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Long-term risk of chronic kidney disease in living kidney donors at a single center in Thailand

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Background : *Although the results of several studies support the safety of live kidney donation, there is no functional deterioration, some donors have proteinuria and hypertension (HT). Most of the studies were done in Europe and America, in Asia, however, the information about donors living with one kidney is lacking.*

Objective : *To study the long-term risks of chronic kidney disease (CKD) in living kidney donors at one medical center in Thailand.*

Design : *A retrospective study.*

Setting : *Division of Urology, Department of Surgery, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.*

Materials and Methods : *Donors who were followed up for more than 1 year after nephrectomy were included. We assessed each donor's blood pressure, urine protein, and estimated glomerular filtration rate (eGFR).*

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Results : *The donors had a mean age of 37.5 ± 9.78 years at donation. The median follow-up period was 3.62 years (range 1 - 11 yrs). There were statistically significant increases in SBP from 113.3 ± 11.15 to 120.5 ± 11.99 mm Hg. and BMI from 22.9 to 23.6 (P <0.001). 4 (4.7%) developed hypertension and 2 (2.3%) displayed proteinuria. Serum Cr significantly changed from 0.72 ± 0.2 to 1.02 ± 0.22 mg/dL. (P <0.001) and eGFR from 114.6 ± 36.62 to 74.26 ± 14.46 mL/min/1.73 m^2. (P <0.001) 5(5.8%) had CKD (eGFR<60 mL/min/1.73 m^2). After transplantation, eGFR decreased by < 1 mL/min/1.73 m^2 each year. Age at donation and longer follow-up time were significant risk factors for renal functional deterioration (CKD, HT, proteinuria) (P = 0.04, OR = 1.092 (1.004 - 1.188) and P = 0.012, OR = 1.425 (1.079 - 1.881), respectively).*

Conclusion : *Renal function was well preserved after donor nephrectomy in early period. A significant proportion of living donors might develop renal deterioration upon long-term follow-up.*

Keywords : *Chronic kidney disease, living kidney donation, King Chulalongkorn Memorial Hospital.*

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นนท์ ว่องวิทวัส, จุลินทร์ โอภานุรักษ์, กมล ภานุมาตรัศมี, ชนธีร์ บุณยะรัตเวช, กวิรัช ตันติวงศ์, สุพจน์ รัชชานนท์, อภิรักษ์ สันติงามกุล, เกรียงศักดิ์ ประสพสันติ. การศึกษาโอกาสในการเกิดโรคไตเรื้อรังในผู้ที่บริจาคไตให้แก่ผู้อื่นในโรงพยาบาลจุฬาลงกรณ์. จุฬาลงกรณ์เวชสาร 2558 มี.ค – เม.ย; 59(2): 127 – 36

เหตุผลของการทำวิจัย : *การผ่าตัดเปลี่ยนไตจากผู้บริจาคที่ยังมีชีวิตเป็นการรักษาที่ดีที่สุดสำหรับผู้ป่วยไตวายระยะสุดท้าย แต่สำหรับผู้ที่บริจาคไตจะมีความเสี่ยงจากการผ่าตัดและจากการลดลงของไตเหลือแค่ครึ่งเดียว ถึงแม้การศึกษาส่วนใหญ่พบว่าการทำงานของไตของผู้ที่บริจาคไตไม่แตกต่างจากในคนปกติ แต่การศึกษาส่วนใหญ่ทำในประเทศทางตะวันตก*

วัตถุประสงค์ : *เพื่อศึกษาการเกิดโรคไตเรื้อรัง ความดันโลหิตสูงและภาวะโปรตีนในปัสสาวะในผู้ที่บริจาคไตที่โรงพยาบาลจุฬาลงกรณ์*

รูปแบบการวิจัย : *การศึกษาแบบไปข้างหลัง*

สถานที่ทำการศึกษา : *หน่วยศัลยกรรมทางเดินปัสสาวะ ภาควิชาศัลยศาสตร์ คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย*

ตัวอย่างและวิธีการศึกษา : *ศึกษาผู้ที่บริจาคไตที่โรงพยาบาลจุฬาลงกรณ์ตั้งแต่ปีพ.ศ. 2546 -2556 ที่มาตรวจติดตามตั้งแต่ 1 ปีขึ้นไป โดยศึกษาโอกาสในการเกิดโรคไตเรื้อรัง ความดันโลหิตสูงและภาวะโปรตีนในปัสสาวะ และปัจจัยเสี่ยงต่อการเกิดโรคไตเรื้อรังในผู้ที่บริจาคไต*

ผลการศึกษา : *พบว่าผู้ที่บริจาคไตมีอายุเฉลี่ย 37.5 ปี ระยะเวลาติดตามเฉลี่ย 4.4 ปี มีการเปลี่ยนแปลงอย่างมีนัยสำคัญของความดัน systolic (113.3 เป็น 120.5 mmHg, P <0.001) BMI (22.9 เป็น 23.6, P <0.001) creatinine ในเลือด (0.72 เป็น 1.20, P <0.001) eGFR (114.6 เป็น 74.6 mL/min/ 1.73 m^2, P <0.001) อัตราการเกิดไตเรื้อรัง ความดันโลหิตสูงและภาวะโปรตีนในปัสสาวะเท่ากับ 5.8%, 4.7% และ 2.3%ตามลำดับ หลังบริจาคไตอัตราการทำงานของไตลดลง <1 mL/min/ 1.73m^2 ต่อปี และพบว่าอายุขณะที่บริจาคไตและระยะเวลาที่ตรวจติดตามมีผลต่อการทำงานที่แย่ลงของไต*

สรุป : *การบริจาคไตไม่ได้ทำให้การทำงานของไตแย่ลงในระยะแรก อายุที่น้อยกว่าจะทำให้การทำงานของไตดีกว่าแต่เมื่อตรวจติดตามไปนานขึ้นจะพบว่าการทำงานของไตแย่ลง*

คำสำคัญ : *โรคไตเรื้อรัง, การปลูกถ่ายไต, โรงพยาบาลจุฬาลงกรณ์.*

Living kidney donation has become an essential part of transplantation practice. Historically, this has been attributed to the shortage of decreased donor kidneys and the growing waiting list of potential recipients. However, kidney transplantation from a living donor has become the treatment of choice for many patients, i.e., better graft survival, low rejection rates, shorter times on dialysis and the possibility of preemptive transplantation.[1, 2] Although the medical benefits for the recipient are unquestionable, a living-donor transplant does have a serious and obvious disadvantage: the donor needs a major operative procedure associated with morbidity, mortality, and a above all the potentially negative long-term consequences of living with a single kidney. Concerns about long-term risks to the donor after uninephrectomy are accentuated by reports that animal renal ablation is associated with compensatory changes in the remaining nephrons which lead to renal failure[3, 4], its early marker is proteinuria. Although the results of several studies support the safety of live kidney donation, i.e., there is no functional deterioration, some donors did have proteinuria and hypertension.[5 - 9] Most of the studies were studied in Europe and America, data about Asian donors are lacking. [10 - 12] Therefore, the aim of the present study was to analyze hypertension, renal function, and proteinuria in living donors after nephrectomy at a medical center in Thailand.

Methods

We retrospectively reviewed medical records of the donors. We identified 86 donors from whom follow-up data of more than 1 year were available. Parameters collected from the medical records included: gender, height, weight, BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), 24-hour urine proteinuria (> 150 mg/24 h), urinalysis, age at donation, age at follow-up, follow-up duration (years), Cr (mg/dL) initially and at follow-up, eGFR (mL/min/1.73 m^2) initially and at follow-up. Renal function was evaluated by Cr (mg/dL) and eGFR, using the formula of modification of diet in renal disease (MDRD), namely, eGFR (mL/min/1.73 m^2) = 186.3 X $Scr^{-1.154}$ X $Age^{-0.203}$ X 0.742 (if female).[13] We collected the following data: gender, age at donation, age at follow-up, follow-up duration (years), Cr (mg/dL) initially and at follow-up, eGFR (mL/min/1.73 m^2) initially and at follow-ups. We defined proteinuria as documented by urine analysis > 1+ or daily urine protein > 150 mg, and hypertension (HT) as systolic blood pressure of >140 mmHg or diastolic blood pressure of >90 mm Hg or the prescription of an antihypertensive drug. Renal functional deterioration was evaluated via the eGFR < 60 mL/min/1.73 m^2, HT, or proteinuria.

Statistical Methods

Data were expressed as mean values and standard deviations or percentages. Paired student t tests were used to compare initial with follow-up renal function values (Cr and eGFR). Risk factors for HT, proteinuria, and eGFR < 60 mL/min/1.73 m^2 were analyzed by logistic regression model (presented as odds ratio [OR], P values and 95% confidence intervals). eGFR decline per year were analyzed using a general linear regression model. All analyses were performed with SPSS version 16.0 software.

Results

The demographic data of our live-kidney donor population are shown in Tables 1. The donor consisted of 32 (37.2%) males and 54 (62.8%) females. Mean age at the time of donor nephrectomy and at the final follow-up were 37.5 ± 9.78 years (range 20 –71 years) and 41.9 ± 10.27 years (range 21– 87 years), respectively. The median follow-up period was 3.62 years (range 1 - 11 yr). There were statistically significant increases in SBP from 113.3 ± 11.15 to 120.5 ± 11.99 mm Hg. and BMI from 22.9 to 23.6 (*P* <0.001). Four of 86 donors (4.7%) developed hypertension that required antihypertensive treatments. After transplantation, 2 donors (2.3%) displayed proteinuria at the final follow-up. Renal functional decline was observed between donation and follow-up time with Cr concentration of -0.3 mg/dL (P <0.001) namely, from 0.72 ± 0.2 to 1.02 ± 0.22 mg/dL and eGFR of -40.36 mL/min/1.73 m^2 (P <0.001) namely, from 114.6 ± 36.62 to 74.26 ± 14.46 mL/min/1.73 m^2. The eGFR was < 60 mL/min/1.73 m^2 for 5 (5.8%) donors, one donor developed HT and another proteinuria. After transplantation, their eGFR decreased by < 1 mL/min/ 1.73 m^2 each year. (Figure 1.)

Possible factors associated with renal functional deterioration (eGFR < 60, HT, and proteinuria) are listed in Table 2. Gender, BMI, SBP, serum Cr and eGFR at donation were not related to renal functional deterioration. Age at donation and longer follow-up time caused greater likelihood of renal functional deterioration (P = 0.04, OR = 1.092 and P = 0.012, OR = 1.425) Table 3.

Table 1. Characteristics of the kidney donor population.

Female	54 (62.8%)		
Median of follow-up (range)	3.62 yr (1 - 11.76)		
	At Donation	At Follow up	P value
Age (yr)	37.5 (9.78)	41.9 (10.27)	
BMI	22.96 (2.92)	23.63 (3.53)	<0.001
Serum Cr (mg/dL)	0.72 (0.2)	1.02 (0.22)	<0.001
eGFR (mL/min/1.73 m^2)	114.6 (36.62)	74.26 (14.46)	<0.001
SBP	113.3 (11.15)	120.5 (11.99)	<0.001
DBP	71.3 (8.19)	71.3 (8.61)	0.929
		No. of patients at follow-up	
eGFR < 60 mL/min/1.73 m^2		5 (5.8%)	
Hypertension		4 (4.7%)	
Proteinuria		2 (2.3%)	

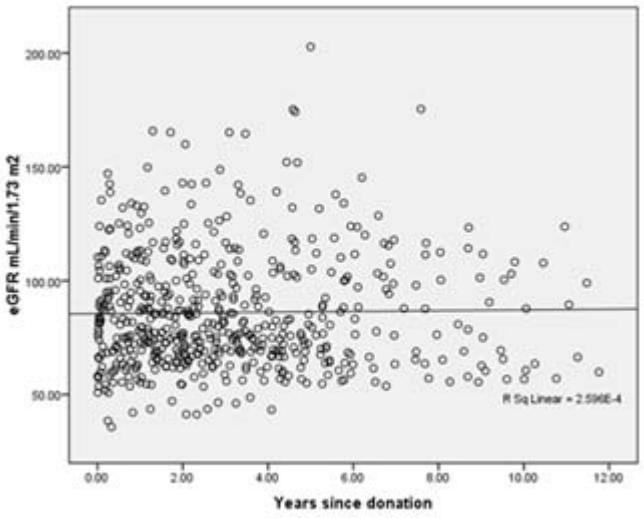

Figure 1. eGFR all 86 donors shows for after kidney donation a linear regression curve for the data is also shown.

Table 2. Univariable analysis of risk factor for renal function deterioration.

Variable	P value
Age at donation	0.027
Serum Cr	0.356
Systolic BP	0.321
BMI at donation	0.381
BMI after donation	0.561
Duration	0.005
Gender	0.072

Table 3. Multivariate analysis of risk factors for renal function deterioration.

Variable	OR	P (95% CI)
Age at donation	1.092	0.04 (1.004 - 1.188)
Duration	1.425	0.01 (1.079 - 1.881)

Discussion

A major long-term concern regarding the use of living donors is whether unilateral nephrectomy (open or laparoscopic) may be associated with the development of kidney disease and with premature death. In fact, recent data suggest that kidney donors live longer than the age-matched general population. [14] Although this finding may be due to selection bias, it contradicts the concept that donor longevity may be limited.

In some experimental animal studies, significant reduction of kidney mass resulted in proteinuria, glomerulosclerosis, and progressive kidney failure.[3, 4, 15] In humans, no large clinical series supports the fear that, in an individual with two normal kidneys, unilateral nephrectomy does not lead to an increased risk of progressive kidney failure. However, there are individual case reports of patients developing kidney disease, proteinuria, and kidney failure.[8] Thus, long-term follow-up of kidney donors are crucial.

The aim of this study was to assess the long-term risks of chronic kidney disease, in living kidney donors followed for more than 1 year after nephrectomy. After a median follow-up period of 3.62 years, eGFR declined to 74.26 mL/min/1.73 m^2, which was far worse than the mean rate among all 36 studies in the systemic review, namely, 86 mL/min/1.73 m^2 after a 6-year follow-up.[9] The reason that the donor prognosis was far worse in our population may be explained by our use of the eGFR estimates (MDRD-eGFR (mL/min/1.73 m^2) = 186.3 X Scr-1.154 X Age -0.203 X 0.742 (if female)The original eGFR is not suitable for Asian patients. The use of eGFR led to a misclassification of stage of chronic kidney disease (CKD) due to ethnic physiological differences, which was also detected in a study by Praditpornsilpa et al.[16] However, our results showed that the rate of annual decline in eGFR after transplantation was < 1 mL/min/1.73 m^2 and this rate was virtually the same in normal volunteers.[8] The results of this study also showed a significant increase in blood pressure, for which 4.7% of donors required antihypertensive treatments. Meta-analysis revealed that blood pressure was 3 mm Hg higher before compared with after KT.[17] Based on these findings, unilateral nephrectomy is associated with a slight increase in blood pressure.

Older age at donation and longer follow-up time both significantly correlated with the development of renal functional deterioration. These factors indicated that renal function in the donor's remaining kidney may be more susceptible to the deterioration that accompanies the aging process. Greater glomerular hypertension in older compared with younger donors causes more glomerulosclerosis and further renal functional deterioration.[18] Age at donation denotes baseline renal function, and duration of follow-up denotes duration of hyperfiltration injury, which is the sum of baseline renal function and hyperfiltration injury. Even young donors with good baseline renal function suffer from renal functional impairment after a long follow-up period.

There were some limitations to this study. As a retrospective study, there was no a control group in this study. So the development of renal deterioration might be caused from the aging process or longer follow-up time. Furthermore, it was a relatively small population at one single center.

In conclusion, Although younger donors will get better renal function after donation than older donors, a significant proportion of living donors may develop renal deterioration upon long-term follow-up.

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