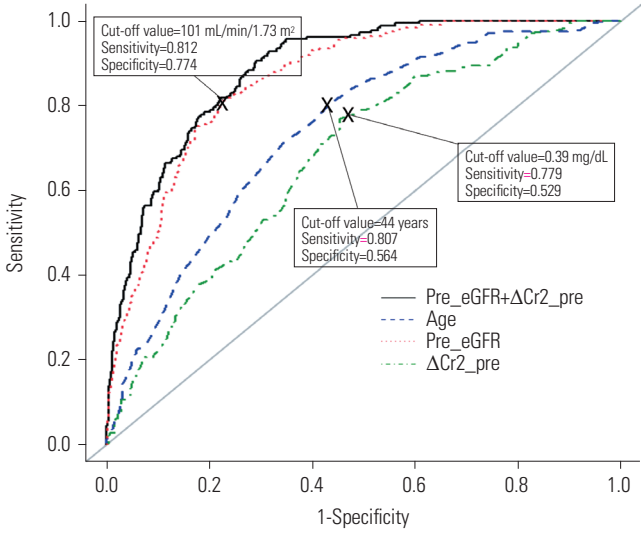

Fig. 2. Receiver operating characteristic curve for determining the cut-off values for predicting $eGFR_{6m}$ <60 in living kidney donors. eGFR, estimated glomerular filtration rate; $eGFR_{6m}$, eGFR at 6 months after donation; Pre_eGFR, preoperative eGFR; ΔCr2_pre, the degree of increase in creatinine levels on postoperative day 2 compared to those before surgery.

Table 5. Multivariate Logistic Regression Model of Risk Factors for $eGFR_{6m}$ <60

Variable	Univariate			Multivariate		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Age	1.092	1.073–1.111	<0.001	1.043	1.018–1.070	<0.001
Female	0.749	0.550–1.019	0.066			
Hypertension	2.243	1.324–3.799	0.003	2.024	1.049–3.905	0.036
BMI	1.103	1.043–1.165	<0.001	1.005	0.926–1.092	0.901
Current smoker	0.927	0.638–1.347	0.693			
First-degree relatives	0.797	0.584–1.088	0.153			
Preoperative eGFR (mL/min/1.73 m^2)	0.880	0.864–0.896	<0.001	0.878	0.858–0.899	<0.001
Preoperative cholesterol	1.010	1.005–1.015	<0.001	1.005	0.998–1.011	0.139
Preoperative albumin	0.595	0.366–0.967	0.036	0.605	0.296–1.240	0.170
TIVA	0.991	0.709–1.385	0.956			
Intraoperative pRBC transfusion	1.922	0.370–9.979	0.437			
Intraoperative systolic blood pressure	1.023	1.012–1.034	<0.001	1.002	0.987–1.018	0.786
ΔCr2_pre (unit: 0.1 mg/dL)	1.425	1.298–1.564	<0.001	1.655	1.458–1.879	<0.001

eGFR, estimated glomerular filtration rate; $eGFR_{6m}$, eGFR at 6 months after donation; OR, odds ratio; CI, confidence interval; BMI, body mass index; TIVA, total intravenous anesthesia; ΔCr2_pre, the degree of increase in creatinine levels on postoperative day 2 compared to those before surgery.

the importance of meticulous donor selection and risk stratification is being highlighted. Furthermore, early identification of patients at a high risk of developing ESRD would enable timely intervention to improve postoperative renal function.

Notably, Massie, et al.[6] found that $eGFR_{6m}$ could be an early marker for predicting ESRD in living kidney donors. It was suggested that $eGFR_{6m}$ was more important than preoperative eGFR or eGFR decline after surgery for predicting the risk of ESRD, since donors with similar preoperative eGFRs showed different degrees of eGFR reduction after donation. Immediately after donation, there is an initial drop in renal function, followed by an adaptive hyperfiltration of the remaining kidney, which commences as soon as 8 h.[2,5,7,12] If incomplete compensatory hyperplasia occurs, it results in drastic renal dysfunction within 6 months after donation,[24] and the lowest eGFR during this period is comparable to $eGFR_{6m}$.[8-10] In this respect, the recognition of these patients during the early postoperative period might be important, although it has not been investigated heretofore.

A substantial number of patients (17.3%) exhibited $eGFR_{6m}$ <60 in the current study, and preoperative eGFR <101 mL/min/1.73 m^2, older age (≥44 years), and history of hypertension were among the preoperative parameters that increased the risk of $eGFR_{6m}$ <60 (OR=0.878, 1.043, and 2.024, p<0.001, <0.001 and 0.04, respectively). Aging and hypertension bi-directionally affect eGFR and ESRD development,[25,26] although collinearity was not observed herein. In addition, the acute compensatory mechanism is less efficient in elderly donors since it relies upon the renal functional reserve.[7] The preoperative eGFR was lower by as much as 20 mL/min/1.73 m^2 in donors with $eGFR_{6m}$ <60 compared to those with $eGFR_{6m}$ >60. Furthermore, these significant gaps were maintained throughout the study period. It is noteworthy that the cutoff value of the preoperative eGFR for $eGFR_{6m}$ <60 was 101 mL/min/1.73 m^2, which is higher than 90 mL/min/1.73 m^2, a value that was never considered incompatible with donation in the current guideline for living kidney donor evaluation.[15] These results can lead to the necessity for precise evaluation of the renal functional reserve and identification of the "phantom menace" within "healthy" kidney donors who are at risk of $eGFR_{6m}$ <60.

In addition to the generally predictable preoperative risk factors, ΔCr2_pre was found to be closely related to $eGFR_{6m}$ in this study. The elevation in serum creatinine immediately after donor nephrectomy is considered to be inevitable due to the 50% reduction in nephron mass. As donors may not tolerate the insult of nephrectomy equally, resulting in variable creatinine levels, we hypothesized that an increase in serum creatinine above a certain level could be an early warning sign for poor renal outcomes, akin to canaries in a coal mine. In our study, an initial increase of 0.1 mg/dL in ΔCr2_pre after donation was associated with a 1.655 OR in the incidence of $eGFR_{6m}$ <60 (p<0.001), and the cutoff value for ΔCr2_pre was 0.39 mg/dL (p<0.001). Interestingly, this value is similar to the degree of increase in creatinine level in the definition of AKI (0.3 mg/dL) according to the Kidney Disease: Improving Global Outcomes criteria,[27] despite the substantial loss of nephron mass in the donor. The results of the present study seem to be consistent with the well-known finding that the occurrence of AKI or minimal increase in serum creatinine is a predictor of poor long-term renal function after surgery.[28] Our results support the imperatives of early measurement and monitoring of serum creatinine levels immediately after donor nephrectomy for the identification of high-risk donors and appropriate intervention. Further prospective clinical studies are needed to devise interventions and determine their effects in preventing eGFR reduction.

In the comparison of several indices for predicting $eGFR_{6m}$ <60, the preoperative eGFR had a higher predictive power than ΔCr2_pre [AUC=0.862 (95% CI, 0.838–0.887) vs. 0.682 (95% CI, 0.642–0.722)], whereas the combination of both preoperative eGFR and ΔCr2_pre showed a higher predictive power than the preoperative eGFR alone [AUC=0.886 (95% CI, 0.863–0.908), p<0.001] in this study. This has important clinical implications since both parameters can be easily measured using routine perioperative laboratory tests, which would allow accurate prediction of the risk in every donor in daily practice.

The strength of the current study is that it was the first to evaluate the perioperative risk factors associated with $eGFR_{6m}$ <60, which is a midterm prognostic factor closely associated with progression to ESRD. The results of this study support the necessity of monitoring the early postoperative changes in the serum creatinine level. Moreover, our study allows to establish the quantified preoperative criteria for kidney donors who are at high risk of $eGFR_{6m}$ <60 and require an intensive perioperative surveillance and management.

This study has several limitations. First, there is an inherent limitation of being a single-center, retrospective study. Second, we could not analyze the relationship between $eGFR_{6m}$ <60 and ESRD due to the high rates of loss to long-term follow-up for a diagnosis of ESRD, although it has already been demonstrated in a previous large-scale study.[6] Given the frequency of ESRD after donor nephrectomy, the number of patients included in the current study was insufficient, and examining this association was beyond the scope of our study.

In conclusion, the incidence of $eGFR_{6m}$ <60 was 17.3%, and factors such as older age, lower preoperative eGFR, history of hypertension, and greater ΔCr2_pre were associated with the occurrence of $eGFR_{6m}$ <60 after living donor nephrectomy. In addition, the combination of the preoperative eGFR and ΔCr2_pre showed the highest power for predicting $eGFR_{6m}$ <60 in this retrospective study.

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