

## Long-term compensation of renal function after donor nephrectomy

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Received April 18, 2019

Revised February 17, 2020

Accepted March 20, 2020

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**Background:** Living donors are the major source of kidneys in countries with a shortage of deceased donors. Kidney donation after careful donor selection is generally accepted as a safe procedure, but the physiologic consequences after donor nephrectomy are not fully verified. In this study we retrospectively reviewed the renal function of the residual kidney in living donors.

**Methods:** Post-nephrectomy laboratory data of 1,175 living donors (60.7%) from 1,933 living donors who received uninephrectomy from January 1999 to December 2017 at Yonsei University, Severance Hospital, Korea were retrospectively collected. Post-nephrectomy renal function was monitored by the relative ratio of estimated glomerular filtration rate (e-GFR; pre-nephrectomy e-GFR ratio vs. post-nephrectomy e-GFR) that was calculated by the Modification of Diet in Renal Disease formula.

**Results:** During 36.3±37.6 months of mean follow-up, two cases (0.17%, 2/1,175) of renal failure developed. The mean e-GFR decreased to 64.3±14.2 mL/min/1.73 m<sup>2</sup> immediately after nephrectomy from 99.2±19.9 mL/min/1.73 m<sup>2</sup> of the pre-nephrectomy e-GFR. Early decrement of e-GFR was prominent in male and obese donors (body mass index >25 kg/m<sup>2</sup>, P<0.05). The e-GFR ratio increased according to post-nephrectomy duration, and the mean increment degree of e-GFR ratio after nephrectomy calculated by linear regression analysis was 1.94% per year. Unlike the early decrement of e-GFR ratio after nephrectomy, donor factors such as degree of obesity and donor sex did not affect the late increment of e-GFR ratio after nephrectomy (P>0.05).

**Conclusions:** Our data showed that long-term compensation of the renal function after nephrectomy occurs independently of preoperative donor characteristics.

**Keywords:** Glomerular filtration rate; Nephrectomy; Living donors; Kidney transplantation

### INTRODUCTION

Following the introduction of kidney transplantation in the 1950s, it has become essential for the improvement of quality of life for end-stage renal disease (ESRD) patients. However, as the demand for donor kidneys has increased,

living donors are now a major source for kidney transplantation in Korea [1]. Improved outcomes and reduced waiting times are some of the merits of living donor kidney transplantation [2], but is not without its shortcomings, and the risk of mortality or renal failure of living donors remains a concern [3].

## HIGHLIGHTS

- The immediate postoperative estimated glomerular filtration rate decreased to about 65.5% of its primary function which is affected by the sex and body mass index of the donor.
- In the long term, we found that compensation of renal function occurs over time, regardless of donor factors.

Compensatory hypertrophy has been observed after unilateral or partial nephrectomy [4-6], and the renal functional reserve has also been assessed along with the consequences of hyperfiltration [7-11]. Preoperative factors, such as obesity, hypertension, and proteinuria have been known to influence the renal function after unilateral nephrectomy [12-14]; in addition, old age has been associated with reduced renal reserve [15]. Older or overweight kidney donors have a lower post-donation reserve capacity, but obesity has a greater impact on loss of renal reserve in younger donors, suggesting that younger donors with obesity must be monitored carefully [16]. Most of the previous studies have focused on the risk factors and pathophysiology of renal failure or other comorbidities [10,17-19]. Edgren et al. [4] reported that renal function reached 77% of its initial level in kidney donors after a mean follow-up of 3 years. Several studies on donor renal function have also reported that renal function reaches 70%–75% of its initial pre-nephrectomy renal function [17,20,21].

This study retrospectively reviewed the renal function of living donors after nephrectomy in order to understand the long-term postoperative changes in renal function, and also define the factors related to renal function compensation.

## METHODS

Data for 1,933 living kidney donors from January 1999 to December 2017 at Yonsei University, Severance Hospital, Korea were collected. The follow-up hospital records of 1,175 donors (60.7%) were available. The selection criteria of donors at donor nephrectomy were: (1) pre-nephrectomy serum creatinine level below 1.5 mg/dL, (2) no radiologic abnormality in bilateral kidneys, and (3) no history of

hypertension, diabetes or active hepatitis. Donor nephrectomy was performed by conventional open nephrectomy or video assisted mini-laparotomy surgery. The estimated glomerular filtration rate (e-GFR), as determined by the Modification of Diet in Renal Disease (MDRD) study, was used. Hospital records were retrospectively reviewed to evaluate the residual renal function and renal impairment.

Early e-GFR was defined as the e-GFR at the early period (usually within 5 days of nephrectomy) and late e-GFR was defined as e-GFR at the time of the most recent follow-up. The e-GFR ratio was the relative e-GFR represented by the ratio of post-nephrectomy e-GFR versus pre-nephrectomy e-GFR. Renal failure was defined using the Kidney Disease Outcomes Quality Initiative Chronic Kidney Disease classification, the need for dialysis, or e-GFR < 15 mL/min/1.73 m<sup>2</sup>.

Donor sex, age, and body mass index (BMI) were analyzed for variables affecting the donor residual renal function after nephrectomy. Patients were categorized and analyzed according to their BMI (BMI < 25 kg/m<sup>2</sup> and ≥ 25 kg/m<sup>2</sup> groups; normal and obese groups, respectively) and age (< 35 years and ≥ 35 years) and analyzed [22,23]. Statistical analysis was performed using Student t-test. The relevance between factors was analyzed using linear regression. Multivariate linear regression was used to determine factors significantly related to post-nephrectomy e-GFR. A general linear model was applied to compare the donor factors in combination with follow-up period. A P-value < 0.05 was defined as statistically significant.

**Table 1.** Donor demographics

Clinical manifestation	Value
Number	1,175
Age at nephrectomy (yr)	40.1±11.4 (16–69)
Sex (male:female)	547 (46.6):628 (53.4)
BMI (kg/m <sup>2</sup> )	23.2±2.7 (15.6–33.3)
Living donor type (related:unrelated)	775 (66.0):400 (34.0)
Mean follow-up duration (mo)	36.3±37.6 (0–193)

Values are presented as mean±standard deviation (range) or number (%). BMI, body mass index.

## RESULTS

### Donor Characteristics and Renal Failure after Donor Nephrectomy

The clinical characteristics of 1,175 donors whose hospital records were retrospectively collected are shown in Table 1. Of the 1,175 donors, two donors developed renal failure and were on dialysis (2/1,175; 0.17%); renal failure occurred at 34 months and 57 months after nephrectomy. The cause of ESRD was hypertension in one case and disease of unknown origin in the other case.

### Early Change of Renal Function after Donor Nephrectomy

The mean age at the time of donation was  $40.1 \pm 11.4$  years (16–69 years). The pre-nephrectomy mean e-GFR was  $99.2 \pm 19.9$  mL/min/1.73 m<sup>2</sup>, and the mean serum creatinine was  $0.82 \pm 0.17$  mg/dL. In the immediate post-operative period, the early e-GFR dropped to  $64.3 \pm 14.2$  mL/min/1.73 m<sup>2</sup>, and the serum creatinine increased to  $1.21 \pm 0.29$  mg/dL.

Donor sex and BMI showed statistically significant relevance with early decrease in renal function, and the early e-GFR was significantly lower in males compared to females. The mean early e-GFR was  $62.1 \pm 12.2$  mL/min/1.73 m<sup>2</sup>,  $66.1 \pm 15.4$  mL/min/1.73 m<sup>2</sup> in males and females, respectively. The decrement of the early e-GFR ratio was statistically greater in males than in females ( $64.1\% \pm 10.2\%$  vs.  $66.7\% \pm 13.0\%$ ,  $P < 0.001$ ). Donor BMI also showed negative correlation with the early e-GFR ratio, and the slope of the relationship between the early e-GFR ratio and BMI was  $-0.53$  ( $P < 0.001$ ) by linear regression analysis.

The early e-GFR ratio in BMI  $< 25$  kg/m<sup>2</sup> and  $\geq 25$  kg/m<sup>2</sup> groups were compared and showed significant difference ( $P < 0.001$ ). However, age was not significantly associated with early e-GFR, and by linear regression analysis, age at donation showed no significant relationship to the early e-GFR ratio. The early e-GFR ratio was analyzed in groups age  $< 35$  years and  $\geq 35$  years, and there was no significant difference between the two age groups ( $P = 0.277$ ) (Table 2).

Stepwise multiple linear regression was used for verification of donor factors affecting renal function after nephrectomy. Donor BMI and sex showed significant correlation with the early change of renal function (Table 3).

### Late Change of Renal Function after Donor Nephrectomy

The mean follow-up period was  $36.3 \pm 37.6$  months (0–193 months), and the mean late e-GFR was  $70.2 \pm 13.3$  mL/min/1.73 m<sup>2</sup> (e-GFR ratio,  $72.0\% \pm 13.5\%$ ) (Fig. 1). The late e-GFR ratio significantly increased according to the follow-up period, and the e-GFR increased  $1.94\% \pm 0.10\%$  of its initial e-GFR per year ( $P < 0.001$ ) (Fig. 2).

**Table 3.** Stepwise multiple linear regression analysis for early changes in renal function

Variable	Beta	Standard error	P-value
Constant	77.219	2.956	<0.001
BMI	-0.460	0.128	<0.001
Sex	-2.174	0.705	0.002

$R^2 = 0.023$ ,  $F = 9.515$ ,  $P < 0.001$ . Excluded variable: age.

BMI, body mass index.

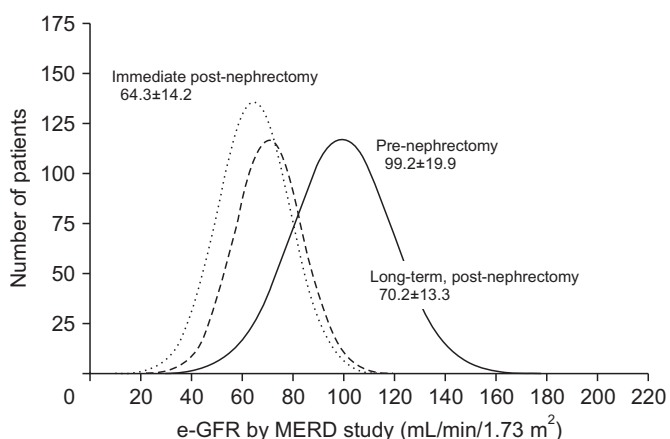
**Table 2.** Early changes of renal function after donor nephrectomy (n=1,175)

Donor variable	n	e-GFR by MDRD formula (mL/min/1.73 m <sup>2</sup> )		e-GFR ratio (B/A, %)	P-value <sup>a)</sup>
		Pre-nephrectomy (A)	Early e-GFR (B)		
Overall	1,175	$99.2 \pm 19.9$	$64.3 \pm 14.2$	$65.5 \pm 11.9$	
Sex					<0.001
Male	547	$97.9 \pm 17.7$	$62.1 \pm 12.2$	$64.1 \pm 10.2$	
Female	628	$100.4 \pm 21.6$	$66.1 \pm 15.4$	$66.7 \pm 13.0$	
Age (yr)					0.277
<35	768	$105.5 \pm 18.7$	$69.0 \pm 14.5$	$66.0 \pm 11.9$	
$\geq 35$	407	$95.9 \pm 19.3$	$61.8 \pm 13.3$	$65.2 \pm 11.9$	
BMI (kg/m <sup>2</sup> )					<0.001
<25	294	$100.4 \pm 20.4$	$65.6 \pm 14.6$	$66.1 \pm 12.5$	
$\geq 25$	881	$95.7 \pm 17.9$	$60.4 \pm 12.0$	$63.5 \pm 9.4$	

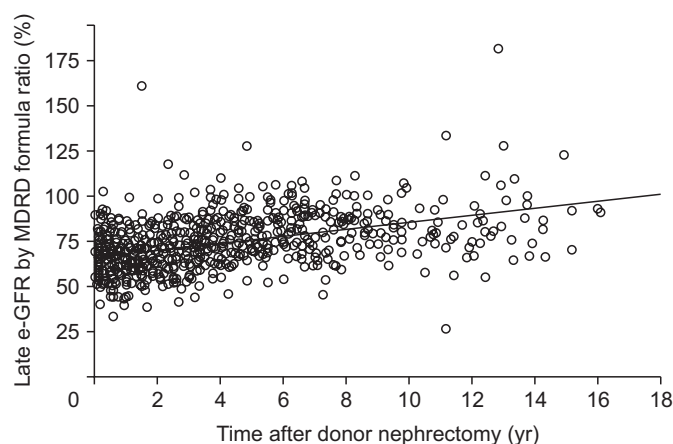
Values are presented as mean  $\pm$  standard deviation.

e-GFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; BMI, body mass index.

<sup>a)</sup>P-value calculated by comparison mean (Student t-test) of e-GFR ratio by variables.



**Fig. 1.** Change of estimated glomerular filtration rate (e-GFR) by Modification of Diet in Renal Disease (MDRD) formula at pre- and post-nephrectomy. Values are presented as mean±standard deviation.



**Fig. 2.** Late compensation of residual renal function after donor nephrectomy.  $y=66.216+0.162*x$  ( $R^2=0.199$ ,  $P<0.001$ ). e-GFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease.

**Table 4.** Late changes of renal function after donor nephrectomy (n=1,173, excluding two cases of renal failure)

Donor variable	n	e-GFR by MDRD formula (mL/min/1.73 m <sup>2</sup> )		e-GFR ratio (C/A, %)	P-value <sup>a)</sup>
		Pre-nephrectomy (A)	Late e-GFR (C)		
Overall	1,173	99.2±19.9	70.2±13.3	72.0±13.5	
Sex					0.883
Male	545	97.9±17.7	69.6±13.2	72.1±13.2	
Female	628	100.4±21.6	70.7±13.5	72.0±13.7	
Age (yr)					0.053
<35	766	105.5±18.7	76.1±14.0	73.1±13.4	
≥35	407	95.9±19.8	67.1±11.9	71.5±13.5	
BMI (kg/m <sup>2</sup> )					0.931
<25	294	100.4±20.4	71.0±13.5	72.0±13.22	
≥25	879	95.7±17.9	67.7±12.6	72.0±14.4	

e-GFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; BMI, body mass index.

<sup>a)</sup>P-value calculated by comparison mean (Student t-test) of e-GFR ratio by variables.

Donor age, sex, and BMI showed no significant correlation with the late e-GFR. The age of the donor at the time of donation had no linear correlation to the late e-GFR ratio. The BMI of the donor at the time of donation also had no correlation with the late e-GFR ratio, although in the immediate postoperative period, a higher donor BMI resulted in a greater decrease in e-GFR. The late e-GFR ratio showed no significant difference in terms of sex, age (<35, ≥35 years), or BMI (<25, ≥25 kg/m<sup>2</sup>) (Table 4).

The donor variables and the late e-GFR ratio were analyzed by stepwise multiple linear regression. Results showed that the follow-up period was the only significant factor explaining the compensation of the donor renal function. The donor variables: sex, age, and BMI at dona-

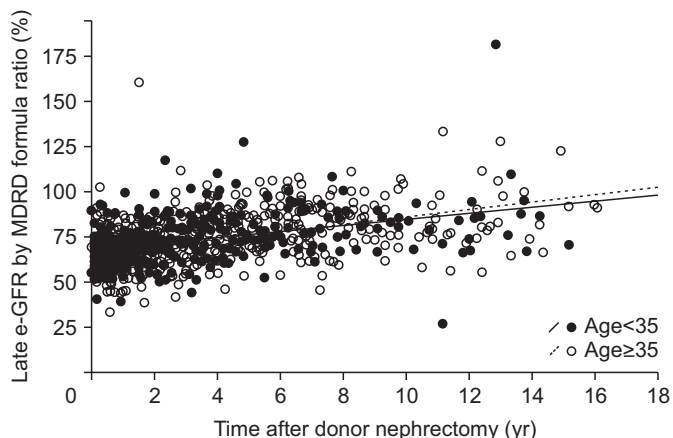
tion were excluded ( $P<0.001$ ) (Table 5).

The effects of the donor variables combined with the follow-up period on the late e-GFR ratio were analyzed. Donors <35 years and ≥35 years were analyzed in combination with follow-up time. We found no significant difference in the effects of the two age groups combined with follow-up period on the late e-GFR ratio ( $P=0.104$ ) (Fig. 3). When BMI was grouped into <25 kg/m<sup>2</sup> and ≥25 kg/m<sup>2</sup> groups, there was no significant difference between the effects of the two groups in combination with follow-up period on the late e-GFR ratio ( $P=0.466$ ) (Fig. 4). There was a statistically significant difference in the late e-GFR ratio between males and females when they were analyzed in combination with follow-up time. Female donors

**Table 5.** Stepwise multiple linear regression analysis for late changes of renal function

Variable	Beta	Standard error	P-value
Constant	66.216	0.495	<0.001
Post-nephrectomy period	0.162	0.009	<0.001

$R^2=0.199$ ,  $F=291.921$ ,  $P<0.001$ . Excluded variable: age, sex, and body mass index.



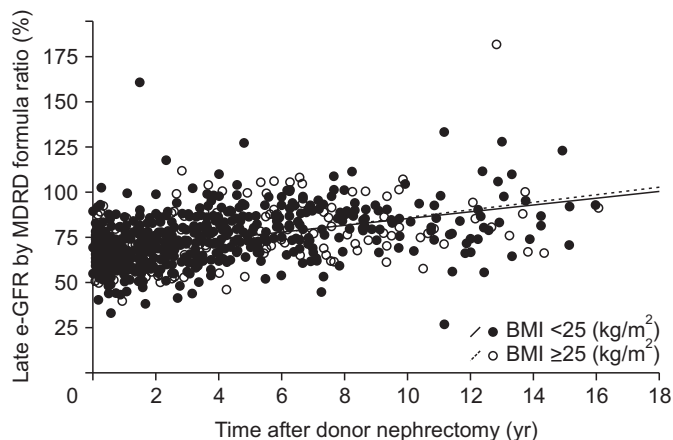
**Fig. 3.** Late compensation of residual renal function after donor nephrectomy between two age groups (age <35, ≥35 years;  $P=0.136$ ). e-GFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease.

showed a greater renal compensation rate compared to male donors ( $P=0.004$ ) (Fig. 5).

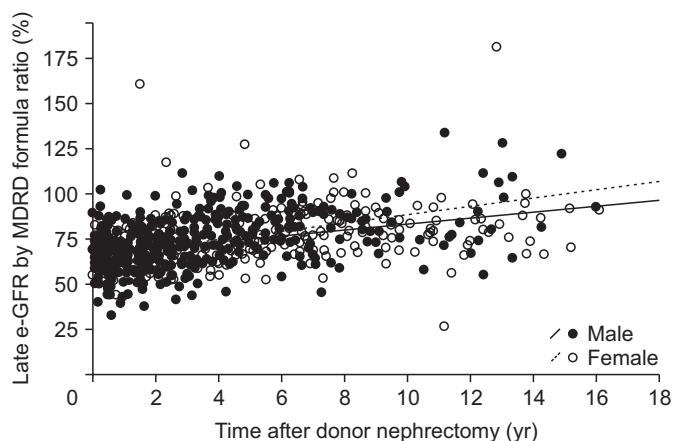
## DISCUSSION

The safety of the donors has been the primary concern of the transplant society since the introduction of living donor kidney transplantation [24]. Although there are concerns about glomerular hyperfiltration, proteinuria, hypertension, and other cardiovascular risks, several studies have reported that kidney donation is relatively safe and that the survival of donors is similar to that of the general population [25,26]. While the risk of ESRD in donors is higher, the absolute risk remains low [27,28]. The rate of ESRD was 0.17% (2/1,175) in our study.

The e-GFR of the donor decreases immediately after donor nephrectomy. After nephrectomy, the renal function is partially compensated and is reported to recover 70%–75% of its initial GFR [17,20,21]. ter Wee et al. [29] reported



**Fig. 4.** Late compensation of residual renal function after donor nephrectomy between two body mass index (BMI) groups ( $P=0.466$ ). e-GFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease.



**Fig. 5.** Late compensation of residual renal function after donor nephrectomy in female donors and male donors ( $P=0.004$ ). e-GFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease.

that the GFR of kidney donors increased for years after donation, probably due to compensatory hypertrophy of the remaining kidney. Furthermore, Rook et al. [30] reported that baseline GFR, BMI, and age were independent predictors for renal function impairment after living donor donation. However, this study had a relatively short follow-up period after donation. We studied the factors affecting the rate of compensation and demonstrated that the immediate decrease in renal function was affected by the sex and BMI of the donor. Overweight donors showed a greater decrease in e-GFR after nephrectomy; however, during follow-up, the compensatory rates were similar



between the normal donors and obese donors.

We compared the donor variables in combination with follow-up period to verify the effect on the compensation of renal function and found that the compensatory rate showed no significant difference according to donor variables, with the exception of donor sex. Sex affected the decrease in e-GFR immediately after nephrectomy, as well as the compensatory rate during follow-up. Previous studies have reported that men have a higher GFR than women before nephrectomy [30,31]. Gossmann et al. [32] found that a higher GFR at the time of donation was the only significant factor for a larger than average loss of GFR. Similarly, our results demonstrated that males had a higher pre-nephrectomy GFR, which may support the greater decrease in postoperative e-GFR. We also showed that males had a lower compensatory rate than females, which may be due to a larger kidney volume and larger muscle mass in males compared to females. Although the compensation rates were statistically different, both sexes showed a compensation rate of over 70%.

In meta-analyses, Kasiske et al. [20] reported an immediate decrease in renal function after nephrectomy, and an increase in GFR was noted per decade during long-term follow-up. Moreover, Garg et al. [33] reported that after an initial decrement in GFR after nephrectomy, the renal function remained stable over 15 years. Our results show a significant linear increment in late e-GFR ratio that was only relevant in terms of the follow-up period. This may imply that donor factors such as sex and BMI only affect the renal function in the immediate postoperative period, but after time, the donor factors have little or no impact on the compensation of the renal function in healthy donors.

There are certain limitations of our study. The data were collected retrospectively and the donors were not asked to come for follow-up testing specifically for this study, only the data available at our center were used. Therefore, the donor pool that was analyzed may not adequately represent the total donor population. Furthermore, the donor pool did not include higher risk donors, such as hypertensive donors or elderly donors, compared to other reports. Therefore, our results may have not fully exhibited the impact of donor factors on the compensation of renal function. In addition, the consequences of hyperfiltration, such as albuminuria and hypertension, could not be evaluated due to our data collection method. Further studies should be carried out in a prospective fashion with an adequate control group in order to study the risk of such

comorbidities and the survival of the donors.

In conclusion, we found that in healthy donors with no major comorbidities, donor factors such as sex and BMI may affect renal function immediately after nephrectomy, but that compensation of renal function occurs over time, regardless of donor factors. The compensation rate reaches an average of over 72% of its initial renal function.

## ACKNOWLEDGMENTS

### Conflict of Interest

No potential conflict of interest relevant to this article was reported.

### Funding/Support

This study was supported by research grant from the Korean Society for Transplantation (2020-02-01001-003).

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Conceptualization: MSK. Data curation: YPL, SJK. Formal analysis: YPL. Funding acquisition: MSK. Methodology: SJK, JL, JGL, KHH, DJJ. Project administration: MSK, SIK, YSK, KHH, JL. Visualization: YPL. Writing—original draft: SJK. Writing—review & editing: YPL, SJK, MSK.

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