Original Article

Selection and Short-Term Outcomes of Living Kidney Donors in Singapore – An Analysis of the Donor Care Registry

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Abstract

Introduction: Transplant rates in Singapore have been falling and there is limited information on baseline characteristics and clinical outcomes of living kidney donors nationally. This study aimed to determine the safety of living kidney donor transplant in Singapore by exploring the proportion of donors that meets international selection guidelines and describing short-term clinical outcomes. Materials and Methods: We analysed 472 donors who underwent nephrectomies from 1 January 2010 to 31 December 2014 from the Donor Care Registry. We described donor characteristics against 5 international guidelines and measured post-nephrectomy outcomes in 150 local donors for up to 24 months. A multivariate analysis was performed to determine the baseline variables associated with poorer outcomes. Results: There were more foreign than local donors, with differences in gender and hospital types. Selection was generally aligned with international recommendations although 3.0% (using the Chronic Kidney Disease Epidemiology [CKD-EPI] equation) to 8.5% (using radionuclide and creatinine clearance methods) of donors had inappropriate baseline estimated glomerular filtration rates (eGFR) for age. Post-procedure, many foreign donors were lost to follow-up. Over 24 months, eGFR decreased by 33.8% from baseline before recovering gradually to 29.6%. During this period, only 2 donors were admitted for renal or urological conditions and there were no cases of end-stage renal failure or deaths. A lower baseline eGFR (HR: 1.05; 95% CI, 1.02 to 1.09) and older age (HR: 1.04; 95% CI, 1.00 to 1.08) were associated with a post-nephrectomy eGFR of less than 60 mL/kg/1.73 m^2. Conclusion: Kidney donation is safe in Singapore. Donor selection is in keeping with international guidelines and short-term outcomes are comparable to other cohorts.

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Key words: Guidelines, Nephrectomy, Renal, Safety

Introduction

Persons with end-stage renal disease (ESRD) require either dialysis or a kidney transplant to survive. Transplant is preferred as it is considered a life-extending procedure; the typical patient lives an average of 10 to 15 years longer with a kidney transplant than if kept on dialysis.[1] In Singapore, data collected by the Singapore Renal Registry showed an increasing incidence of ESRD from 210.2 (1999) to 392.6 (2012) per million population. Yet transplant rates have fallen from 35.5 per million in 2006 to 16.2 per million in 2012.[2]

A cross-sectional study was conducted in 2012 to examine public attitudes to living kidney donation. It showed that only 48.4% of respondents expressed that they were willing to donate while alive. The main reasons given by those not willing to donate were fears of surgical risks (86.5%) and poorer health consequent to donation (87.5%).[3] There is presently limited published data regarding baseline characteristics and clinical outcomes of living kidney donors in Singapore at the national level.

There are currently a number of major guidelines used internationally for living kidney donation eligibility.

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The more commonly used are: i) the Amsterdam Forum on the Care of the Live Kidney Donor; ii) the British Transplantation Society/Renal Association United Kingdom guidelines for living donor transplantation; iii) the Guidelines for the Medical Evaluation of Living Kidney Donors by the United States (US) Organ Procurement and Transplant Network; iv) the Guidelines on Renal Transplantation by the European Association of Urology; and v) the Living Kidney Donor Guideline Caring for Australasians with Renal Impairment.[4-9]

In 2009, sub-legislation for the Donor Care Registry (DCR) of the National Registry of Diseases Office (NRDO), Ministry of Health (MOH), Singapore was established, mandating detailed reporting of all new and yearly follow-up information for living kidney donors. The aim of this study was to use data collected in the registry to determine the safety of living kidney donor transplantation in Singapore by exploring the proportion of donors that meets international selection guidelines and describing short-term clinical outcomes.

Materials and Methods

Living kidney donation in Singapore is governed through the Human Organ Transplant Act (HOTA) and the transplant ethics committee of each hospital. This is a retrospective case series which included all living donors reported to the DCR from 1 January 2010 to 31 December 2014 (inclusive).

Outcomes

The first primary outcome was the proportion of donors who met a list of parameters based on the 5 most commonly used international guidelines at baseline (Table 1). As there were variations in the absoluteness of contraindications, these were grouped into stronger and weaker relative contraindications. Conservative laboratory thresholds for haematuria and pyuria were used. Renal function at baseline was based on radionuclide glomerular filtration rate (eGFR) or urine creatinine clearance. eGFR was also calculated using serum creatinine using the 2009 Chronic Kidney Disease Epidemiology (CKD-EPI) formula. All laboratories had also indicated that their serum creatinine measurements were calibrated to isotope dilution mass spectrometry.

The second primary outcome was only performed for Singaporean citizens and permanent residents (locals) due to the likely high rate of loss to follow-up for foreign donors. These were clinical outcomes at less than 6 months, 6 to 12 months and 12 to 24 months of follow-up (Table 2). Complications and clinical complaints were documented as free-text and classified by an investigator (MZJ Ho) into mild (e.g. postoperative fever that resolved without antibiotics) as well as moderate and severe events (e.g. chest infections).

Table 1. Parameters for Baseline Analysis of Donors

	Baseline Parameters	Based On
Age	Less than 18 years old	USA, Europe: <18-year-old an absolute CI
	Less than 21 years old	USA: <21-year-old a relative CI
	More than 60 years old	No recommendations for upper limit
Hypertension	BP of >130/90 mmHg	USA: 130/90, Others: 140/90
	BP of >140/90 mmHg	>3 Absolute CI in USA guidelines
	On 3 or more anti-hypertensives	>3 Relative CI in UK guidelines
Dyslipidaemia	On hypolipidaemics	Generally not contraindicated
Diabetes	Diagnosed with DM	Absolute CI in European guidelines
	2-hour OGTT of ≥7.8 mmol/L	USA, Australia: ≥7.8 mmol/L
	2-hour OGTT of ≥11.1 mmol/L	Amsterdam: ≥11.1 mmol/L
Obesity	BMI of >30.0 kg/m^2	USA, Australia: >30 relative CI
	BMI of >35.0 kg/m^2	USA: >35 absolute CI
Renal function	Inappropriate eGFR for age	Amsterdam, USA, Australian, UK guidelines
Urine protein	24-hour urine protein >300 mg/24H	All guidelines
Urinary stones	Any stones on x-ray (size of stones not captured in registry)	USA: Any stones a relative CI
		Europe: >1 cm a relative CI
	Nephrocalcinosis or bilateral stones	Amsterdam: >1.5 cm a relative CI
		Amsterdam and Europe: Absolute CI
Anatomical abnormalities	Any significant abnormalities on x-ray	USA: Absolute CI
		European: Relative CI
Pulmonary issues	Any smoking history	Other pulmonary issues not directly captured

BP: Blood pressure; CI: Contraindication; DM: Diabetes mellitus; eGFR: Estimated glomerular filtration rate; OGTT: Oral glucose tolerance test; RBC: Red blood cell; UK: United Kingdom; USA: United States of America; WBC: White blood cell

Data Collection

Collection of data from new and follow-up donors was conducted by doctors and nurses within transplant clinics and hospitals. Although the extent and manner of data

gathering was left to clinicians, these were in accordance to structured electronic forms.[10,11] The National Organ Transplant Unit of MOH regularly generates a list of known donors and 2 NRDO renal transplant coordinators visited clinics and hospitals to record data using structured forms via an electronic database. Data was gathered through the access and review of clinical case notes, investigations and medication records.

On registration, basic demographic data, baseline pre-donation clinical state and investigations were collected. This was followed by nephrectomy details and complications noted during donors' hospitalisation. Registration of new donors to the registry was conducted ad-hoc, and not later than 3 months post-procedure. Donors were also followed-up annually, including documenting complications and clinical outcomes. At the first follow-up visit, clinical outcomes within the first 3 months post-transplant were also collected. Mortality data was obtained through the Singapore death registry.

Data Analysis

Demographics and clinical characteristics of patients were described using frequencies and percentages. Means and standard deviations were used for approximately normally distributed continuous variables, and medians and interquartile ranges (IR) for skewed distributions. Differences in demographics and clinical states between sub-groups of donors at the point of donation were examined. Paired sample t-test was used for differences in means while Fisher's exact test was used for differences in proportions.

Statistical analysis was performed using STATA, version 11.0. For all analysis, a two-sided *P* value of <0.05 was used as cutoff for statistical significance. Univariate analysis for renal function after donation was performed. Bivariate analysis for specific risk factors such as age, gender, baseline body mass index (BMI), baseline renal function and operative techniques, and association with changes in post-donation renal function were quantified using hazard ratios (HR) and 95% confidence intervals (CI). These are variables that had been previously shown to have had some effect on post-donation clinical outcomes in other cohorts.

Multivariate analysis was conducted through Cox proportional hazards regression analysis for 5 variables using an eGFR of <60 mL/min/1.73 m^2 as the outcome. Next, a receiver operating curve (ROC) was constructed with baseline eGFR as a predictor for postoperative eGFR of <60 per mL/min/1.73 m^2 to determine an optimal binary cutoff for baseline eGFR. This was followed by constructing a Kaplan-Meier curve for time to reach eGFR of <60 mL/min/1.73 m^2 based on the cutoff baseline eGFR.

Ethical Considerations

Collection of data and subsequent publication were covered by the 2009 National Registry of Diseases Act

Table 2. Clinical Outcomes for Follow-up Analysis

Outcomes	Definition
Post-donation renal function	eGFR (calculated using the 2009 CKD-EPI formula, as suggested by the 2012 KDIGO guidelines*); % change in GFR in each donor from baseline
Poor post-donation renal function	Last eGFR of less than 60 mL/min/1.73 m^2
Sign of possible end-stage renal failure	Last eGFR of less than 15 mL/min/1.73 m^2
Post-donation blood pressure	Systolic and diastolic blood pressure (in mmHg) compared to baseline
New onset hypertension	Use of blood pressure medications and not on medication pre-donation
New onset DM	Diagnosis of DM and did not have the diagnosis pre-donation
New onset proteinuria	Urinary protein of more than 300 mg/24 hours and did not have elevated urinary protein pre-donation
New onset elevated urinary RBC	RBC in urine of >2 RBC/hpf or RBC in urine of >3 RBC/u
New onset elevated urinary WBC	WBC in urine of >4 WBC/hpf OR WBC in urine of >6 WBC/uL
Complications and clinical complaints	Free text records of any significant clinical complaints during the admission of procedure, within 3 months post-donation and within 24 months post-donation
Readmission to Hospital	Any re-admission to hospital within 3 months and within 24 months post-donation
Death	Any deaths as recorded through clinical notes or registered in the National Death Registry

CKD-EPI: Chronic Kidney Disease Epidemiology; eGFR: Estimated glomerular filtration rate; KDIGO: Kidney Disease: Improving Global Outcomes; RBC: Red blood cell; WBC: White blood cell

*Kidney Disease: Improving Global Outcomes (KDIGO). KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl 2013;3:1-150.

Table 3. Demographic Characteristics of Donors at Baseline (n = 472)

	Number of Donors	%
Age		
Median age (IQR)	40 (31 – 50)	
Gender		
Male	255	54.0
Resident status		
Foreigners	322	68.2
Singapore citizens and PRs	150	31.7
Marital status		
Married	289	61.2
Single	143	30.3
Divorced/separated	31	6.6
Widowed	9	1.9
Education status		
No formal education	10	2.1
Primary/PSLE	54	11.4
Secondary/GCE N/O Level	183	38.8
Pre-university/ diploma	87	18.4
University and above	135	28.6
Unknown	3	0.6
Employment status		
Working full-time	358	75.8
Working part-time	8	1.7
Not working	10	2.1
Housewife	80	16.9
Retired	13	2.8
Student	3	0.6
Donor relationship status		
Biologically-related	247	52.3
Emotionally-related	221	46.8
Others	4	0.8

GCE: Singapore-Cambridge General Certificate of Education; IQR: Interquartile range; PR: Permanent resident; PSLE: Primary School Leaving Examination

which takes into consideration ethical issues. Data was anonymised by NRDO prior to analysis and the database was large enough to prevent inferential deduction of identities. Confidentiality was also maintained and the study did not influence clinical care nor provide direct benefits to donors.

Results

Demographics

There were 472 persons who underwent living kidney donation from January 2010 to December 2014. There were more foreign than local donors and slightly more males than females. The median age of donors was 40 years (IQR: 31 to 50 years) with an almost equal proportion of biologically- and non-biologically-related donors (Table 3).

Most nephrectomies were between foreign donors and foreign recipients (65.7%), and between local donors and local recipients (30.9%). Majority of foreign donors underwent nephrectomies at private hospitals (89.8%), whereas local donors had majority of their procedures performed at public hospitals (74.0%). Gender distribution was also different – there were more females among local donors and more males among foreign donors (59.3% and 39.8% females, respectively). Relationships between donors and recipients were similar in both groups.

Selection of Kidney Donors

Pre-donation, there were 471, 459 and 47 donors with serum creatinine, urinary creatinine clearance and radionuclide eGFR data, respectively. Although there were few donors with stronger relative contraindications for living kidney donation, there were 8.5% of donors who fell below the recommended kidney function for their age based on radionuclide eGFR and urinary creatinine clearance. This was 3.0% based on the CKD-EPI formula (Table 4). All of these donors were more than 60 years of age, which may indicate increased caution among older donors. There were 3 donors who had a BMI of more than 35.0 kg/m^2 and another 3 who had a 24-hour urine protein of >300 mg in 24 hours.

The number of patients with weaker relative contraindications was higher, though none exceeded 10%. Although 7.5% of donors had a BMI of more than 30.0 kg/m^2, only 0.6% had a BMI of over 35.0 kg/m^2. There were 8.3% and 3.0% of donors with high systolic and diastolic blood pressure reading record, respectively, but none had 3 or more medications for chronic hypertension. Furthermore, there were 4.2% and 2.0% of donors with red and white cells detected on pre-donation urine microscopy, though 78% of these were female donors.

Quality of life, captured through the Euro-QoL 5 Dimensions (EQ-5D) questionnaire, was found to be generally good. Of 382 donors with data captured, only 2 reported moderate anxiety and depression, 1 reported some problems with self-care, and 1 reported some problems with mobility.

Table 4. Donors with Relative Contraindications and Other Indices

Stronger Relative Contraindications	**Donors with Data***	**No. of Donors**	**%**
Inappropriate eGFR for age (radionuclide eGFR or urinary creatinine clearance)†	459	39	8.5
Inappropriate eGFR for age (CKD-EPI)	471	14	3.0
Body mass index ≥35.0 kg/m^2	466	3	0.6
24-hour urine protein >300 mg/24H	373	3	0.8
Diagnosed with diabetes mellitus	472	1	0.2
Nephrocalcinosis or bilateral stones	465	1	0.2
Age less than 18 years	472	0	0
On 3 or more anti-hypertensives	472	0	0
2-hour OGTT of ≥11.1 mmol/L	58	0	0
Weaker Relative Contraindications	**Donors with Data**	**No. of Donors**	**%**
Systolic blood pressure ≥140 mmHg	472	39	8.3
Diastolic blood pressure ≥90 mmHg‡	472	14	3.0
Body mass index ≥30.0 kg/m^2	466	35	7.5
Red blood cells on urine microscopy§	452	19	4.2
White blood cells on urine microscopy‖	452	9	2.0
2-hour OGTT of ≥7.8 mmol/L	58	0	0
Other Indices	**Donors with Data**	**No. of Donors**	**%**
Other non-specific findings on x-ray¶	465	82	17.6
Current smoker	472	85	18.0
Age more than 60 years	472	30	6.4
On anti-hyperlipidaemia medication	472	26	5.5
Any stones on x-ray	465	18	3.9
Age less than 21 years	472	0	0

eGFR: Estimated glomerular filtration rate; CKD-EPI: Chronic Kidney Disease Epidemiology; OGTT: Oral glucose tolerance test
*Differences in number of donors with data due to missing entries for some variables.
†Appropriate eGFR for age was based on the table for age-appropriate eGFR by the British Transplant Society.
‡Thirteen of these individuals also had high systolic blood pressure.
§Considered elevated if urine RBC >2 hpf or RBC >3 uL.
‖Considered elevated if Urine WBC >4 hpf or WBC >6 uL.
¶Any other x-ray findings apart from renal stones and cysts (e.g. double ureter).

Operative Techniques and Immediate Outcomes

There were more open surgeries in private hospitals (73.8% vs 9.0%), and more laparoscopic techniques in public hospitals. The median length of hospital stay was 5 days (IQR: 4,5). There were 10 (2.1%) and 6 (1.3%) donors respectively who had clinically moderate to severe events during their stay (chest infections, surgical site infections, acute urinary retention and pneumothorax) and there were no incidents of acute kidney failure or death. There were no differences in incidence of these events between public and private hospitals (P = 1.00) or operative techniques (P = 1.00).

Follow-up

There was high loss to follow-up for foreign donors (only 43.1% returned for any follow-up visit). In contrast, there were 96.4% of Singaporean citizens and permanent resident donors (locals) with at least 1 follow-up visit, and across the cohorts, an average of 72.8% (range: 65.5% to 87.9%) complied with annual follow-up.

Short-Term Kidney Function

Outcomes up to 24 months after transplant were thus only analysed for donors who were locals. Renal function decreased from pre-donation levels by a mean of 33.8% before recovering gradually to 70.4% of baseline renal function after 12 to 24 months post-nephrectomy (Fig. 1). Though 26.3% of the patients had an eGFR of <60 mL/min/1.73 m^2, there were no patients with eGFRs of <15 mL/min/1.73 m^2 or deaths.

Baseline renal function was higher in those less than 50 years of age (eGFR 108.4 mL/min/1.73 m^2 [SD: 12.7]

vs 95.5 mL/min/1.73 m^2 [SD 10.7]) and slightly higher among females (eGFR 105.9 mL/min/1.73 m^2 [SD 13.2] vs 99.7 mL/min/1.73 m^2 [SD 9.2]). Using the most recent post-nephrectomy eGFR result of <60 mL/min/1.73 m^2 as an outcome, multivariate analysis found a higher risk associated with lower baseline eGFR (HR: 1.05; 95% CI, 1.02 to 1.09) and to a lesser extent, older age (HR: 1.04; 95% CI, 1.00 to 1.08). There were no differences in gender, surgical approach and BMI (Table 5).

A baseline eGFR to predict postoperative eGFR of <60 mL/min/1.73 m^2 or ≥60 mL/min/1.73 m^2 yielded an area under the ROC curve (AUC) of 0.85 (95% CI, 0.78 to 0.93). An optimal sensitivity of 85.7% and specificity of 71.4% was achieved with a baseline eGFR cutoff value of 97 mL/min/1.73 m^2. Using this cutoff, a Kaplan-Meier curve was subsequently constructed. The probability of having a post-donation eGFR of <60 mL/min/1.73 m^2 was lower for patients with baseline eGFR ≥96.8 mL/min/1.73 m^2 (HR 0.18; 95% CI, 0.09 to 0.37; P <0.001) and the median time to reach post-donation eGFR of <60 mL/min/1.73 m^2 was shorter for baseline eGFRs lower than 96.8 mL/min/1.73 m^2 (424 days as compared to 693 days) (Fig. 2).

Other Outcome Measures

There were no significant differences in mean systolic (P = 0.843) and diastolic blood pressure (P = 0.200) in donors post-nephrectomy and there were no donors with newly diagnosed diabetes mellitus. Next, there were no donors with urinary protein above the upper limit of 300 mg/24 hours although a small number had new instances of elevated red (n = 8) and white blood cells (n = 9) in their urine. There were 10 donors (7.5%) who reported clinical complaints within 3 months of discharge, and of these, 4 required hospitalisation for reasons related to the procedure (e.g. surgical site infection) but not for poor renal function. Over a 24-month period, the proportion of patients hospitalised since their previous visit was 1.2%, 7.4% and 5.7% for within 6 months, 6 to 12 months and 12 to 24 months after donation, respectively. Of these, only 2 donors were admitted for renal or urological conditions.

Discussion

Donor Characteristics

This is the first study detailing baseline characteristics of living kidney donors in Singapore. The surprisingly high numbers of donations between foreign donors and foreign recipients suggest a strong medical tourism sector in keeping with overall trends seen during that period, and the difference in distribution between local and foreign donors in terms of hospital type may be due to subsidies available for locals at public hospitals.

Gender disparity among living kidney transplant has been a topic of much debate over the past few years. Among most cohorts, both in the West as well as a number of Asian countries such as China and India, it seemed that there was a female predominance.[12-14] The proportion of local female donors in Singapore is in keeping with these trends, whereas that of foreign donors seemed more akin to a handful of transplant centres from purportedly conservative societies such as Saudi Arabia, Iran and Korea.[15-17] Our study was unable to determine the cause for this difference, and it would necessitate further studies.

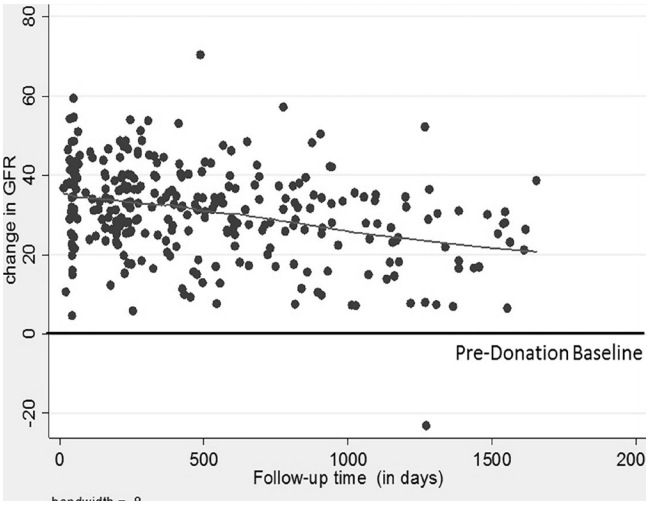

Fig. 1. Lowess plot of kidney function over time (locals).

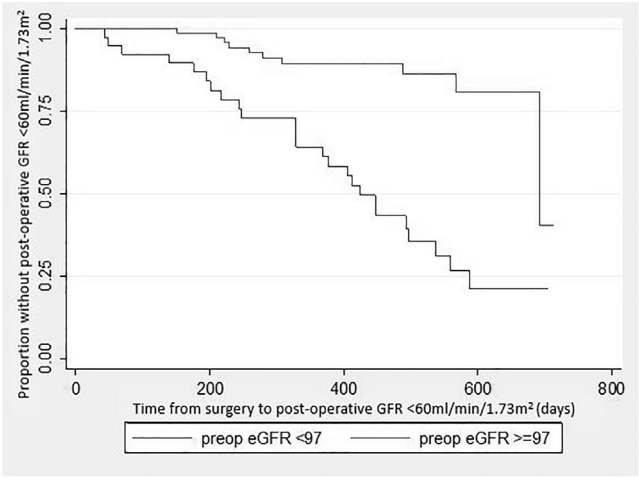

Fig. 2. Kaplan Meier curve for post-donation renal function of <60 mL/min/1.73m^2.

Table 5. Multivariate Analysis for Post-Donation Renal Function of <60 mL/min/1.73 m^2

	Post-Donation eGFR <60 mL/min/1.73 m^2 (n = 35)		Post-Donation eGFR ≥60 mL/min/1.73 m^2 (n = 98)		Crude Hazards Ratio			Adjusted Hazards Ratio		
	n	%	n	%	HR	95% CI	*P* Value	HR	95% CI	*P* Value
Gender										
Male	20	57.1	33	33.7	1.00	-	0.068	1.00	-	0.388
Female	15	42.9	65	66.3	0.54	0.27 – 1.05	0.068	0.69	0.30 – 1.60	0.388
Surgical approach										
Laparoscopy	31	88.6	81	82.7	1.00	-	0.198	1.00	-	0.391
Open	4	11.4	17	17.4	0.50	0.18 – 1.43	0.198	0.61	0.20 – 1.89	0.391
	Mean	**SD**	**Mean**	**SD**	**HR**	**95% CI**	***P* Value**	**HR**	**95% CI**	***P* Value**
Baseline eGFR	90.8	12.1	107.6	11.5	1.06	1.04 – 1.10	<0.001	1.05	1.02 – 1.08	<0.001
Age at surgery	52.3	10.0	44.6	11.2	1.06	1.03 – 1.10	0.001	1.04	1.00 – 1.08	0.047
BMI	24.2	3.1	23.8	3.8	1.03	0.94 – 1.13	0.480	1.02	0.91 – 1.14	0.751

BMI: Body mass index; eGFR: Estimated glomerular filtration rate; HR: Hazards ratio

Selection of Donors

Donor selection in Singapore is aligned with international guidelines, with stringent adherence as compared to transplant centres overseas. In the United Kingdom, there were 70% and 86% of transplant centres that did not have lower and upper age limits, respectively; some (9%) did not have an upper limit for BMI, and only 30% collected 24-hour urine protein.[18] Similar variations were seen in transplant centres in the US.[19] Furthermore, in the US, 12.8% of donors had a BMI of ± 30 kg/m^2; there were 10.3% and 4.2% who were hypertensive and had a renal function of <60 mL/min/1.73 m^2, respectively, and 2.7% with more than one of these risk factors.[20] For direct comparison, only 0.4% of cases in our study fell below the more liberal cutoff of <60 mL/min/1.73 m^2. Selection of living kidney donors in Singapore is thus comparable, if not safer, than other countries.

Some donors would have required further workup. High blood pressure readings may have been due to natural fluctuations and the presence of red and white blood cells in urine may be due to physiological reasons (especially since majority with this abnormality were women). Unfortunately, details on any workup were not captured in the registry.

Clinical Outcomes

This is the first study detailing immediate and short-term outcomes of living kidney donors at a national level in Singapore. Immediate outcomes showed that surgical procedures were safe. A small number of donors had moderate to severe events during their admission post-surgery and the duration of their stay was fairly short and uniform.

Tan L et al conducted a study among 86 donors at a single public hospital in Singapore who had undergone nephrectomy from 1987 to 2008.[21] A significant proportion (55%) of donors had donated before the publication of the Amsterdam guidelines. Preoperative GFR was higher in our study (103.4 mL/min/1.73 m^2 vs 88.7 mL/min/1.73 m^2) and although this may have been due to differences in measurement techniques (Modification of Diet in Renal Disease [MDRD] formula was used), it may also suggest stricter selection of donors over time. Indeed, a more recent study by Han X et al among 82 prospectively recruited kidney donors noted a preoperative eGFR of 95.5 mL/min/1.73 m^2, which was closer to our findings.[22]

Tan L et al also found that 24.4% of donors had Stage 3 or worse chronic kidney disease (CKD) after an average of 6.4 years. Another study by Chen KW et al also found a mean postoperative eGFR of 68.9 mL/min/1.73 m^2 after an average of 52.9 months, with 24.1% of donors in Stage 3 CKD.[23] Both studies thus had similar results to our finding that 26.3% of donors had a last eGFR of less than 60 mL/min/1.73 m^2 within 24 months.

Tan L et al also found that the baseline eGFR rate of less than 82 mL/min/1.73 m^2 was an independent risk factor for post-donation CKD.[21] This cutoff was higher in a separate study by Tsai SF et al among 105 donors in Taiwan (90.2 mL/min/1.73 m^2), than the cut-off of 96.8 mL/min/1.73 m^2 in our study.[24] These may again be due to differences in measurement techniques (MDRD formula vs CKD-EPI formula used by our study). Another possible reason was that the time to follow-up in our study was still short (2 years, as compared to 6.4 years and 5.4 years in studies by Tan L

et al and Tsai SF et al respectively)[21,24] and some donors' renal function may have improved further. Another study by Tan RY et al similarly found a 6% risk reduction for each unit increase in pre-nephrectomy eGFR, pointing towards high pre-nephrectomy eGFR conferring protection against low post-donation eGFR.[25]

Baseline eGFR thus continues to play an important role in the safe selection of living kidney donors in relation to donors' eventual risk of developing CKD. International guidelines continue to be useful in laying out minimum acceptable standards to which transplant centres should adhere to. However, many use a single or range of stratified cutoffs and it is important to keep in mind that such risks to otherwise healthy donors actually exist on a continuum.

The decrease in renal function of 33.8% from baseline is in keeping with local studies and other international cohorts. Of note, this is less than the 50% that would have been expected after removing 1 of 2 kidneys. At a local institution, Han X et al noted a fall in postoperative eGFR to 71.0 mL/min/1.73 m^2 (a decrease of 25.7%) over a median follow-up of 7.8 years. Furthermore, 43.1% of donors regained 75% of more of preoperative eGFR after 5 years.[22] Kasiske BL et al showed that donors had a drop in renal function post-nephrectomy of 33.6%, with a gradual rise over the subsequent 3 years.[26] We found a similar trend, with gradual recovery to 29.6% by 24 months.

Guerra J et al showed that donor kidney function was 32% lower post-nephrectomy as compared to baseline, with 21% having an eGFR of less than 60 ml/min/1.73m^2, influenced by age and baseline eGFR.[27] Among Japanese donors, eGFR dropped by an average of 37% and was negatively associated with older age and lower preoperative eGFR.[28] Our study likewise showed these associations as well.

Although earlier studies had shown equal longer-term mortality among kidney donors as compared to the general population,[29] more recent studies showed that mortality was still higher than matched healthy non-donors. These were accompanied by increases in blood pressure, proteinuria, and ESRD.[30-35] None of these changes were observed in our cohort, although a longer period of follow-up and future studies would be required to draw more definitive conclusions.

Limitations and Strengths

The retrospective nature restricts the amount of information available for analysis as data that was not collected or poorly recorded could not be analysed. In addition, recorded data were assumed to be accurately captured. For example, we were unable to ensure that adequate urine was collected by clinicians when determining urine creatinine clearance as this depended on individual practice protocols. During follow-up visits, certain portions deemed less important were sometimes not assessed by clinicians. Medical visits in other settings would also not be captured. Furthermore, there was also a high rate of loss to follow-up for foreign donors, thus results may not be generalisable to this group. Intervals of follow-up visits were dependent on clinician preference; as such, not all donors had results within each time bracket, thereby reducing the amount of data available for analysis.

The presence of legislation ensured that data capture of all living kidney donors in Singapore was generally expected to be good. There were also relatively good follow-up rates among local donors. The use of trained coordinators for data collection reduces interpersonal variability and a structured form to record findings would lower the need for subjective interpretation. Majority of outcome indicators were also derived through investigation results (e.g. serum creatinine), hospitalisation events and medication data, thus providing more objective data.

Conclusion

The demand for renal donations in Singapore is expected to continue, driven by the increase in persons with end-stage renal failure. The enactment and subsequent revisions of HOTA have sought to improve organ donation numbers; however, these have not resulted in an increase in kidney transplants that commensurates with demand. Deceased donor transplants are also not without downsides, with studies showing that graft survival was lower as compared to living transplants.[36]

Since fear of surgical complications and postoperative outcomes were found to be the main barriers to living kidney donations in Singapore, presenting an accurate reflection of these risks is important to help allay some of these concerns.[4] Findings from our study show that after 24 months of post-donation monitoring, although there is some expected decrease in renal function, transplant operating procedures in Singapore remain safe. As long as clinical practice adheres rigorously to internationally accepted guidelines, kidney donation in Singapore will be as effective and free of adverse outcomes as other high-performing transplantation programmes.

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