

Compensation Capacity of the Living-Related Donor's Remnant Kidney and Recipient's Transplanted Kidney

Xin Huang^{1†}, Binbin Ma^{2†}, Wenhao Lin¹, Kun Shao¹, Huimin An¹, Jun Dai¹, Fukang Sun¹, Danfeng Xu¹, Peijun Zhou^{1,*}, and Juping Zhao^{1,*}

¹Department of Urology, School of Medicine, Ruijin Hospital, Shanghai Jiaotong University, Shanghai, China

²Department of Urology, School of Medicine, Ruijin Hospital Luwan Branch, Shanghai Jiaotong University, Shanghai, China

[†]These authors contributed fully and equally to this work

***Corresponding author:** Juping Zhao, Department of Urology, School of Medicine, Ruijin Hospital, Shanghai Jiaotong University, #197 Ruijin Er Road, Shanghai, 200025, China, Tel: 086-02164370045-666061; E-mail: zjp11317@rjh.com.cn

***Co-correspondence:** Peijun Zhou, Department of Urology, School of Medicine, Ruijin Hospital, Shanghai Jiaotong University, #197 Ruijin Er Road, Shanghai, 200025, China, Tel: 086-02164370045-666061; E-mail: zpj11282@rjh.com.cn

Received: 21 Aug, 2021 | **Accepted:** 21 Sep, 2021 | **Published:** 26 Sep, 2021

Citation: Huang X, Ma B, Lin W, Shao K, An H, et al. (2021) Compensation Capacity of the Living-Related Donor's Remnant Kidney and Recipient's Transplanted Kidney. *Int J Nephrol Kidney Fail* 7(4): dx.doi.org/10.16966/2380-5498.218

Copyright: © 2021 Huang X, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Introduction: We try to explore the compensatory capacity of living-related donor's remnant kidney and recipient's transplanted kidney in terms of the glomerular filtration rate (GFR).

Patients and Methods: Clinical data of 94 patients who received living-related kidney transplantation in our hospital between June 2007 and December 2017 were reviewed retrospectively. GFR_{SCr} was estimated by using the Cockcroft-Gault equation. The GFR_{SCr} compensatory capacity of donor's remnant and donated kidneys in their new milieu after transplantation was compared. The differential value (D-value) of split renal function was defined as postoperative ipsilateral GFR_{SCr}-preoperative split GFR_{SCr}. The compensatory percentage (C-percentage) of split renal function was defined as (postoperative ipsilateral GFR_{SCr}-preoperative split GFR_{SCr})/preoperative split GFR_{SCr}.

Results: The median D-value of the donor's remnant kidney increased by 20.8 ml/min/1.73m² [IQR=8.9-29.6 ml/min/1.73m²] with a C-percentage of 46.6% (IQR=17.0%-73.0%). The median D-value of the donated kidney increased by 30.6 ml/min/1.73m² [IQR=19.8-42.3 ml/min/1.73m²] with a C-percentage of 67.8% (IQR=39.6%-94.7%). Multivariable analysis showed that only split preoperative GFR_{SCr} in the donor was the independent predictor for C-percentage of the split kidney.

Conclusions: Renal function could be well preserved and compensated after kidney donation in most donors and recipients in Chinese population. Healthy donors with a good GFR before operation possessed a mighty functional compensation capacity.

Keywords: Renal function; Glomerular filtration rate; Compensatory capacity; Kidney transplantation; Living-Related donor

Abbreviations: BMI: Body Mass Index; C-percentage: Compensatory Percentage; D-value: Differential Value; GFR: Glomerular Filtration Rate; GFR_{SCr}: Glomerular Filtration Rate Based on Serum Creatinine; IQR: Interquartile Range; LDN: Laparoscopic Donor Nephrectomy; LKT: Living-Donor Kidney Transplantation; ODN: Open Donor Nephrectomy; ROC: Receiver Operator Characteristic; SCr: Serum Creatinine

Introduction

Compensatory growth of the contralateral kidney to promote significant restoration of the lost renal function is a common phenomenon after unilateral radical nephrectomy [1,2]. The glomerular filtration rate (GFR) is a generally accepted parameter to evaluate the renal function. Living-donor kidney transplantation (LKT) has been recommended as a safe treatment for patients with end-stage renal failure worldwide by virtue of a short duration of organ ischemia, rapid recovery of the graft, and fewer complications [3]. However, the application of LKT in China is still restricted due to

the traditional idea and the insufficiency of the evidence in the renal compensation capacity.

LKT is an optimal model to explore the compensatory capacity of split renal function from the donor kidney in real world, because GFR alteration in a recipient who has progressed to uremia before transplantation can clearly show the compensatory capacity of the donated kidney. So we sought to make a retrospective analysis on GFR changes of the recipient's transplant kidney from his/her live-related donor and the donor's remnant kidney, and explore the GFR compensation capacity of donor's both kidneys in their new milieu.

Patients and Methods

Patients

We reviewed all cases (136 pairs) of LKT performed in our center between June 2007 and December 2017. A total of 94 pairs of LKT with integrated information were enrolled in this study. In accordance with the Kidney Disease: Improving Global Outcomes guideline and the Regulations of Organ Transplantation of the People's Republic of China, living organ recipients are limited to people who are spouses, lineal blood relatives or collateral blood relatives within three generations of living organ donors [3]. Donor evaluation included the performance status, anatomical parameters by spiral computed tomography angiography, serum creatinine (SCr), GFR, and the psychosocial condition. Each pair of the donor and the recipient underwent blood grouping, HLA typing and lymphocytotoxicity cross-matching test. In the majority of patients, the immunosuppressive protocol includes a calcineurin inhibitor, an antimetabolite and a corticosteroid. The methylprednisolone dose was tapered over time from 500 mg/d intraoperatively to 20 mg/d intravenously one week after transplantation. Then oral prednisone was administered at the dosage from 15 mg/d to 5 mg/d one month after transplantation. We focus the maximal renal compensation capacity as the main endpoint, so we exclude those cases who occurred super-acute rejection, severe complication, severe adverse events of immunosuppression drugs.

Renal function assessment

Before operation, GFR_{ECT} was calculated by 99m Tc-DTPA detection to measure preoperative split renal function in the donor. GFRSCr was estimated by using the Cockcroft-Gault formula, based on the equation $= (140 - \text{age}) \times \text{weight (kg)} / (\text{SCr (mg/dl)} \times 72) \times 0.85$ (if female) [4]. To maintain pre and postoperative consistency, we calculated preoperative split GFRSCr by the percentage GFR% detected by GFR_{ECT} . GFRSCr of the donated kidney was estimated by SCr of the corresponding recipient with end-stage renal failure before transplantation who acquired renal function mainly dependent upon the kidney donated.

D-value was defined as postoperative ipsilateral GFRSCr-preoperative split GFRSCr. C-percentage was defined as (postoperative ipsilateral GFRSCr-preoperative split GFRSCr)/preoperative split GFRSCr. Knowing that several factors may influence the renal function after surgery in most scenarios, we chose the optimal SCr as the main parameter or primary endpoint within one month after LKT [4].

Statistical analysis

Continuous variables were expressed as median and interquartile range (IQR) and compared using Mann-Whitney test. Categorical variables were compared using the chi-square and Fisher's exact tests. Association between C-percentage of split renal function and the clinical parameters was evaluated using linear regression analysis. All p values were two-tail and $p < 0.05$ was considered statistically significant. Data were analyzed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA).

Results

Demographics and general data

This study included 94 donors (35 men and 59 women), who ranged in age from 21 to 64 years with a median of 49 (IQR=39-54) years at the time of kidney donation, and the demographics are listed in table 1. There were 66 men and 28 women in recipient population, the median age 30 (IQR=26-38) years, and the median BMI 20.7

(IQR=19.3-22.7) (kg/m^2). Laparoscopic donor nephrectomy (LDN) was performed in 12 donors who donated left kidneys, and open donor nephrectomy (ODN) was applied in the rest 82 donors. The 94 donors included 4 pairs of spouses and 90 pairs of blood relatives within three generations.

Change of donors' remnant kidneys in terms of GFRSCr

The median GFRSCr of the donor's remnant kidney was 46.1 ml/min/1.73m² [IQR=41.2-51.0 ml/min/1.73m²] before surgery and 66.8 ml/min/1.73m² [IQR=58.5-76.5 ml/min/1.73m²] 1 month after nephrectomy (Table 1). The median D-value of GFRSCr increased by 20.8 ml/min/1.73m² [IQR=8.9-29.6 ml/min/1.73m²] with a C-percentage of 46.6% (IQR=17.0-73.0%). The renal function was well preserved in 84(89.4%) donors (positive compensatory in GFRSCr), and slightly decreased in the other 10(10.6%) donors within a month, with a median negative C-percentage of 16.9% (IQR=8.4-25.6%).

Using 20% as the criterion for qualified compensation of the remnant kidney, we found that 67 cases met with the criterion and the remaining 27 cases failed, with an overall qualified compensation rate of 71.3% (67/94). Using receiver operator characteristic (ROC) curve for analysis of the subjects (Figure 1), the best cutoff point of GFRSCr of the donors' remnant kidney was 44.7 ml/min/1.73m² before surgery, sensitivity 0.82 and specificity 0.63.

The clinical data at one-year follow-up showed that the median D-value of GFRSCr increase of the donor's remnant kidneys was 23.5 ml/min/1.73m² (IQR=15.7-29.4 ml/min/1.73m²), and the median C-percentage was 49.5% (IQR=32.2-64.9%), showing no significant difference as compared with that at one month after surgery. These results showed that the donor's renal function remained at a safe and stable level one month after donation.

Change of recipients' transplanted kidneys in terms of GFRSCr

The median GFRSCr of the donated kidneys was 47.0 ml/min/1.73m² [IQR=41.8-52.5 ml/min/1.73m²] before surgery; the median GFRSCr of the donors' donated kidneys was 81.0 ml/min/1.73 m² [IQR=68.4-89.0 ml/min/1.73m²] after 1 month surgery, showing that the D-value increased by 30.6 ml/min/1.73m² [IQR=19.8-42. ml/min/1.73m²] and C-percentage was 67.8% (IQR=39.6%-94.7%).

Correlation between the side of donation and the GFRSCr C-percentage

Eighteen donors donated their right kidneys, in whom postoperative GFRSCr of the remnant kidneys was 64.0 ml/min/1.73m² [IQR=61.1-75.4 ml/min/1.73m²], with the D-value increasing by 20.6 ml/min/1.73m² [IQR=6.9-28.2 ml/min/1.73m²] and an overall GFRSCr C-percentage of 45.4% (14.5%-74.0%). The other 76 donors donated their left kidneys, in which the overall postoperative GFRSCr C-percentage was 46.6% (18.5%-72.2%) ($p=0.870$). The GFRSCr C-percentage of the right-kidney donated was 79.4% (28.2%-112.8%), and that of the left-kidney donated was 64.8% (39.9%-93.6%) ($p=0.834$) (Table 1).

Correlation between donor age and the GFRSCr C-percentage

They were categorized in two groups: group A ≤ 50 years ($n=55$), and group B >50 years ($n=39$). The median GFRSCr C-percentage of the remnant kidneys was 58.2% (IQR=31.8%-86.3%) in group A and 26.6% (IQR=6.7%-51.9%) in group B ($p=0.005$). The median GFRSCr C-percentage of the donated kidneys was 67.9% (IQR=47.6%-93.9%) and 67.8% (IQR=36.1%-95.0%) in group A and B respectively ($p=0.675$) (Table 2).

Table 1: Change in split renal function of the remnant and donated kidneys before donation and within 1 month after transplantation in terms of donation side.

| | Overall | Right donated | Left donated | P |
|--|------------------|------------------|------------------|-------|
| Donors (n) | 94 | 18 | 76 | - |
| Male (%) | 35(37.2) | 7(38.9) | 28(36.8) | 0.872 |
| Age [yr, median(IQR)] | 49(39-54) | 48(34-54) | 49 (40-54) | 0.713 |
| BMI [(kg/m ²), median(IQR)] | 23.3(21.0-25.2) | 22.0(20.5-25.1) | 23.4 (21.3-25.2) | 0.856 |
| Overall GFRSCr before donation [ml/min/1.73m ² , median(IQR)] | 93.6(85.7-102.8) | 90.7(83.8-100.3) | 93.6(87.2-103.2) | 0.696 |
| GFRSCr of remnant kidney before donation [ml/min/1.73m ² , median(IQR)] | 46.1(41.2-51.0) | 45.4(40.8-50.3) | 46.4(41.3-51.1) | 0.967 |
| Optimal GFRSCr of remnant kidney after donation [ml/min/1.73m ² , median(IQR)] | 66.8(58.5-76.5) | 64.0(61.1-75.4) | 67.0(57.6-76.9) | 0.798 |
| GFRSCr D-value of remnant kidney [ml/min/1.73m ² , median(IQR)] | 20.8(8.9-29.6) | 20.6(6.9-28.2) | 20.8(9.3-30.0) | 0.837 |
| GFRSCr C-percentage of remnant kidney [% , median(IQR)] | 46.6(17.0-73.0) | 45.4(14.5-74.0) | 46.6(18.5-72.2) | 0.870 |
| GFRSCr of donated kidney before donation [ml/min/1.73m ² , median(IQR)] | 47.0(41.8-52.5) | 44.64(40.5-50.4) | 47.2(42.6-53.9) | 0.524 |
| Optimal GFRSCr of donated kidney after transplantation [ml/min/1.73m ² , median(IQR)] | 81.0(68.4-89.0) | 80.6(71.4-97.9) | 81.0(68.3-89.0) | 0.796 |
| GFRSCr D-value of donated kidney [ml/min/1.73m ² , median(IQR)] | 30.6(19.8-42.3) | 31.5(18.4-54.4) | 29.4(20.0-42.0) | 0.902 |
| GFRSCr C-percentage of donated kidney [% , median(IQR)] | 67.8(39.6-94.7) | 79.4(28.2-112.8) | 64.8(39.9-93.6) | 0.834 |

IQR = Interquartile Range; BMI = Body Mass Index; GFRSCr = Glomerular Filtration Rate Based on Serum Creatinine; D-value = Differential Value; C-percentage = Compensatory Percentage.

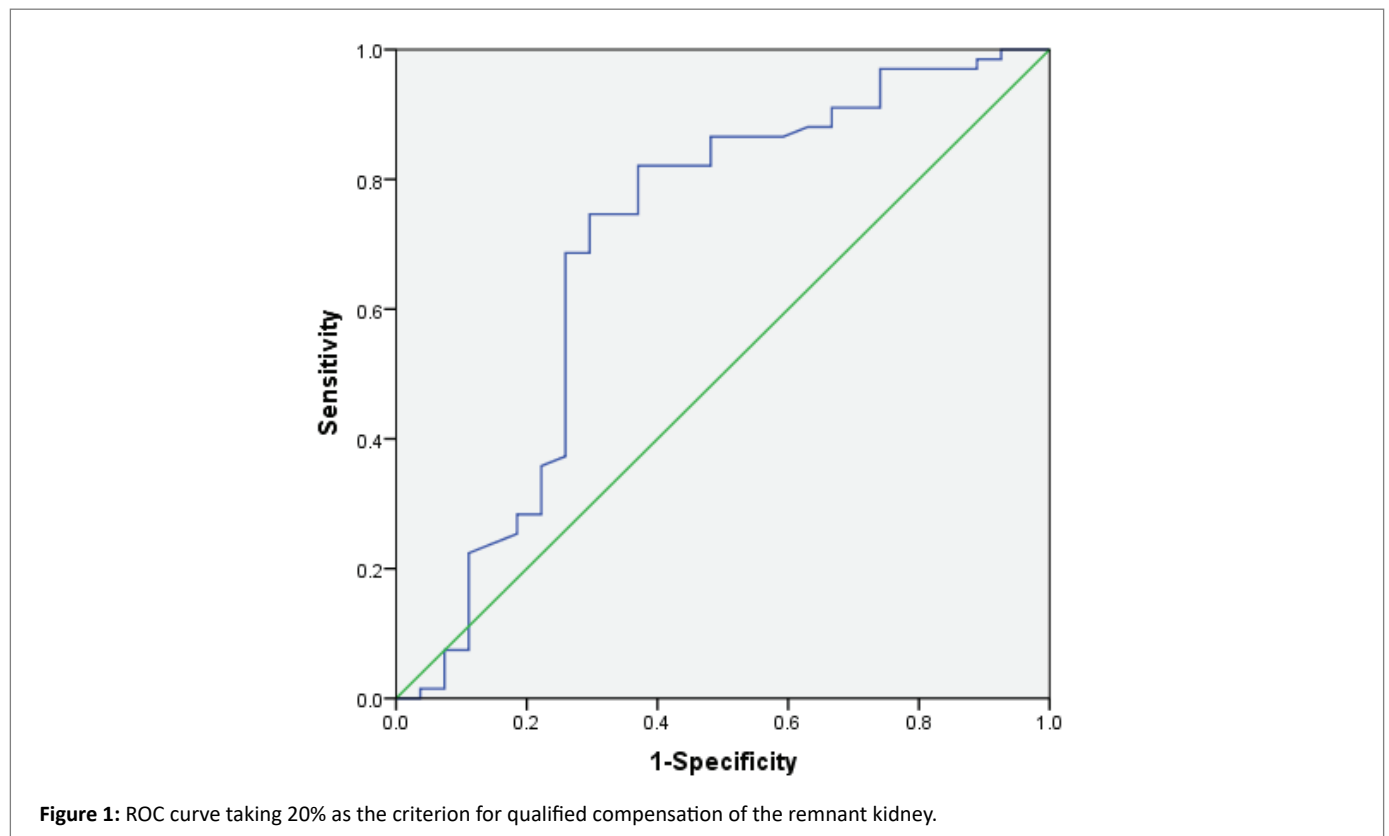


Figure 1: ROC curve taking 20% as the criterion for qualified compensation of the remnant kidney.

Correlation between donor gender and the GFRScR C-percentage

The median D-value of GFRScR increase of the male and female donors after surgery was 17.9 ml/min/1.73m² [IQR=4.8-29.5 ml/min/1.73m²] and 23.1 ml/min/1.73m² [IQR=11.2-29.7 ml/min/1.73m²] respectively (p=0.489). The GFRScR C-percentage of the male and female donors was 82.7% (IQR=43.8%-108.1%) and 61.3% (38.5%-86.2%) respectively (P=0.050) (Table 3).

Correlation between the renal transplantation procedures and the GFRScR C-percentage

The median C-percentage of the remnant kidneys in ODN and LDN groups was 42.8% (IQR=13.3%-70.6%) and 56.6% (IQR=31.4%-82.5%) respectively (p=0.179). The median C-percentage of the donated kidneys in ODN and LDN was 67.8% (IQR=38.9%-94.4%) and 75.9% (IQR=56.3%-99.6%) respectively (p=0.427). No significant difference was observed in the GFRScR compensation rate in either the remnant and transplanted kidneys.

Multivariate analysis of factors affecting the GFRScR C-percentage

Univariate analysis showed that donors aged ≤ 50 years and the preoperative GFRScR of the remnant kidney were significantly associated with C-percentage of the remnant kidneys after operation (p=0.006 and p<0.001), while donors' gender and the side of donation were not significantly associated with it (p=0.562 and p=0.870 respectively). Multivariable analysis showed that preoperative GFRScR of the donors' remnant kidneys was an independent predictor of its remnant GFRScR compensation capacity after operation. C-percentage of the donated kidneys was independently associated with preoperative GFRScR of the donated kidneys (p<0.001), but not donor's age (p=0.675), gender (p=0.051) or the side of donation (p=0.834).

Discussion

The kidney presents a functional reserve capacity after unilateral nephrectomy [1,2]. Many studies reported that the donor's global renal function decreased immediately after kidney donation [5]. Although

Table 2: Change in split renal function of the remnant and donated kidneys sorted by donors' age.

| | ≤ 50 year (group A) | >50 year (group B) | P |
|--|---------------------|--------------------|--------|
| Donors (n) | 55 | 39 | - |
| Male (%) | 34.5 | 41.0 | 0.522 |
| Age [yr, median(IQR)] | 43(31-47) | 55(54-57) | <0.001 |
| Global GFRScR of donor before donation [ml/min/1.73m ² , median(IQR)] | 93.6(85.9-101.4) | 93.7(85.4-104.7) | 0.474 |
| GFRScR of remnant kidney before donation [ml/min/1.73m ² , median(IQR)] | 46.0(41.4-50.3) | 46.6(41.2-54.6) | 0.288 |
| Optimal GFRScR of donated kidney after transplantation [ml/min/1.73m ² , median(IQR)] | 68.1(62.1-78.3) | 63.0(54.8-71.3) | 0.675 |
| GFRScR D-value of donated kidney [ml/min/1.73m ² , median(IQR)] | 25.1(16.4-36.6) | 11.8(3.9-23.6) | 0.005 |
| GFRScR C-percentage of remnant kidney [%, median(IQR)] | 58.2(31.8-86.3) | 26.6(6.7-51.9) | 0.005 |
| GFRScR D-value of donated kidney [ml/min/1.73m ² , median(IQR)] | 31.6(23.3-42.6) | 27.1(19.1-40.2) | 0.829 |
| GFRScR C-percentage of donated kidney [ml/min/1.73m ² , median(IQR)] | 67.9(47.6-93.9) | 67.8(36.1-95.0) | 0.675 |

IQR = Interquartile Range; GFRScR = Glomerular Filtration Rate Based on Serum Creatinine; D-value = Differential Value; C-percentage = Compensatory Percentage.

Table 3: Change in split renal function of the remnant and donated kidneys by donor's gender.

| | Male | Female | P |
|---|------------------|------------------|-------|
| Donors (n) | 35 | 59 | |
| Age [yr, median(IQR)] | 49(26-54) | 48(43-54) | 0.01 |
| Global GFRScR of donor before donation [ml/min/1.73m ² , median(IQR)] | 93.7(90.4-102.4) | 93.6(85.3-102.7) | 0.582 |
| GFRScR of remnant kidney before donation [ml/min/1.73m ² , median(IQR)] | 47.8(43.6-51.3) | 45.6(41.1-50.3) | 0.559 |
| Optimal GFRScR of remnant kidney after donation [ml/min/1.73m ² , median(IQR)] | 62.2(55.6-74.1) | 67.5(61.9-76.8) | 0.673 |
| GFRScR D-value of remnant kidney [ml/min/1.73m ² , median(IQR)] | 17.9(4.8-29.5) | 23.1(11.2-29.7) | 0.489 |
| GFRScR C-percentage of remnant kidney [%, median(IQR)] | 36.7(9.1-83.3) | 52.1(21.6-70.6) | 0.562 |
| GFRScR D-value of donated kidney [ml/min/1.73m ² , median(IQR)] | 34.6(24.4-47.7) | 28.7(18.9-39.2) | 0.045 |
| GFRScR C-percentage of donated kidney [ml/min/1.73m ² , median(IQR)] | 82.7(43.8-108.1) | 61.3(38.5-86.2) | 0.050 |

IQR = Interquartile Range; GFRScR = Glomerular Filtration Rate Based on Serum Creatinine; D-value = Differential Value; C-percentage = Compensatory Percentage.

most of these studies compared the global GFR of the bilateral kidneys before donation with that of the single kidney preserved after nephrectomy, they did not compare the functional change of the same donor's remnant and donated kidney in their new milieu after operation [5]. The renal function of split kidneys from living donors can be monitored perioperatively in real world. In this study, we sought to measure the initial GFR_{SCr} of the split kidney and compare it with the kidney preserved and donated respectively, aiming to explore the potential compensation capacity of the split kidney from living donors.

Time and mechanism of the renal compensation phenomenon

Compensatory renal growth of the remnant kidney starts within hours following nephrectomy and reaches a stable compensatory state in varying periods post-operation. For human living kidney donation, GFR of donors and recipients was compensated and remained stable about one month after operation [6,7]. Gong NQ, et al. reported that donor's mean GFR remained stable at (85.2 ± 17.6) ml/min/1.73m², (87.2 ± 15.9) ml/min/1.73m², (82.1 ± 14.6) ml/min/1.73m² and (83.0 ± 13.7) ml/min/1.73m² 5 days, 3 months, 1 year and more than one year after LKT respectively [6]. Knowing that the GFR reached stability about one month after operation in most related studies, we used GFR at one month after operation as the main parameter for analysis [4-7].

Compensatory renal growth following nephrectomy is predominantly due to renal cell hypertrophy [1,8]. The mechanisms that sense and respond to renal volumetric reduction which generate renal growth remain elusive.

Cleper R reported that two main mechanisms have been proposed in 2012. One ascribes it to the increased activity of the remnant kidney that leads to hypertrophy, and the other attributes it to the release of kidney specific factors such as insulin-like growth factor 1, epidermal growth factor and hepatocyte growth factor and pathways such as mammalian target of rapamycin in response to unilateral nephrectomy. In 2018, Srivastava T, et al. proposed the hyperfiltration-mediated injury in the remaining kidney of a transplant donor and considered that tensile stress invokes the RAAS, fluid flow shear stress predominantly activates the COX2-PGE2-EP2 axis [9]. In 2020, McArdle et al. reported that alterations in the renal sympathetic nerves, the renal RAS and the nitric oxide system may be strong contributing factors to compensatory mechanism [10].

GFR compensation capacity of the remnant kidney

Several studies have reported on the compensatory capacity of remnant kidneys after nephrectomy [2,4,11]. Chien CH, et al. reported that GFR of donor's remnant kidney compensated from 58.2 ml/min/1.73m² to 79.6 ml/min/1.73m², with a 36.9% increase in C-percentage [4]. Our finding is consistent with the results from other centers in term of the tendency, indicating an acceptable and reasonable compensation in the remnant kidney. In our study, GFR in the remnant kidney averaged a 46.6% increase, which is better than 36.9% reported by Chien CH.

We also observed a case with the highest C-percentage in a 43-year-old father who donated the left kidney to his 22-year-old son. GFR_{SCr} of the father's right kidney was 51.3 ml/min/1.73m² before operation and increased to 107.0 ml/min/1.73m² after operation, with a C-percentage of 108.6%, indicating that the remnant kidney of a healthy donor possesses a powerful compensation capacity after donation to meet the physiological needs of the donor.

Impact of donor's age on renal function compensation

Serrano et al. reported that donors in the optimal group were

significantly younger, the optimal/suboptimal ratio being 56.0 ± 10.4 vs 60.7 ± 8.7 years (p=0.018) [12]. Univariate analysis in our study showed a significantly higher GFR C-percentage of the remnant kidneys in younger donor's ≤ 50 years than those in older donors (58.2% vs 26.6%, p=0.005). The above results showed that the remnant kidneys of younger donors have higher compensation capabilities, which is in line with the natural psychological tendency that the renal function decreases with age in ordinary healthy people. However, it is interesting to find that there was no significant difference in the GFR compensation rate of the donated kidneys in the recipients' bodies between the young and old donor age groups [67.9% (IQR=47.6-93.9%) vs 67.8% (IQR=36.1-95.0%), p=0.675]. The reason may be that transplanted kidneys are affected by multiple factors in the new milieu of the recipients, such as immunological and hemodynamic factors, all of which may attenuate the impact of age on the grafts.

Preoperative assessment of nadir GFR for the kidney to be donated

The donated kidney has to adapt to the new milieu before it can gradually recover its function and compensatorily develop its infiltrating capacity in the recipient's body. In this study, there were 36 (38.3%) donors whose eGFR were less than 90 ml/min/m² before donation, and among them 12 donated kidneys' eGFR was <40 ml/min/m². Further sub-group analysis of our study showed that the median GFR D-value in the 12 donors with GFR <40 ml/min/1.73m² before operation was 30.4 ml/min/1.73m² (IQR=25.7-37.1 ml/min/1.73m²) and C percentage was 90.2% (IQR=67.8-127.4%). In the group with GFR_{SCr} of the donated kidneys ≥ 40 ml/min/1.73m², the median GFR_{SCr} D-value was 18.2 ml/min/1.73m² (IQR=6.8-28.1 ml/min/1.73m²) and C-percentage was 62.0% (38.4%-92.7%). This indicates that kidneys with a relatively low GFR before operation have an even more powerful compensatory capability because the donated kidney is fully compensated in the body of the recipient. One possible reason could be the high corticosteroids dosage used perioperatively, which could induce some hyperfiltration in the donated kidney.

Currently, it is difficult to define the acceptable nadir GFR value of the kidney to be donated before operation. Most transplantation centers recommend ≥ 40 ml/min/1.73m² as the cutoff value [3,13]. But as the compensation capability of the donated kidney is higher than that of the remnant kidney as shown in our study, donors with an estimated GFR value <40 ml/min/1.73m² before operation can still be considered as potential candidates for donation. We suggest that the GFR criterion for kidney donation could be reduced to 30 ml/min/1.73m² in specific population. Of course, the baseline GFR of the remnant kidney should be maintained at a ≥ 40 ml/min/1.73m² level so as to guarantee that the donor's remnant kidney has a good filtering function after nephrectomy [14].

Limitations

Our study has some limitations. First, it is of retrospective nature with all data retrieved from a single center, which may bring about tertiary selection bias. Sample is relative limited due to the gradual application of LKD in China over recent years. In addition, though GFR_{SCr} based on Cockcroft-Gault formula is not definitely precise, we take the C-percentage of pre- and postoperative kidney as the main parameter, which may attenuate the influence of other factors (muscle mass, fluid status, nutritional state, etc.). Obviously, further studies are required to explore the compensatory growth after kidney surgery.

Conclusion

The human kidney has a powerful compensation capability. Renal

function could be well compensated after kidney donation in living-donor kidney transplantation within one month. Healthy donors with a good GFR before operation possess a mighty functional compensation capacity although long-term follow-up are needed.

Ethical Statement

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All experiments, including methods and operations were approved by the Ethics Committee of Ruijin Hospital of Shanghai Jiaotong University School of Medicine, China. This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments (as revised in 2013) or comparable ethical standards. Informed consent was obtained from all participants and/or their legal guardian/s. We attested that no organs were procured from prisoners. All living kidneys donated were procured under the supervision of the Regulations of Organ Transplantation of the People's Republic of China, without violating the privacy of donors.

Conflicts of Interest

The authors declare no competing interests.

Consent for Publication

Not applicable.

Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Funding

None.

Author Contributions

All authors listed above have contributed sufficiently to be included as authors. All of the authors had full access to the data for this study and take full responsibility for the integrity of the data and the accuracy of the data analysis. Juping Zhao, Danfeng Xu and Peijun Zhou conceived and designed the study. Xin Huang, Binbin Ma, Kun Shao and Huimin An performed the surgeries. Binbin Ma, Jun Dai and Juping Zhao analyzed the data and drafted the manuscript. All of the authors revised the article critically, gave final approval of submission and agreed to be accountable for all aspects of the work.

Acknowledgements

We show more respect to these donors and patients during this study. We are very grateful to Professor Peijun Zhou, Xianghui Wang and Da Xu from Ruijin Hospital of Shanghai Jiaotong University

School of Medicine in China for their valuable kidney transplantation and total devotion to their job.

References

1. Rojas-Canales DM, Li JY, Makuei L, Gleadle JM (2019) Compensatory renal hypertrophy following nephrectomy: When and how? *Nephrology (Carlton)* 24: 1225-1232.
2. Drozdik M, Domanski L, Rozanski J, Gorecka B (2003) Functional evaluation of the remaining kidney in patients after unilateral nephrectomy. *Scand J Urol Nephrol* 37: 159-163.
3. Lentine KL, Kasiske BL, Levey AS, Adams PL, Alberú J, et al. (2017) KDIGO Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors. *Transplantation* 101: S1-S109.
4. Chien CH, Wang HH, Chiang YJ, Chu SH, Liu HE, et al. (2010) Change in renal function after laparoscopic donor nephrectomy for kidney transplantation. *Transplant Proc* 42: 692-695.
5. Bieniasz M, Domagala P, Kwiatkowski A, Gozdowska J, Krzysztof O, et al. (2009) The assessment of residual kidney function after living donor nephrectomy. *Transplant Proc* 41: 91-92.
6. Gong NQ, Ming CS, Zeng FJ, Zhang WJ, Lin ZB, et al. (2011) Renal function of donors and recipients after living donor kidney transplantation in a Chinese cohort. *Chin Med J (Engl)* 124: 1290-1295.
7. Shirley DG, Walter SJ (1991) Acute and chronic changes in renal function following unilateral nephrectomy. *Kidney Int* 40: 62-68.
8. Cleper R (2012) Mechanisms of compensatory renal growth. *Pediatr Endocrinol Rev* 10: 152-163.
9. Srivastava T, Hariharan S, Alon US, McCarthy ET, Sharma R, et al. (2018) Hyperfiltration-mediated Injury in the Remaining Kidney of a Transplant Donor. *Transplantation* 102: 1624-1635.
10. McArdle Z, Schreuder MF, Moritz KM, Denton KM, Singh RR (2020) Physiology and Pathophysiology of Compensatory Adaptations of a Solitary Functioning Kidney. *Front Physiol* 11: 725.
11. van Londen M, Kasper N, Hessels NR, Messchendorp AL, Bakker SJL, et al. (2018) Renal functional reserve capacity before and after living kidney donation. *Am J Physiol Renal Physiol* 315: F1550-F1554.
12. Serrano OK, Yadav K, Bangdiwala A, Vock DM, Dunn TB, et al. (2018) Age alone is not a contraindication to kidney donation: Outcomes of donor nephrectomy in the elderly. *Clin Transplant* 32: e13287.
13. Goldfarb DA, Matin SF, Braun WE, Schreiber MJ, Mastroianni B, et al. (2001) Renal outcome 25 years after donor nephrectomy. *J Urol* 166: 2043-2047.
14. Lewandowska D, Galazka Z, Pazik J, Szmidi J, Durlik M (2014) When less is more--case report of successful renal transplantation from a living unrelated donor to a high-risk female recipient. *Transplant Proc* 46: 2927-2928.