Yearly Trends of Chronic Kidney Disease III Progressions in Living Kidney Donors

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ABSTRACT

Purpose. We aim to see the rate of progression to chronic kidney disease stage III after living donor nephrectomy in a single institution annually.

Methods. Between May 2006 and July 2017, a total of 753 living kidney donors who were followed up more than 6 months were enrolled in the study. We divided normal function vs chronic kidney disease III at 6 months postoperatively. We compared the incidence rate of chronic kidney disease stage III annually. For analysis, the entire period was divided into Era 1 (2006–2008), Era 2 (2009–2011), Era 3 (2012–2014), and Era 4 (2015–2017).

Results. During the period, the incidence of chronic kidney disease stage III was 258 living donors (34.3%). The prevalence of chronic kidney disease stage III was 39.3%, 36.6%, 35.5%, and 29.3% in Era 1, Era 2, Era 3, and Era 4, respectively. The rate of chronic kidney disease stage III incidence serially decreased as the era passed ($P = .046$). There was no difference in age, smoking status, drinking status, body mass index, preoperative cholesterol, and uric acid among the eras. However, preoperative estimated glomerular filtration rate was 90.86 (SD, 4.12), 94.47 (SD, 16.62), 103.82 (SD, 0.68), and 105.66 (SD, 19.57) mL/min/1.73 m^2 in Era 1, Era 2, Era 3, and Era 4, respectively ($P = .001$).

Conclusions. The incidence of chronic kidney disease stage III in living kidney donors for the last 3 years (Era 4) has decreased compared with the past (Era 1 and 2). The reason for this might be the effect of the change in the living donor guideline. Also, pre- and post-operative management method had an effect on renal function at 6 months.

IN KIDNEY donation, the living donor who is at no risk of chronic renal failure is important. Ibrahim et al reported on 12-year follow-up and found no significant difference in end-stage renal disease (ESRD) ratio compared with the normal group [1]. In contrast, Muzaale et al reported a matched comparison study with nondonor populations that ESRD progression was 8-fold higher in the kidney donors during a period of 7.6 years [2]. In both studies, however, the absolute rate of progression to ESRD was low, reinforcing the predominating low risk characterization of donation. As living donation has been increasingly used in the United States, it is likely that this trend will continue and grow in demand for living kidney donors in the future [3]. The increased demand for living kidney donors has been studied, and there are also studies on the risk of ESRD in living kidney donors. However, there is a lack of reports of progression to annual chronic kidney disease (CKD) in living kidney donors. Understanding trends to CKD in the living kidney donor can help to guide physicians in clinical practice as well as plan for proper management. The purpose of this study was to evaluate the changing

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incidence of ESRD. Thus, we evaluated the cause of CKD III annually and which factor affects disease progression in living kidney donors.

METHODS

This study was performed from May 2006 to July 2017 at Severance Hospital. A total of 1183 donors underwent live donor nephrectomy in this period. Among them, 753 living kidney donors who were followed up more than 6 months were enrolled in the study.

In this period, all donor nephrectomies were performed by using video-assisted mini-incision surgery. Recorded donor characteristics, including age, sex, height, weight, body mass index, and pre- and postoperative blood test were extracted, as were results of routine diagnostics performed in each instance, including diethylenetriamine-penta acetic acid (DTPA) renal scans and computerized tomographic angiography. In accordance with donor criteria, candidates with estimated glomerular filtration rate (eGFR) values < 80.0 mL/min/1.73 m^2 at baseline and those with diabetes or hypertension inadequately controlled were excluded as donors. Baseline levels of total cholesterol, triglyceride, low-density lipoprotein, and high-density lipoprotein in standard testing were also collected. Renal function was estimated, using the Modification of Diet in Renal Disease formula to calculate eGFR pre-and postoperatively, and donors were grouped by eGFR at last follow-up examination, creating healthy (> 60.0 mL/min/1.73 m^2) and CKD III (< 60.0 mL/min/1.73 m^2) groups 6 months post operation. We compared the incidence rate of CKD III annually. For analysis, the entire period was divided into Era 1 (2006–2008), Era 2 (2009–2011), Era 3 (2012–2014), and Era 4 (2015–2017). During this period, living kidney donor surgery was performed by using video-assisted minilaparotomy surgery. In Era 1, we managed living kidney donors in the same way after radical nephrectomy. From Era 2, we have changed the preoperative and postoperative management. First, the use of antibiotics was limited to once on the day of surgery. We also used eGFR in combination with serum creatinine and cystatin C in donor selction since Era 2. In addition, the renal function was evaluated by conducting 3 to 4 blood tests before donation. Also, we assessed 24-hour urine creatinine clearance and DTPA clearance to accurately evaluate renal function in the live kidney donor. From Era 3, the Life Style Modification was implemented for all donors. We performed multidetector computed tomography (MDCT), which enabled the evaluation of renal function in the live kidney donors. To determine the side of the nephrectomy, DTPA scintigraphy was used to evaluate split renal function. Also, the MDCT reconstruction images yielded accurate measurements of the kidney volume. In addion, MDCT provided anatomic details of the kidney, vasculature, and the collecting system and aided in the diagnosis of kidney abnormalities. In Era 4, fluid therapy has been administered at a rate of 80.0 to 120.0 mL/h from 2 days before surgery, and maintained for 2 to 3 days after surgery. Group differences were compared using 1-way analysis of variance and χ^2 tests when appropriate. A value of $P < .05$ was considered statistically significant. Statistical analyses were performed, using SPSS software version 23.0 (IBM, Armonk, NY, United States).

RESULTS

A total of 753 living kidney donors were analyzed in Eras 1, 2, 3, and 4. The median follow-up time for donors was 6 months. Characteristics of donors were similar in each era, except for a donor side and preoperative eGFR (Table 1). Right donor side rates were 22.3% (25/112), 13.7% (24/175), 8.7% (19/217), and 6.4% (16/249) in Era 1, Era 2, Era 3, and Era 4, respectively. Preoperative eGFRs were

Table 1. Living Kidney Donor Preoperative Characteristics

	Era 1	Era 2	Era 3	Era 4	*P* Value
Age, mean (SD), y	40.74 (10.71)	39.41 (12.17)	42.46 (11.63)	42.63 (11.43)	.19
Sex, No.					
Male	51	82	93	99	
Female	61	93	124	150	.49
HTN, No.					
Yes	2	6	14	19	
No	110	169	203	230	.07
DM, No.					
Yes	0	0	2	1	
No	112	175	215	248	.45
Smoking, No.					
Yes	38	56	69	78	
No	74	119	148	171	.97
Alcohol, No.					
Yes	54	94	118	131	
No	58	81	99	118	.75
Side, No.					
Left	87	151	198	233	
Right	25	24	19	16	< .001
BMI, mean (SD)	23.36 (2.71)	23.26 (2.82)	23.35 (2.66)	23.43 (2.73)	.72
eGFR (preop), mean (SD), mL/min/1.73 m^2	90.86 (13.14)	94.47 (16.62)	103.82 (20.68)	105.66 (19.57)	.001
Cholesterol, mean (SD), mg/dL	185.86 (35.18)	184.27 (37.06)	189.10 (32.64)	196.01 (32.80)	.26
Uric acid, mean (SD), mg/dL	4.89 (1.36)	4.70 (1.20)	5.00 (1.45)	4.82 (1.29)	.68

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HTN, hypertension; preop, preoperative.

Table 2. Difference of eGFR According to Era (Pre- and Postoperation)

	Era 1	Era 2	Era 3	Era 4	*P* Value
eGFR (preop), mL/min/1.73 m^2	90.86 (13.14)	94.47 (16.62)	103.82 (20.68)	105.66 (19.57)	< .001
Era 1		$P = .37$	$P < .001$	$P < .001$	
Era 2			$P < .001$	$P < .001$	
Era 3				$P = .71$	
eGFR (postop), mL/min/1.73 m^2	62.82 (10.85)	65.42 (12.28)	66.12 (12.71)	66.75 (11.77)	.03
Era 1		$P = .28$	$P = .09$	$P = .02$	
Era 2			$P = .94$	$P = .67$	
Era 3				$P = .94$	

Abbreviations: eGFR, estimated glomerular filtration rate; postop, postoperative; preop, preoperative.

90.86 (SD, 13.14), 94.47 (SD, 6.62), 103.82 (SD, 20.68), and 105.66 (SD, 19.57) mL/minute/1.73 m^2 in Era 1, Era2, Era3, and Era 4, respectively. There were significant differences in donor side and preoperative eGFR in any era ($P < .05$). The rate of progression to CKD III at 6 months after living donor nephrectomy was 39.3% (44/112), 36.6% (64/175), 35.5% (77/217), and 29.3% (73/249) in Era 1, Era 2, Era 3, and Era 4, respectively ($P = .046$).

Preoperative eGFR showed a significant difference between Era 1, 2 and Era 3, 4. Postoperative eGFR showed a statistically significant difference between Era 1 and Era 4 (Table 2). There was a statistically significant reduction of CKD III in women from Era 1 to Era 4 ($P = .04$) (Table 3). Also, we compared Era 1 and Era 4, and there was a statistically significant decrease in CKD III for 6 months after living donor nephrectomy ($P < .05$) (Fig 1).

DISCUSSION

In the US Renal Data System, there were 687,093 people with ESRD in the United States in 2015 [4]. End-stage renal disese is a major outcome of CKD, with an important effect on mortality, morbidity, quality of life, and health resource utilization. Kidney transplant is the criterion standard for treating patients with ESRD because it provides patients with better survival and quality of life than dialysis [5]. More than 27,000 living donor kidney transplants have been performed; there is an increasing demand for living kidney donation [3]. With increasing numbers of patients with ESRD, there is a growing need for kidney transplant, yet the number of donors is limited. Thus, there are emerging concerns regarding the preservation of renal function of living donors. To ensure the preservation of renal function after donation, the predonation renal function of all potential donors is rigorously evaluated, and those with conditions such as kidney disease, diabetes, hypertension, and end-organ damage are excluded, as these conditions are anticipated to deteriorate renal function in the future. The postdonation glomerular filtration rate (GFR) has been reported to reach 65% to 70% of the predonation GFR in healthy donors [6], and factors reported to be associated with the risk of decreased GFR are older age, high body mass index, and race. Living kidney donors have a single kidney after donor nephrectomy; it is unexpected that any health problems will affect a single kidney. Evidence implies that living kidney donation greatly elevates the relative risk of ESRD, although this outcome remains uncommon: less than 0.5% over 15 years [7,8]. Unfortunately, few data for long-term renal outcomes have been published. The incidence of ESRD in donors was lower than in the unscreened general population controls but higher than in matched healthy nondonors [1]. Muzaale et al extrapolated data to a longer time horizon and estimated that the 15-year cumulative incidence of ESRD was 0.31% in living kidney donors vs 0.03% in healthy nondonors [2,7].

Table 3. No. of CKD III Incidents Between Sexes

	Era 1	Era 2	Era 3	Era 4	*P* Value
eGFR < 60, mL/min/1.73 m^2					
Male	19	25	38	34	.54
Female	25	39	39	39	.04
eGFR ≥ 60, mL/min/1.73 m^2					
Male	32	57	55	65	
Female	36	54	85	111	
Total (N)	112	175	217	249	

Abbreviation: eGFR, estimated glomerular filtration rate.

A previous report said that renal function stabilized in living kidney donors at 1 month after nephrectomy; this effect persisted through at least the entire first postsurgical year [9]. Based on this report, we confirmed the presence of CKD III in the living kidney donors who were observed for more than 6 months from 2006 to 2017. Chronic kidney disease III occurred in about 34%, and there was no progression to ESRD. Previous reports have shown that progression from living kidney donor to ESRD occurred in 0.1% [2]. In the living kidney donors, the deterioration of CKD III to ESRD is relatively low compared with the normal population. These results suggest that CKD III in living kidney donors is different from pathologic CKD III.

The incidence of CKD III in each era tended to decrease. The change in the lower limit of normal for predonation eGFR in the Kidney Disease: Improving Global Outcomes guideline seems to be the reason for the difference in occurrence of CKD III during this period. In addition, changes in the management of living kidney donor in each era according to guideline alteration may have influenced the reduction of CKD III. For example, the Kidney Disease: Improving Global Outcomes guideline on blood pressure

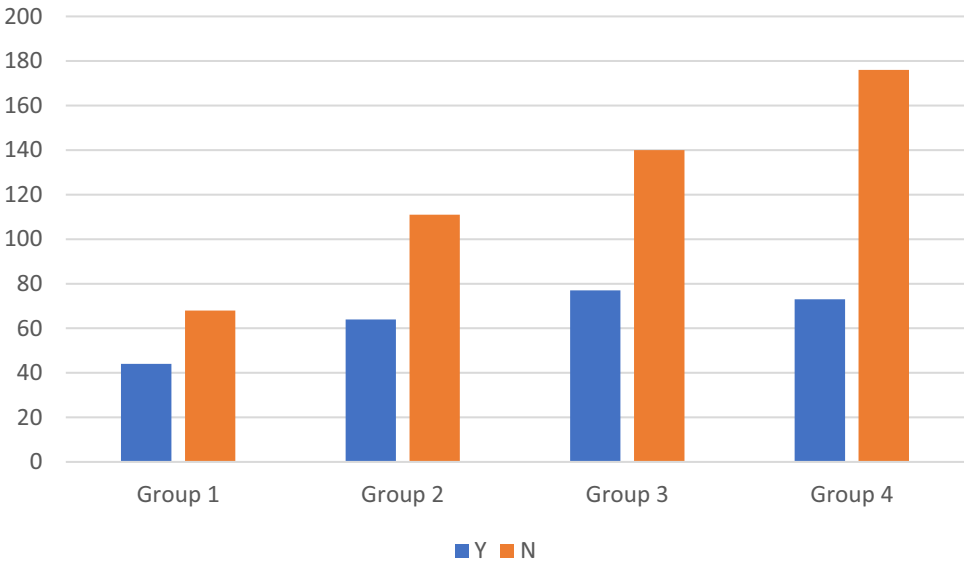

Fig 1. CKD III after 6 months among 4 groups. CKD, chronic kidney disease, N, no; Y, yes. $^{*}P < .05$.

has been changing since 2005, and our institution has also thoroughly managed hypertension in living kidney donors after Era 3. An antihypertension drug was taken as soon as possible when the living kidney donor was observed as a high-risk group for blood pressure.

Perioperative death or major complication from kidney transplant is a rare event. Unfortunately, our institutions encountered an event in 2012 when a young woman died after donor nephrectomy. We performed retrospective chart review of this woman and found preoperative microscopic hematuria and microscopic proteinuria. Since then, microscopic hematuria and microscopic proteinuria have been thoroughly controlled in donor selection. Because the preoperative eGFR affects postoperative eGFR, thorough lifestyle modification and any amount of hydration were performed for 6 months before living donor nephrectomy. This change in management seems to be the cause of CKD III reduction. Regarding the difference in CKD III incidence according to sex (Table 3), women seem to be more effective on preoperative or postoperative management than men.

This present study has some limitations, including the short postoperative monitoring period (up to 6 months) of the donors. We could not analyze the long-term effects of all variable on renal function after donation because of high rates of loss to follow-up, recall bias, and inadequate sample size to detect clinically important risks. It was a retrospective study and a relatively small number of patients were included. However, all patients underwent the same surgical procedure and were followed up according to routine protocol; the postoperation data were collected in a prospective method, and because all patients with sufficient data were included, there is a low chance of selection or recall bias. To our knowledge, however, no studies have addressed the clinical implications of the era change in kidney donors. Based our study, we recommend thorough management in living kidney donors; the CKD III risk posed by these conditions might plausibly depend on the donor's age at donation, lifestyle, and the availability of pre- and postoperative health care. The perception of CKD III in living donor needs to be converted into a manageable condition, not a pathologic one.

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