Characteristics and clinical outcomes of living renal donors in Hong Kong

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A B S T R A C T

Introduction: In Asia, few reports are available on the outcomes for living renal donors. We report the short- and long-term clinical outcomes of individuals following living donor nephrectomy in Hong Kong.

Methods: We retrospectively reviewed the characteristics and clinical outcomes of all living renal donors who underwent surgery from January 1990 to December 2015 at a teaching hospital in Hong Kong. Information was obtained from hospital records and territory-wide electronic patient records.

Results: During the study period, 83 individuals underwent donor nephrectomy. The mean (± standard deviation) follow-up time was 12.0 ± 8.3 years, and the mean age at nephrectomy was 37.3 ± 10.0 years. A total of 44 (53.0%), four (4.8%), and 35 (42.2%) donors underwent living donor nephrectomy via an open, hand-port assisted laparoscopic, and laparoscopic approach, respectively. The overall incidence of complications was 36.6%, with most being grade 1 or 2. There were three (9.4%) grade 3a complications; all were related to open donor nephrectomy. The mean glomerular filtration rate was 96.0 ± 17.5 mL/min/1.73 m^2 at baseline and significantly lower at 66.8 ± 13.5 mL/min/1.73 m^2 at first annual follow-up (P<0.01). The latest mean glomerular filtration rate was 75.6% ± 15.1% of baseline. No donor died or developed renal failure.

Of the donors, 14 (18.2%) developed hypertension, two (2.6%) had diabetes mellitus, and three (4.0%) had experienced proteinuria.

Conclusion: The overall perioperative outcomes are good, with very few serious complications. The introduction of a laparoscopic approach has decreased perioperative blood loss and also shortened hospital stay. Long-term kidney function is satisfactory and no patients developed end-stage renal disease. The incidences of new-onset medical diseases and pregnancy-related complications were also low.

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New knowledge added by this study
- The overall perioperative outcomes are good, with very few serious complications, among living renal donors. The introduction of a laparoscopic approach has decreased perioperative blood loss and also shortened hospital stay.
- Long-term kidney function was satisfactory and no patients developed end-stage renal disease (ESRD).
- The incidences of new-onset medical disease and pregnancy-related complications were also low.

Implications for clinical practice or policy
- Medical practitioners should encourage relatives of patients with ESRD to consider the possibility of kidney donation.

Introduction

Chronic kidney disease (CKD) is the progressive loss of kidney function over a period of time. End-stage renal disease (ESRD) is the final stage of CKD. Patients with ESRD require renal replacement therapy that includes haemodialysis, peritoneal dialysis, and renal transplantation.

Currently, there are approximately 7000 patients on various forms of renal replacement therapy being cared for in the public sector in Hong Kong. As of 31 December 2016, 2047 patients were on the renal transplant waiting list. Nonetheless, between 2007 and 2016, only 58 to 87 cadaveric renal transplants were performed in Hong Kong each year.[1] With the long waiting list and low number of cadaveric kidneys available, living donor renal transplant is the only possible alternative. It offers advantages over other renal replacement

香港活體捐腎者的特徵及臨床結果

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引言：亞洲只有少數關於活體捐腎者臨床結果的報導。本文報告香港捐腎者的長短期臨床結果。

方法：回顧分析1990年1月至2015年12月期間，在香港一所教學醫院內接受手術的所有捐腎者的特點和臨床結果。資料來自醫院紀錄及全港電子醫療紀錄。

結果：研究期間共83名捐腎者接受腎切除術。平均（±標準差）隨訪時間為12.0±8.3年，捐腎者接受腎切除術時的平均年齡為37.3±10.0歲。他們進行腎切除術的方式為開放式44例（53.0%），手助式腹腔鏡4例（4.8%），以及腹腔鏡手術35例（42.2%）。總併發症發生率為36.6%，大部分屬1級或2級；有3名（9.4%）捐腎者的併發症屬3a級，均與開放式手術有關。平均腎小球濾過率方面，基線為96.0±17.5 mL/min/1.73 m²，首次隨訪時為66.8±13.5 mL/min/1.73 m²的顯著較低水平（P<0.01）。最後一次的平均腎小球濾過率為基線的75.6%±15.1%。沒有捐腎者死亡或出現腎衰竭。捐腎者中有14人（18.2%）患有高血壓，2人（2.6%）有糖尿病，3人（4.0%）有蛋白尿。

結論：捐腎者的圍手術期結果良好，只有少數出現嚴重併發症。引入腹腔鏡手術減少了圍手術期失血，並縮短了住院時間。捐腎者的長期腎功能令人滿意，沒有患者出現末期腎病。新出現的內科疾病和妊娠相關併發症的發生率也偏低。

therapies, as it provides better long-term results, shortens the waiting time for an organ, lowers the risk of complications or rejection, and provides better quality of life after recovery. Despite these advantages, only seven to 15 living donor transplants were performed each year between 2007 and 2015 at the hospitals of the Hong Kong Hospital Authority.[1]

One of the major fears of an individual who is considering living organ donation concerns possible clinical outcomes. Although studies show that living donors have a similar to or better life expectancy than the general population, they are nevertheless at increased risk of developing ESRD, hypertension, gestational hypertension, and pre-eclampsia.[2-4]

In Hong Kong, few reports on the perioperative, short-term, and long-term clinical outcomes are available, especially those related to the minimally invasive surgical approach now employed for donor nephrectomy. This study reports our observation of characteristics of donors, and the short- and long-term clinical outcomes following living donor nephrectomy in Hong Kong.

Methods

Study design

We retrospectively reviewed the characteristics and short- and long-term clinical outcomes of all patients who underwent living donor nephrectomy at the Prince of Wales Hospital in Hong Kong between January 1990 and December 2015. Information was obtained from the Clinical Management System that includes the majority of electronic patient records—including consultation histories, operation records, radiology results, laboratory results, and medication records—collected and filed under the Hospital Authority since 2000. Medical records before 2000 and pregnancy-related information were reviewed manually by formally trained medical students and cross-checked by a urologist, and retrieved from the medical records of the involved patients.

The study was conducted in accordance with the principles outlined in the Declaration of Helsinki, and approved by the Joint Chinese University of Hong Kong–New Territories East Cluster Clinical Research Ethics Committee, with the requirement of patient informed consent waived because of its retrospective nature.

Study measures

Baseline demographics including sex, age at donation, ethnicity, relationship with recipient, diabetes mellitus status, hypertension status, body mass index, and serum creatinine level were obtained. Glomerular filtration rate (GFR) was derived from the serum creatinine level using a modified equation from the Modification of Diet in Renal Disease (MDRD) study.[5] Operation details, including surgical approach, laterality of donated kidney, operating time, warm ischaemia time, blood loss, and need for transfusion were retrieved.

Short-term complications within 30 days of surgery were classified according to the Clavien-Dindo classification of surgical complications.[6] Long-term outcomes were also assessed, with particular reference to development of hypertension, diabetes mellitus, renal stones, proteinuria, and renal failure. Serial changes in GFR were also assessed.

For female donors, pregnancy-related variables were recorded and included any pregnancy after surgery, records of pregnancy-related hydronephrosis, pregnancy-related urinary tract infection, pre-eclampsia, gestational diabetes mellitus, gestational hypertension, and any fetal loss.

Statistical analyses

All statistical analyses were performed using the SPSS (Windows version 23.0; IBM Corp, Armonk [NY], United States). Categorical variables were presented in counts and percentages while continuous variables were presented as mean ± standard deviation. Outcomes following open and laparoscopic techniques were compared by Chi squared test or Fisher's exact test for categorical variables, and independent t test or Mann-Whitney

U test for continuous variables. Paired *t* test or Wilcoxon rank sum test, whichever was appropriate, was used to evaluate the pre- and post-difference in GFR. A P value of <0.05 was considered statistically significant. Missing data were excluded from analysis.

Results

Donor characteristics

Between 1 January 1990 and 31 December 2015, a total of 83 donors underwent unilateral nephrectomy at the Prince of Wales Hospital. In one donor, records could not be traced, with only information about the sex, age at nephrectomy, and type of surgical technique.

Of the 83 donors, 56 (67.5%) were female. The mean age at nephrectomy was 37.3 ± 10.0 years. The majority were Chinese (97.6%) and a first-degree relative of the recipient (79.3%). None had hypertension or diabetes mellitus. The mean preoperative GFR was 96.0 ± 17.5 mL/min/1.73 m². Nine (11.0%) donors had thalassaemia trait, four (4.9%) had hepatitis B, and two (2.4%) had asthma (Table 1).

TABLE 1. Baseline characteristics of kidney donors

Baseline characteristic	No. (%) of donors or mean ± SD
Sex, n=83	
Male	27 (32.5)
Female	56 (67.5)
Age at nephrectomy (years), n=83	37.3 ± 10.0
Ethnicity, n=82	
Chinese	80 (97.6)
Indonesian	1 (1.2)
Filipino	1 (1.2)
Relationship with recipient, n=82	
First-degree relative	65 (79.3)
Sibling	49 (59.8)
Parent to child	8 (9.8)
Child to parent	8 (9.8)
Spouse	15 (18.3)
Second-/third-degree relative	2 (2.4)
Baseline BMI (kg/m²), n=37	23.1 ± 2.5
Baseline serum Cr (µmol/L), n=76	74.2 ± 15.2
Baseline GFR (mL/min/1.73 m²), n=76	96.0 ± 17.5
Other health condition, n=82	
With thalassaemia trait	9 (11.0)
Hepatitis B carrier	4 (4.9)
Asthma	2 (2.4)

Abbreviations: BMI = body mass index; Cr = creatinine; GFR = glomerular filtration rate; SD = standard deviation

Operation details and short-term outcomes

Around half (n=44, 53.0%) of the donors underwent open living donor nephrectomy, as this was the only technique used at our centre until 2002. After 2002, a hand-port assisted laparoscopic approach (n=4, 4.8%) and later a laparoscopic approach (n=35, 42.2%) were adopted. In most instances, the left kidney was donated (n=77, 93.9%) [Table 2].

Comparing laparoscopic or hand-port assisted laparoscopic living donor nephrectomy (LDN) with open donor nephrectomy (ODN), LDN was associated significantly with longer warm ischaemia time (309.0 ± 113.0 s vs 62.0 ± 17.9 s; P<0.01), less blood loss (55.3 ± 33.7 mL vs 532.2 ± 270.0 mL; P<0.01), and shorter hospital stay (5.7 ± 2.0 days vs 8.1 ± 1.9 days; P<0.01). In addition, LDN was associated significantly with more short-term complications (53.8% vs 20.9%; P<0.01). The most commonly experienced complication was epigastric pain/nausea and vomiting (n=18, 56.3%), followed by fever requiring medication (n=4, 12.5%). Most complications were grade 1 on the Clavien-Dindo classification scale (n=16, 50.0%), only three (9.4%) were grade 3a and all were related to ODN. The grade 3a complications were wound dehiscence that required a second operation for re-suturing, persistent pancreatic fluid discharge that required insertion of a pancreatic stent, and pneumothorax with chest drain inserted.

Long-term outcomes

The mean follow-up time was 12.0 ± 8.3 years. The mean GFR was 96.0 ± 17.5 mL/min/1.73 m² at baseline and it dropped significantly to 66.8 ± 13.5 mL/min/1.73 m² at 1-year follow-up (P<0.01). The GFR then gradually improved until 8 years after surgery and became stable (Fig). Of 73 living donors with at least one follow-up (mean follow-up time, 12.0 ± 8.2 years) and baseline serum creatinine level available, the latest GFR was 75.6% ± 15.1% of baseline GFR with the mean latest GFR being 71.3 ± 14.2 mL/min/1.73 m². The mean GFR was 70.4% ± 12.3% of baseline level 1 year after surgery. Comparison of latest GFR with that 1 year after surgery revealed that it was stable (± 10% change) in 23 (39.0%) of 59 patients and higher (>10% increment) in 29 (49.2%) patients. None of the donors had died or developed ESRD. Fourteen (18.2%) donors developed hypertension, two (2.6%) had diabetes mellitus, and three (4.0%) had experienced proteinuria (Table 3).

Pregnancy-related complications

Of 56 female donors, 11 (19.6%) became pregnant after kidney donation: 17 pregnancies were reported. None of the pregnant donors experienced gestational hydronephrosis or gestational hypertension. Three donors each had gestational diabetes mellitus, pre-

TABLE 2. Comparison of operation details and short-term outcomes by operation techniques

	Total		Open technique		Laparoscopic or hand-port assisted laparoscopic		P value
	No. of donors	Data*	No. of donors	Data*	No. of donors	Data*	
Left or right kidney	82		43		39		0.362
Left		77 (93.9)		39 (90.7)		38 (97.4)	
Right		5 (6.1)		4 (9.3)		1 (2.6)	
Operating time (hours)	40	3.5 (0.9)	3	3.0 (0.7)	37	3.6 (0.9)	0.354
Warm ischaemia time (s)	39	277.4 ± 134.6	5	62.0 ± 17.9	34	309.0 ± 113.0	<0.01
Blood loss (mL)	29	137.5 ± 212.1	5	532.2 ± 270.0	24	55.3 ± 33.7	<0.01
In-patient hospital stay (days)	79	6.9 ± 2.3	40	8.1 ± 1.9	39	5.7 ± 2.0	<0.01
Complication	82		43		39		<0.01
Yes		30 (36.6)		9 (20.9)		21 (53.8)	
No		52 (63.4)		34 (79.1)		18 (46.2)	
Complication by episode: type	32		10		22		0.217
Epigastric pain/nausea and vomiting		18 (56.3)		4 (40.0)		14 (63.6)	
Fever (treated with medication)		4 (12.5)		0		4 (18.2)	
Leak		2 (6.3)		1 (10.0)		1 (4.5)	
Bleeding		2 (6.3)		1 (10.0)		1 (4.5)	
Infection		2 (6.3)		1 (10.0)		1 (4.5)	
Other		4 (12.5)		3 (30.0)		1 (4.5)	
Complication by episode†	32		10		22		0.021
Grade 1		16 (50.0)		3 (30.0)		13 (59.1)	
Grade 2		13 (40.6)		4 (40.0)		9 (40.9)	
Grade 3a		3 (9.4)		3 (30.0)		0	
Total No. of complications	82	0.4 ± 0.5	43	0.2 ± 0.5	39	0.6 ± 0.6	0.005
Latest GFR (mL/min/1.73 m²)	77	71.3 ± 14.2	40	74.7 ± 14.5	37	65.6 ± 12.9	0.025

Abbreviation: GFR = glomerular filtration rate
* Data are shown as No. (%) or mean ± standard deviation
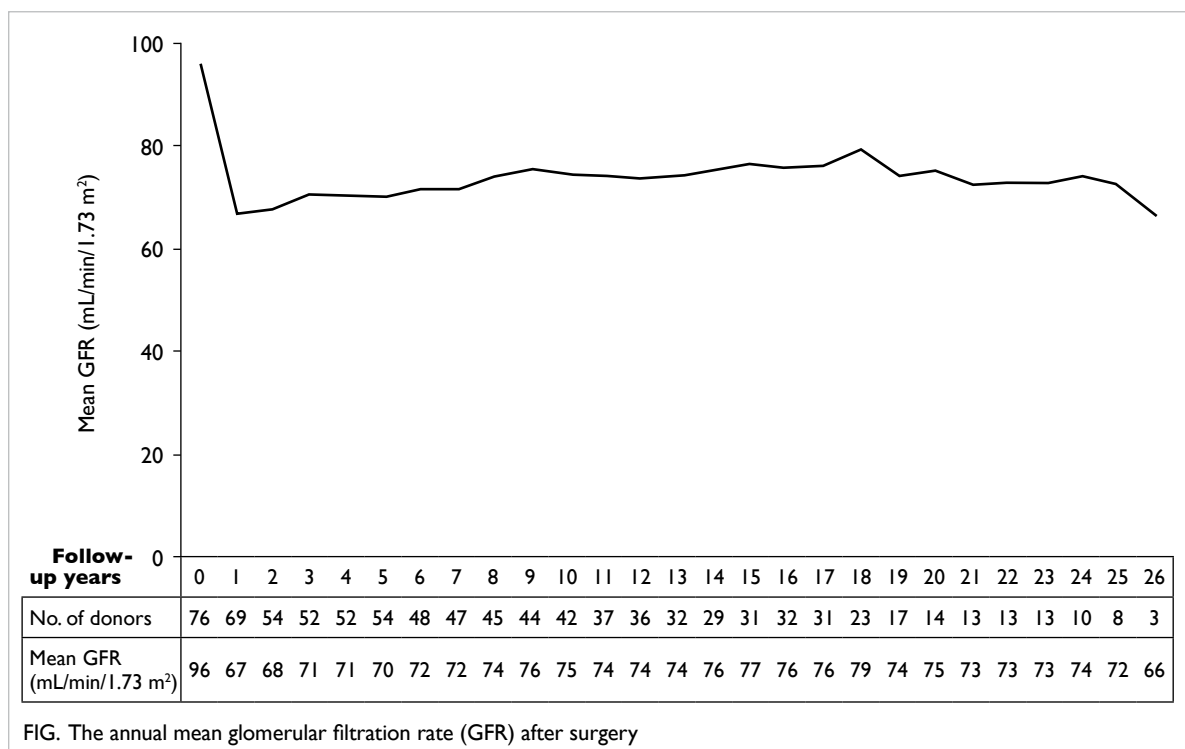† According to Clavien-Dindo classification scale

eclampsia, and post-delivery urinary tract infection. Two donors had experienced fetal loss, one in the first trimester and another one at an unknown gestational age (Table 4).

Discussion

Postoperative morbidity and mortality are the prime concerns when making a decision about kidney donation. Our results confirm that living donor nephrectomy is a relatively safe procedure, with a low incidence of major complications and mortality. In addition, the incidence of developing any other major disease was not particularly high in our series. This form of renal replacement therapy should be further promoted in Hong Kong to benefit more people with ESRD.

Results from previous studies have shown that living renal donors have a similar to or better life expectancy than the general population.[7-10] Mjøen et al,[11] however, reported that compared with healthy matched individuals, living renal donors had an increased risk of death. In Hong Kong, Chu et al[12] reported one death related to multiple myeloma among 95 living renal donors with active follow-up and a mean follow-up period of 13.4 years. There were no deaths recorded in our study with a mean follow-up of 12 years.

Long-term renal function is another major concern of renal donors. Our results revealed that 1 year after living donor nephrectomy, the mean GFR of the kidney donors dropped significantly from 96.0 ± 17.5 mL/min/1.73 m² at baseline to 66.8 ± 13.5 mL/min/1.73 m². Nonetheless, it then

Follow-up years	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
No. of donors	76	69	54	52	52	54	48	47	45	44	42	37	36	32	29	31	32	31	23	17	14	13	13	13	10	8	3
Mean GFR (mL/min/1.73 m²)	96	67	68	71	71	70	72	72	74	76	75	74	74	74	76	77	76	76	79	74	75	73	73	73	74	72	66

FIG. The annual mean glomerular filtration rate (GFR) after surgery

gradually improved. This is probably partly related to the adaptation of the remaining kidney with hyper-filtration. From our series, the mean GFR was 70.4% ± 12.3% of baseline level 1 year after surgery but improved to 75.6% ± 15.1% of baseline level at the last follow-up. In the majority (88.2%) of donors, the last available GFR was static or higher than that 1 year after donation. This is comparable with the report of Rook et al[13] in which GFR usually reached 64% ± 7% of the pre-donation level 1 year after donation.

Despite these changes in GFR, ESRD in renal donors is very rare, with an incidence of less than 0.5% in 15 years after donation.[11,14,15] Ibrahim et al[8] reported that survival and risk of ESRD in kidney donors appeared to be similar to those in the general population. Our study and that of Chu et al[12] observed no ESRD in local kidney donors.

The effect of kidney donation on the development of hypertension is controversial. Although reports suggest that the incidence of hypertension among kidney donors increases,[16-19] others have not confirmed this observation.[20-24] In Hong Kong, the prevalence of hypertension in the general population was 12.6% in 2014,[25] which is lower than our reported figure of 18.2%. With the progression of time after surgery, however, the prevalence of hypertension among living donors is expected to increase as age is a known influence in hypertension. Without a comparable control group, we cannot conclude if there is any actual discrepancy in the prevalence of hypertension among living

TABLE 3. Long-term outcomes for kidney donors

	No. of donors with data available	Data*
Follow-up (years)	79	12.0 ± 8.3
Latest stones	81	
Yes		0
No		17 (21.0)
Investigation not done after surgery		64 (79.0)
Latest hypertension	77	
Yes		14 (18.2)
No		63 (81.8)
Latest diabetes mellitus	76	
Yes		2 (2.6)
No		74 (97.4)
Renal failure	79	
Yes		0
No		79 (100)
Latest proteinuria	75	
Yes		3 (4.0)
No		72 (96.0)

* Data are shown as No. (%) or mean ± standard deviation

donors compared with the general population.

Young female potential donors may have concerns about the impact of kidney donation on

TABLE 4. Pregnancy-related complications

	No. or No. (%) of donors
Pregnancy after kidney donation	56
Yes	11 (19.6)
No	45 (80.4)
Hydronephrosis in pregnancy	9
Yes	0
No	9 (100)
Pregnancy-related urinary tract infection	9
Yes	1 (11.1)
No	8 (88.9)
Pre-eclampsia	9
Yes	1 (11.1)
No	8 (88.9)
Gestational diabetes mellitus	10
Yes	1 (10.0)
No	9 (90.0)
Gestational hypertension	9
Yes	0
No	9 (100)
Fetal loss	9
Yes	2 (22.2)
No	7 (77.8)

any future pregnancy. Garg et al[4] reported that gestational hypertension or pre-eclampsia was more common among living donors than non-donors. Although our study showed an alarmingly high percentage (11%) of pre-eclampsia and absence of gestational hypertension, the small sample size (11 donors reported one or more pregnancies) undermines the ability to infer the actual percentage.

Perioperative complications may also deter potential living donors. Based on the US data, Lentine et al[26] reported that 16.8% of donors experience a perioperative complication; most commonly gastrointestinal (4.4%). Our study showed a higher complication rate of 36.6%, with epigastric pain or nausea and vomiting being the major complication (56.3%). We further examined the techniques used and established that the complication rates of 20.9% or 53.8% respectively in donors who underwent ODN or LDN were significantly different (P<0.01). Despite the above mean complication rates, all complications of LDN were mild and of grade 1 or 2 according to the Clavien-Dindo classification, while three patients who underwent ODN had grade 3a

complications. This is contrary to the majority of previous findings that suggest a lower perioperative complication rate for LDN and increased risk of more serious complications than during an ODN,[27] although other indicators such as longer warm ischaemia time, less blood loss, and shorter hospital stays were still in line with previous findings. Further analysis of the differences between our local data and those of previous studies is warranted.

This study has several limitations. First, this was a retrospective study and the total number of living donors was restricted. Second, data quality could not be controlled and some data were incomplete, in particular for the obstetric records at other hospitals. Some data were also lost either because records were too old and pre-dated the electronic system or donors were no longer followed up at our centre. The oldest record included in the study was from 1990. At that time, record keeping was not always accurate, resulting in some baseline records from the early 1990s being missing. For example, the baseline GFR level of seven (8.4%) patients was not found, and might have affected the overall data quality as well as the analysis and conclusion. Third, although the urologist endeavoured to ensure accurate data entry, initial interpretation of the raw records was by medical students so certain inaccuracies might have occurred. Lastly, it is known that GFR might be underestimated when derived from the MDRD equation.

Conclusion

Living donor kidney transplantation is an important approach to improve the quality of life of patients with ESRD. Good short- and long-term outcome for kidney donors is important for promoting kidney donation. Our results suggest that the overall perioperative outcomes are good, with only very few serious (grade III) complications after surgery, occurring following an open approach. Long-term kidney function of donors was satisfactory and no patients developed ESRD. Although we had no control arm in our study, the overall incidences of new-onset medical diseases and pregnancy-related complications were low. The introduction of a laparoscopic approach for kidney harvesting has helped to decrease blood loss during surgery and also shorten hospital stay. Based on this encouraging result, relatives of patients with ESRD should be encouraged to consider the possibility of kidney donation.

Acknowledgements

Declaration

All authors have disclosed no conflicts of interest.

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