Clinical Kidney Journal

Clinical Kidney Journal, 2017, vol. 10, no. 1, 116–123

doi: 10.1093/ckj/sfw097
Advance Access Publication Date: 4 October 2016
Original Article

ORIGINAL ARTICLE

Does size matter? Kidney transplant donor size determines kidney function among living donors

Meenakshi Narasimhamurthy[1], Lachlan M. Smith[2], Jason T. Machan[3], Steven E. Reinert[4], Reginald Y. Gohh[5], Lance D. Dworkin[1], Basma Merhi[1], Nikunjkumar Patel[1], Michael D. Beland[2] and Susie L. Hu[1]

[1]Division of Kidney Disease and Hypertension, Department of Medicine, Warren Alpert Medical School of Brown University, Rhode Island Hospital, Providence, RI, USA, [2]Department of Diagnostic Imaging, Warren Alpert Medical School of Brown University, Rhode Island Hospital, Providence, RI, USA, [3]Biostatistics Core, Lifespan Hospital System, Departments of Orthopedic and Surgery, Warren Alpert Medical School of Brown University, Providence, RI, USA, [4]Lifespan Information Services, Lifespan Hospital System, Providence, RI, USA and [5]Division of Renal Transplantation, Department of Medicine, Warren Alpert Medical School of Brown University, Rhode Island Hospital, Providence, RI, USA

Correspondence and offprint requests to: Susie L. Hu; E-mail: shu@lifespan.org

Abstract

Background: Kidney donor outcomes are gaining attention, particularly as donor eligibility criteria continue to expand. Kidney size, a useful predictor of recipient kidney function, also likely correlates with donor outcomes. Although donor evaluation includes donor kidney size measurements, the association between kidney size and outcomes are poorly defined.

Methods: We examined the relationship between kidney size (body surface area-adjusted total volume, cortical volume and length) and renal outcomes (post-operative recovery and longer-term kidney function) among 85 kidney donors using general linear models and time-to-chronic kidney disease data.

Results: Donors with the largest adjusted cortical volume were more likely to achieve an estimated glomerular filtration rate (eGFR) ≥60 mL/min/1.73 m^2 over a median 24-month follow-up than those with smaller cortical volumes (P <0.001), had a shorter duration of renal recovery (1.3–2.2 versus 32.5 days) and started with a higher eGFR at pre-donation (107–110 versus 91 mL/min/1.73 m^2) and immediately post-nephrectomy (~63 versus 50–51 mL/min/1.73 m^2). Similar findings were seen with adjusted total volume and length.

Conclusions: Larger kidney donors were more likely to achieve an eGFR ≥60 mL/min/1.73 m^2 with renal recovery over a shorter duration due to higher pre-donation and initial post-nephrectomy eGFRs.

Key words: chronic renal insufficiency, creatinine, glomerular filtration rate, kidney transplantation, nephrectomy

Received: June 24, 2016. **Accepted:** August 16, 2016

Introduction

Living donor kidney function evaluation, primarily focused on recipient outcomes and allograft function, has been studied extensively [1, 2]. Greater attention is being dedicated to the long-term welfare of donors [3–5], particularly as the kidney donor eligibility criteria continue to expand, with growing interest in donor survival or cardiovascular events, kidney function, blood pressure (BP) [6, 7] and proteinuria [8], which have been found to be comparable to that of the general population using national mortality averages [9–12].

In most transplant centers, donor evaluation includes computed tomographic (CT) angiography to define renal anatomy where kidney sizes can be non-invasively assessed [13, 14]. Transplant donor's size (length, weight or volume) is often cited as a predictive factor for recipient allograft function [15–17] but likely also predicts donor outcomes including donor kidney function [18]. Recent publications seem to favor total kidney volume [16] or cortical volume [19] in living donor transplantation. Not only has volumetric measurement of the donor kidneys been shown to be a useful predictor of recipient kidney function [1, 2, 20, 21], but also it may correlate with donor kidney function and possibly with outcomes [16, 22, 23]. We examined the relationship between kidney size [adjusted for patient size using body surface area (BSA)] and renal outcomes including kidney function (pre- and post-donation), longer-term estimated glomerular filtration rate (eGFR) decline, hypertension, proteinuria, cardiovascular events and death.

Materials and methods

Ninety-five potential living kidney transplant donors undergoing scheduled outpatient CT angiography of the kidneys were identified from Rhode Island Hospital between 2009 and 2013 from chart review. For the kidney volume assessment, 10 of 95 identified patients were excluded due to lack of laboratory data or CT angiography, resulting in a total of 85 remaining living donors.

Demographic data (age, gender, race, height and weight), comorbid conditions, medications, creatinine, urinalysis and urine protein quantification, eGFR by the CKD Epidemiology Collaboration (CKD-EPI) equation [24] and blood pressures (BPs) were obtained. Patients were considered to have hypertension if BP exceeded 140/90 mmHg, or were taking antihypertensive medications. Albuminuria >30 mg/g (urine albumin/creatinine) and proteinuria (urine protein/creatinine) >150 mg/g or mg/24 h were defined to be abnormal.

Helical CT angiography of the kidneys for living donor kidney transplantation was performed pre-donation on the same 64-detector row CT scanner. Post-contrast imaging was obtained in the corticomedullary phase after intravenous administration of 100 mL of iohexol (350 mg/mL iodine) at 4 mL/s using smart-prep.

Total renal volumes were calculated from the 3D volume-rendered images. Segmented cortical volumes were calculated on the CT workstation using manual thresholding with a value that differentiated enhancing cortex from the medulla and collecting system (average of 118 Hounsfield Units, HU; range 88–173 HU). Results of each kidney were summed for calculation of cortical volumes for each patient. Renal lengths were also measured as the greatest bipolar dimension obtained from the 3D volume-rendered images. Transplant donor's kidney sizes were measured prior to donor nephrectomy.

Kidney size-dependent donor outcomes including creatinine, CKD-EPI eGFR and renal recovery post-nephrectomy (time to eGFR ≥60 mL/min/1.73 m^2) were assessed. We examined the relationship of baseline kidney function (creatinine and eGFR), initial post-operative kidney function and post-operative renal recovery to (the non-resected) kidney size. Kidney size divided by BSA (m^2) to proportionally adjust for patient size was then categorized (given their nonlinear relationship) into quartile groups (A–D according ascending kidney size) as detailed in the tables and figures for total volume/BSA, cortical volume/BSA and length/BSA. Creatinine and eGFR were estimated by the Y-intercept, and post-nephrectomy renal recovery rate by the slope obtained from post-operative days 1 through 28. Lastly, the likelihood of achieving eGFR ≥60 mL/min/1.73 m^2 from nadir eGFR post-nephrectomy was assessed by survival analysis according to kidney size. BSA was calculated using the formula of DuBois and DuBois [25].

Systolic and diastolic BP changes, new-onset hypertension, presence of proteinuria, cardiovascular events and death were also recorded. Study protocol was approved by the Lifespan Institutional Review Board.

Analyses were carried out using SAS version 9.3 (The SAS Institute, Cary, NC, USA). Creatinine and eGFR were normally distributed and analyzed using general linear models (ANOVA and regression). Measures were expressed as mean ± standard error unless otherwise indicated. Time-to-event data was analyzed using the Kaplan–Meier method to estimate survival function, censoring when patients were lost to follow-up (zero mortality), and comparing survival estimates using Wilcoxon weighting. *Post hoc* comparisons were carried out using the Tukey–Kramer (Kaplan–Meier Survival Analyses) or Holm Test (generalized linear models).

Results

Baseline characteristics and post-nephrectomy renal function

A cohort of 85 potential living kidney transplantation donors undergoing scheduled outpatient renal CT angiography were retrospectively followed for a mean of 21 ± 11 (median 24) months. No donors had proteinuria or diabetes mellitus and 8% had well-controlled hypertension on medication without other comorbidities. Left-sided nephrectomy (smaller kidney) was performed for the majority (82%) unless surgical factors or size favored right-sided nephrectomy. Split renal function assessments were not routinely performed for donor evaluation. The mean total and cortical kidney volume for the non-resected kidney were 163 ± 33 mL (mean ± standard deviation) and 104 ± 23 mL, respectively. The non-resected kidney length was on average 10.9 ± 1.0 cm. The percentage of the non-resected total kidney volume was on average 51 ± 2% (range 42–54) of the pre-donation bilateral volume and only two patients were <45%. Additional baseline characteristics are outlined in Table 1.

Baseline characteristics for the donor groups divided according to kidney size adjusted for BSA (in quartiles) were not significantly different from each other except for age. For both total volume/BSA and cortical volume/BSA, the smallest group A had higher mean age in years (total volume/BSA—A: 50.7 ± 2.2 versus B: 41.1 ± 2.6, C: 43.3 ± 2.0 and D: 44.0 ± 2.1; cortical volume/BSA—A: 52.5 ± 1.9 versus B: 43.6 ± 2.6, C: 42.3 ± 2.3 and D: 41.4 ± 2.2). For length/BSA, age was greatest for group B: 49.6 ± 1.8 versus group A: 45.3 ± 2.6, C: 43.3 ± 2.4 and D: 41.8 ± 2.1. Gender distribution was similar between groups except for length/BSA where group C had a lower distribution of men (C 17% versus A, B, D with 22%, $P < 0.05$ for all comparisons). Only 7% (6/85) of the whole cohort were reported as black and 5% other (Asian and Hispanic); therefore, race was not considered in the subgroup comparisons.

Donor kidney function changed from the baseline mean serum creatinine of 0.79 ± 0.14 mg/dL (eGFR by the CKD-EPI equation 102 ± 17 mL/min/1.73 m^2) to a peak creatinine of 1.35 ± 0.28 mg/dL (eGFR 56.6 ± 13.6 mL/min/1.73 m^2), which fell to 1.09 ± 0.20 mg/dL (mean eGFR 69.6 ± 15.6 mL/min/1.73 m^2) at the 2-year follow-up. eGFR increased by 21% at 1 year and 26% at 2 years from nadir eGFR post-nephrectomy (equivalent to 67% of the pre-donation eGFR). All donors had eGFR ≥60 mL/min/1.73 m^2 prior to nephrectomy. Immediately after nephrectomy, the majority (72%) had an eGFR <60 mL/min/1.73 m^2, which fell to 41% and 30% of donors by the 1-year and the 2-year follow-up.

Table 1. Baseline characteristics of potential kidney transplant donors undergoing computed tomographic angiography[a]

n = 85	
Age (years)	45 ± 10
Gender (% male)	41
Race (%)	
White	88
Black	7
Other	5
Height (inches)	66 ± 4
Weight (lbs)	162 ± 36
BSA (m^2)	1.8 ± 0.2
BMI (kg/m^2)	26 ± 5
BMI >30 kg/m^2 (%)	17
Follow-up (months)	21 ± 11
Baseline creatinine (mg/dL)	0.79 ± 0.14
24-h CrCl (mL/min)	127 ± 27
Baseline eGFR (mL/min/1.73 m^2)	102 ± 17
Bilateral kidney volume	
Total volume (mL)	322 ± 64
Cortical volume (mL)	208 ± 44
Non-resected kidney volume	
Total volume (mL)	163 ± 33
Cortical volume (mL)	104 ± 22
Length (cm)	10.9 ± 1

BMI, body mass index; CrCl, creatinine clearance; eGFR, estimated glomerular filtration rate.
[a]Continuous data expressed as mean ± standard deviation and proportion as percentages.

Baseline kidney function and size

Kidney size adjusted by patient BSA generally correlated with kidney function (Table 2). Cortical volume/BSA was inversely related to baseline creatinine, where the largest cortical volume/BSA group D had the lowest creatinine compared with the smaller-sized group B as detailed. In fact, length/BSA correlated strongly with baseline creatinine, where the smallest length group A had the highest average creatinine compared with the other groups (B–D). Baseline creatinine for group B was also significantly higher than for group D. This relationship was not seen between total volume/BSA and baseline creatinine.

The association between kidney function and kidney size was more apparent with baseline eGFR, which correlated positively with total volume/BSA; group A had a lower mean eGFR compared with that for groups B, C and D. Similarly, cortical volume/BSA was also associated with baseline eGFR, where the smallest group A had lower eGFR compared with groups C and D. The largest group D had eGFR significantly greater than the smaller groups A and B. Moreover, longer length/BSA in group D was likewise significantly associated with higher baseline eGFR than that for the smaller groups A and B.

Post-nephrectomy kidney function and size

Post-operative kidney function significantly differed according to kidney size when adjusted for patient size (Table 3). Although

Table 2. Comparison of baseline kidney function according to kidney size of potential kidney transplant donors undergoing computed tomographic angiography[a]

Baseline								
Total vol/BSA (mL/m^2)			Cortical vol/BSA (mL/m^2)			Length/BSA (cm/m^2)		
Size group (mL/m^2)	Cr (mg/dL)	eGFR (mL/min/1.73 m^2)	Size group (mL/m^2)	Cr (mg/dL)	eGFR (mL/min/1.73 m^2)	Size group (cm/m^2)	Cr (mg/dL)	eGFR (mL/min/1.73 m^2)
A 57.5–78.7 *n* = 22	0.80 ± 0.02	**92.9 ± 3.0**; A versus B, C, D[b]	**A** 36.2–48.5 *n* = 20	0.80 ± 0.03	**91.1 ± 3.7**; versus C: P = 0.0016 versus D: P = 0.0001	**A** 4.6–5.4 *n* = 22	**0.89 ± 0.03**; A versus B, C, D	**98.3 ± 4.0**; **P = 0.017**
B >78.7–84.6 *n* = 18	0.78 ± 0.04	105.9 ± 4.8 P = 0.024	**B** >48.5–57.5 *n* = 20	**0.83 ± 0.03**; versus D; P = 0.011	100.4 ± 3.9; versus D: P = 0.0001	**B** >5.4–6.1 *n* = 20	0.78 ± 0.03; versus A: P = 0.0026; versus D: P = 0.020	**96.4 ± 3.3**; **P = 0.021**
C >84.6–93.7 *n* = 18	0.80 ± 0.03	101.8 ± 3.1; P = 0.042	**C** >57.5–62.9 *n* = 20	0.76 ± 0.03	107.1 ± 3.2	**C** >6.1–6.5 *n* = 20	0.75 ± 0.03; P = 0.0006	102.7 ± 3.9
D >93.7–117.0 *n* = 21	0.76 ± 0.03	108.4 ± 3.1; P = 0.0006	**D** >62.9–80.1 *n* = 19	0.73 ± 0.03	110.5 ± 3.1; D versus A, B	**D** >6.5–7.5 *n* = 20	0.70 ± 0.02; P <0.0001	110.2 ± 2.9; D versus A, B

BSA, body surface area; Cr, creatinine; eGFR, estimated glomerular filtration rate; vol, volume.
[a]Size groups are in order of ascending size (A–D); mean values with standard errors reported; bold numbers represent 'threshold' values where the measures become significantly different; shaded areas represent the groups with lower kidney function separated by these 'threshold points'.
[b]Comparisons of only indicated groups were significant.

Table 3. Comparison of post-nephrectomy kidney function within first 28 days according to kidney size of potential kidney transplant donors undergoing computed tomographic angiography[a]

Post-operative (first 28 days)								
Total vol/BSA			Cortical vol/ BSA			Length/ BSA		
Size group (mL/m^2)	Cr (mg/dL)	eGFR ($mL/min/1.73\ m^2$)	Size group (mL/m^2)	Cr (mg/dL)	eGFR ($mL/min/1.73\ m^2$)	Size group (cm/m^2)	Cr (mg/dL)	eGFR ($mL/min/1.73\ m^2$)
A 57.5–78.7 n = 22	1.38 ± 0.04	**50.3 ± 2.1**; versus D[b]: P = 0.001	**A** 36.2–48.5 n = 20	1.38 ± 0.05	**49.1 ± 2.5**; A versus C, D	**A** 4.6–5.4 n = 22	1.38 ± 0.05	**50.1 ± 2.8**; A versus C, D
B >78.7–84.6 n = 18	1.38 ± 0.06	56.3 ± 2.9	**B** >48.5–57.5 n = 20	**1.47 ± 0.05**; B versus C, D	**51.8 ± 1.9**; B versus C, D	**B** >5.4–6.1 n = 20	**1.47 ± 0.06**; B versus C, D	**51.4 ± 2.0**; B versus C, D
C >84.6–93.7 n = 18	1.37 ± 0.07	57.0 ± 2.9	**C** >57.5–62.9 n = 20	1.27 ± 0.06; versus B; P = 0.015	63.8 ± 3.0; versus A: P = 0.0003; versus B: P = 0.0009	**C** >6.1–6.5 n = 20	1.26 ± 0.06; P = 0.015	62.9 ± 3.0; versus A: P = 0.0024; versus B: P = 0.0021
D >93.7–117.0 n = 21	1.28 ± 0.06	63.4 ± 3.3	**D** >62.9–80.1 n = 19	1.26 ± 0.06; versus B; P = 0.014	63.7 ± 3.3; versus A; P = 0.0007 versus B; P = 0.0021	**D** >6.5–7.5 n = 20	1.26 ± 0.06; P = 0.014	62.7 ± 2.8; versus A: P = 0.0017; versus B: P = 0.0013

BSA, body surface area; Cr, creatinine; eGFR, estimated glomerular filtration rate; vol, volume.

[a]Size groups are in order of ascending size (A–D); mean values with standard errors reported; bold numbers represent 'threshold' values where the measures become significantly different; shaded areas represent the groups with lower kidney function separated by these 'threshold points'.

[b]Comparisons of only indicated groups were significant.

total volume/BSA did not correlate with lower post-operative creatinine across size groups, cortical volume/BSA was significantly associated with creatinine. We found that, for cortical volume/BSA, the larger groups C and D had a considerably lower initial post-operative creatinine than that for group B, yet the rates of creatinine fall (slope) over 28 days were not significantly different among the groups and did not follow any trend according to size. Likewise, shorter kidney length/BSA was associated with worse creatinine post-operatively, where the smaller group B had higher mean initial post-operative creatinine compared with each of the larger kidney length/BSA groups C and D.

Correspondingly, greater initial eGFR after nephrectomy was positively associated with total volume/BSA (A versus D), cortical volume/BSA (A versus C and D; as well as B versus C and D) and length/BSA (A versus C and D; as well as B versus C and D), as shown in Table 3. The rate of change of eGFR (slope of eGFR rise) was not determined by kidney size with any measure of kidney size when it was adjusted by BSA.

Post-nephrectomy achievement of eGFR ≥60 mL/min/ 1.73 m^2 and size

Overall, although no donors began with eGFR <60 mL/min/1.73 m^2 prior to nephrectomy, initial mean post-operative eGFR fell to 56.6 ± 13.6 mL/min/1.73 m^2. Donors with the smallest total volume/BSA (group A) were less likely to reach eGFR ≥60 mL/min/1.73 m^2 from nadir eGFR compared with groups B (P = 0.026), C (P = 0.023) and D (P = 0.003) by time-to-event survival analysis (with a median 24-month follow-up), as shown in Figure 1. The median time to reach eGFR ≥60 mL/min/1.73 m^2 for groups B, C and D (in ascending order of size) was 10.3, 16.4 and 1.3 days, respectively (P <0.025).

Likewise, similar relationships were seen with cortical volume/BSA (Figure 2), where groups A (versus C: P = 0.0012; versus D: P ≤0.0001) and B (versus C: P = 0.046; versus D: P = 0.0043) were each less likely than groups C and D to achieve freedom from eGFR <60 mL/min/1.73 m^2 (median time to eGFR ≥60 mL/min/1.73 m^2—B: 32.5, C: 2.2, D: 1.3 days; P <0.001), and with length/BSA (Figure 3), where group D compared with A (P = 0.0017) and B (P = 0.0042), and additionally C versus A (P = 0.035) were also more likely to reach eGFR ≥60 mL/min/1.73 m^2 (median time to eGFR ≥60 mL/min/1.73 m^2—A: 144.5, B: 193.3, C: 3.2, D: 2.2 days; P = 0.0045).

Notably, the largest total volume/BSA group D not only started with a higher baseline eGFR but also with a higher initial post-operative eGFR as discussed earlier. This was also true for BSA-adjusted cortical volume and length.

Blood pressure, proteinuria, cardiovascular disease events and mortality

Seven donors had pre-existing well-controlled hypertension and only one donor developed new hypertension requiring antihypertensive medication. Neither systolic nor diastolic BPs changed significantly over a mean follow-up of 22 months. No donor had subsequent proteinuria as assessed by follow-up urinalyses. There were no cardiovascular events or death for the duration of follow-up. The association of outcomes and kidney size could not be properly assessed given the exceedingly low event rate.

Discussion

Previous studies have primarily evaluated baseline donor kidney function related to kidney size. This study examined post-operative renal recovery and longer-term kidney function (eGFR). We found that BSA-corrected kidney size was not only associated with baseline kidney function but also determined post-nephrectomy kidney function. Kidney size did not determine the slope of

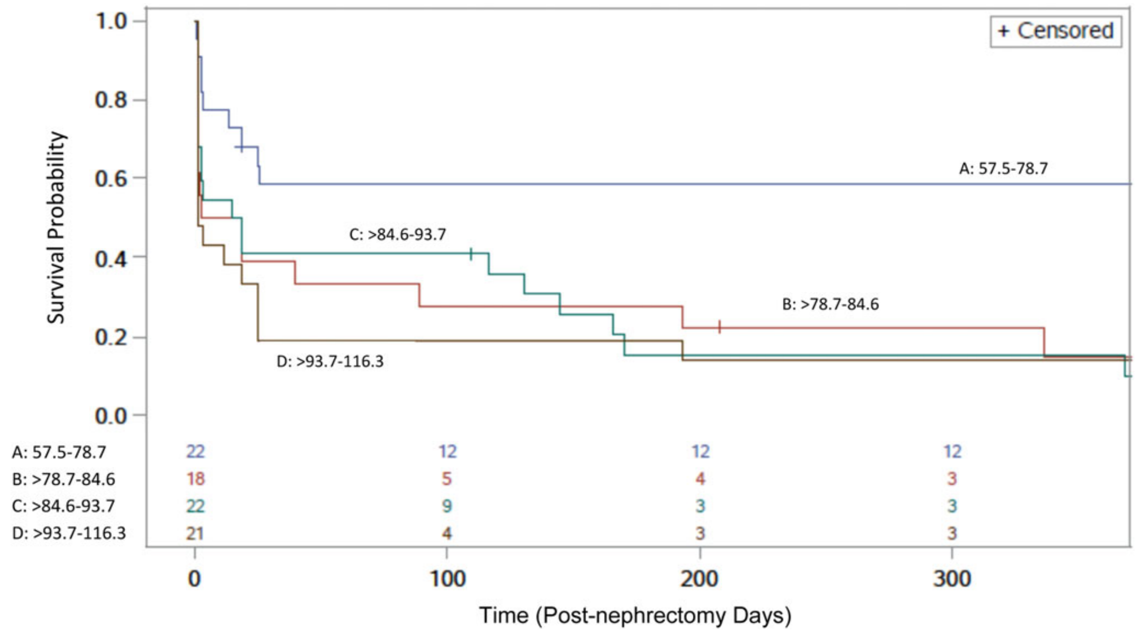

Fig. 1. Time to freedom from estimated glomerular filtration rate <60 mL/min/1.73 m^2 according to total volume/body surface area (mL/m^2) among potential kidney transplant donors.

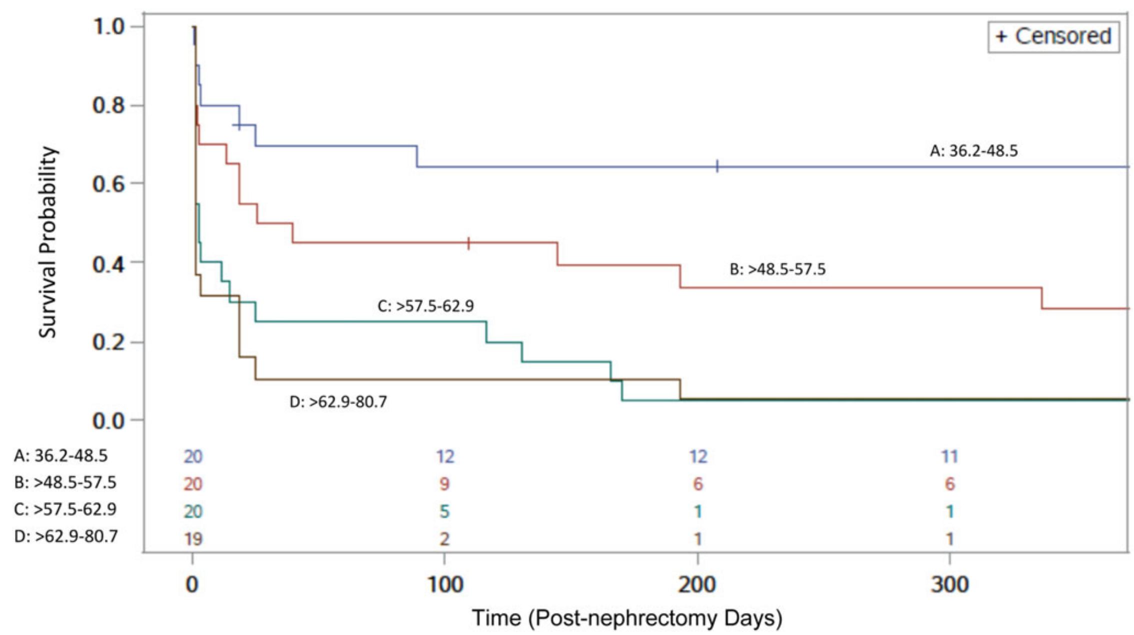

Fig. 2. Time to freedom from estimated glomerular filtration rate <60 mL/min/1.73 m^2 according to cortical volume/body surface area (mL/m^2) among potential kidney transplant donors.

eGFR recovery. Instead, ability to achieve post-nephrectomy eGFR ≥60 mL/min/1.73 m^2 appeared to be primarily related to baseline and initial post-nephrectomy eGFR.

Baseline donor kidney function and kidney size

We found that, for total volume/BSA, the smallest kidney-sized group A had the worst kidney function (eGFR), seemingly with a threshold effect for those with total volume/BSA <78.7 mL/m^2. For cortical volume/BSA, the smaller-sized groups A and B versus C and D had the worse kidney function (eGFR) again, with likely a threshold cortical volume/BSA ≤57.5 mL/m^2. Similar association of better kidney function was also seen with kidneys of longest length/BSA (group D versus A and B) once length/BSA reached ≥6.5 cm/m^2 (Table 2). For total volume/BSA assessment, the older age observed in group A may explain the association of kidney function and size. A large study of 1344 potential kidney donors found significant association of cortical volume with age and gender [26]. However, age did not explain the association of kidney size and function for cortical volume/BSA and length/BSA assessments. Age has been shown to determine kidney function, but acceleration of GFR decline generally occurs by the sixth to seventh decade of life [27]. Our study cohort had a narrow age range (45 ± 10 years) and its impact on size and kidney function

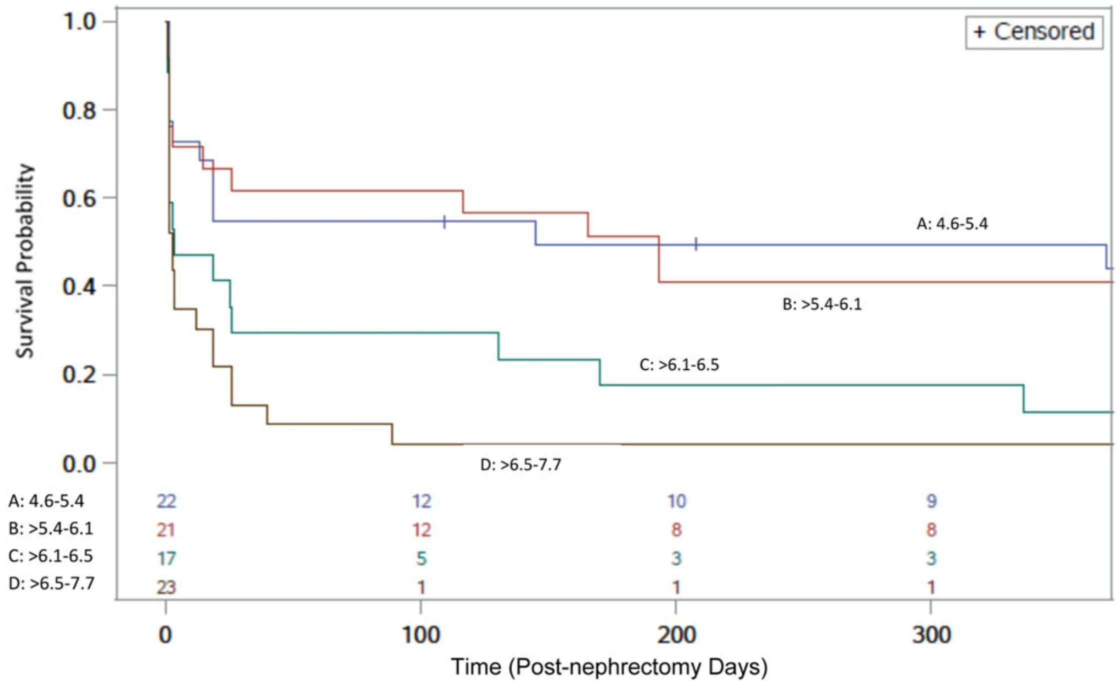

Fig. 3. Time to freedom from estimated glomerular filtration rate <60 mL/min/1.73 m^2 according to length/body surface area (cm/m^2) among potential kidney transplant donors.

measures are arguably minimal. However, the influence of age on outcomes according to kidney size groups should be taken into consideration.

A direct relationship has been shown pre-surgery or at the time of donation between measured GFR and renal parenchymal volume [26, 28] and with total kidney volume [23] from CT angiography, but without further follow-up. Similarly, total kidney volume, parenchymal renal volume and even length using ultrasound have also been shown to correlate with measured GFR (again assessed only at baseline) among potential living donors, actual donors and recipients [15, 29, 30], although others have not demonstrated a significant relationship between kidney volume and baseline eGFR [31]. Most studies did not examine the relationship of kidney size and kidney function over time (post-operatively or longer-term), and they did not adjust kidney size for patient size.

Post-nephrectomy donor kidney function recovery and size

We have long known that the GFR decline post donation does not return exactly to pre-donation GFR levels [32]. Donor kidney function among kidney transplant donors typically declines acutely after donation and then improves rapidly, reported as early as 3 days after nephrectomy [22]. In an observational cohort of 84 donors, 24.4% progressed to 'stage 3 CKD' with a mean follow-up of 6.4 years [33]. We found kidney function decline, with as many as 72% having eGFR <60 mL/min/1.73 m^2 immediately post-nephrectomy, which then improved but still with 30% having eGFR <60 mL/min/1.73 m^2 by 2 years of follow-up. At the end of follow-up, eGFR fell on average to approximately 38% from baseline, which is comparable to reported 30–40% deviations from pre-donation GFR [19, 34, 35].

Our results suggested that initial post-operative creatinine and eGFR (in addition to baseline values) were also determined by kidney size when adjusted for BSA as presented in Table 3. Beyond initial post-nephrectomy factors, we found that once kidney size was adjusted for BSA, the rate of kidney function change (slope) over 28 days was not related to size with any clear pattern. However, those with larger kidney size recovered earlier after nephrectomy, presumably because they started with greater kidney function. Increased renal perfusion and hypertrophy of the kidney have been shown to correspond to an increase in renal cortical volume [19]. Others have reported less hypertrophy among those with larger kidneys [22] and after adjustment of kidney size with BSA [36]. This may explain the loss of association between kidney size and post-nephrectomy renal recovery rate (slope) once adjusted for BSA in our cohort. Possibly, larger kidneys have hypertrophied pre-donation limiting capacity for additional hypertrophy after donation.

The more commonly cited factors for rate of renal recovery include age [22, 34], gender [22] and body mass index [34]. Patients who were younger [22, 34], male [22] and non-obese [34] had a more rapid rate of recovery, whereas tobacco use, hypertension and proteinuria [22] adversely affected GFR recovery after donation. Our donor population tended to be younger, mostly white and female. Although there were some differences for baseline characteristics of age across groups divided in quartiles, the kidney size and function associations remained significant across groups where there were no differences in age. Age alone did not appear to explain this association. We accounted for patient size and gender with division by BSA. Only seven were hypertensive and none had significant proteinuria in our cohort of donors.

Others have reported a pre-operative measure of GFR <82 mL/min/1.72 m^2 as a predictor of donor CKD [33], and rate of renal recovery among transplant donors has been mostly explored generally [22, 23, 28, 37] but not according to kidney size. Although preserved kidney volume has been identified as a predictor of donor eGFR 6 months [36] and 1 year after donation [38] by multivariate logistic regression analysis, no study to our knowledge has examined how kidney size determines rate of renal recovery and the risk of non-recovery to an eGFR ≥60 mL/min/1.73 m^2 post-nephrectomy.

eGFR, other outcomes and kidney size

Given the correlation of kidney size with baseline kidney function [19, 23], kidney size likely also determines longer-term eGFR. Our results indicated that donors with larger total, cortical volume and length corrected for BSA were more likely to achieve eGFR ≥60 mL/min/1.73 m^2 from nadir post-nephrectomy eGFR with a shorter median time to recovery (Figures 1–3). This may be primarily explained by greater pre-donation eGFR and associated higher post-operative eGFR, but not by the rate of eGFR rise as the slope of eGFR decline was no different among groups. In a study of 45 donors, those who were able to increase renal plasma volume (measured by magnetic resonance imaging) by more than 20% after 7 days were more likely to have greater eGFR (Cockroft-Gault) adaptation after 1 year and had associated increase of renal blood flow of 25–32% within 1 week [22]. This group also started with a higher eGFR prior to kidney donation [22]. Surprisingly, the group with more rapid eGFR adaptation had on average smaller kidneys, which increased in size with greater magnitude [22].

The incidence of new-onset proteinuria and hypertension was exceedingly low and there were no cardiovascular events or death during the short follow-up duration for this study. These limitations did not allow for risk assessment of kidney size for these outcomes; however, there was no difference in these events with respect to kidney size. Reported albuminuria between donors and matched controls from the general population have been similar [11], but donor risk of proteinuria increased with time [39]. Hypertension risk among donors was also variable [40]. A meta-analysis found that donor BPs were 5 mmHg higher than that of the control group [41], but without greater risk of GFR decline, end-stage renal disease or mortality over long-term follow-up [11]. No study has examined the impact of kidney size on these outcomes.

In conclusion, we have found that kidney size corrected for BSA determined post-nephrectomy donor eGFR. Donors with larger kidneys were more likely to achieve freedom from an eGFR <60 mL/min/1.73 m^2 post-nephrectomy over a median of 2 years and had shorter duration of renal recovery primarily due to higher pre-donation and initial post-nephrectomy eGFRs.

Conflict of interest statement

M.D.B. is a consultant for Hitachi Aloka America, Inc. The results presented in this paper have not been published previously in whole or part.

References

1. Sikora MB, Shaaban A, Beddhu S *et al*. Effect of donor kidney volume on recipient outcome: does the ‘dose’ matter? *Transplantation* 2012; 94: 1124–1130
2. Yano M, Lin MF, Hoffman KA *et al*. Renal measurements on CT angiograms: correlation with graft function at living donor renal transplantation. *Radiology* 2012; 265: 151–157
3. Mjoen G, Hallan S, Hartmann A *et al*. Long-term risks for kidney donors. *Kidney Int* 2014; 86: 162–167
4. Tsai SF, Shu KH, Ho HC *et al*. Long-term outcomes of living kidney donors over the past 28 years in a single center in Taiwan. *Transplant Proc* 2012; 44: 39–42
5. Foley RN, Ibrahim HN. Long-term outcomes of kidney donors. *Curr Opin Nephrol Hypertens* 2010; 19: 129–133
6. Tent H, Sanders JS, Rook M *et al*. Effects of preexistent hypertension on blood pressure and residual renal function after donor nephrectomy. *Transplantation* 2012; 93: 412–417
7. Mjoen G, Midtvedt K, Holme I *et al*. One- and five-year follow-ups on blood pressure and renal function in kidney donors. *Transpl Int* 2011; 24: 73–77
8. Yoon YE, Lee KS, Choi KH *et al*. Prospective measurement of urinary microalbumin in living kidney donor nephrectomy: toward understanding the renal functional recovery period. *J Urol* 2014; 192: 1172–1177
9. Lam NN, Lentine KL, Levey AS *et al*. Long-term medical risks to the living kidney donor. *Nat Rev Nephrol* 2015; 11: 411–419
10. Fehrman-Ekholm I, Elinder C-G, Stenbeck M *et al*. Kidney donors live longer. *Transplantation* 1997; 64: 976–978
11. Ibrahim HN, Foley R, Tan L *et al*. Long-term consequences of kidney donation. *N Engl J Med* 2009; 360: 459–469
12. Garg AX, Meirambayeva A, Huang A *et al*. Cardiovascular disease in kidney donors: matched cohort study. *BMJ* 2012; 344: e1203
13. Del Pizzo JJ, Sklar GN, You-Cheong JW *et al*. Helical computerized tomography arteriography for evaluation of live renal donors undergoing laparoscopic nephrectomy. *J Urol* 1999; 162: 31–34
14. Engelken F, Friedersdorff F, Fuller TF *et al*. Pre-operative assessment of living renal transplant donors with state-of-the-art imaging modalities: computed tomography angiography versus magnetic resonance angiography in 118 patients. *World J Urol* 2013; 31: 983–990
15. Paleologo G, Abdelkawy H, Barsotti M *et al*. Kidney dimensions at sonography are correlated with glomerular filtration rate in renal transplant recipients and in kidney donors. *Transplant Proc* 2007; 39: 1779–1781
16. Hugen C, Polcari A, Farooq A *et al*. Size does matter: donor renal volume predicts recipient function following live donor renal transplantation. *J Urol* 2011; 185: 605–609
17. Buturovic-Ponikvar J, Cerne S, Arnol M *et al*. Early kidney graft size and Doppler parameters are associated with kidney graft function at 1 year after transplantation. *Transplant Proc* 2010; 42: 4026–4029
18. Herts B, Sharma N, Lieber M *et al*. Estimating glomerular filtration rate in kidney donors: a model constructed with renal volume measurements from donor CT scans. *Radiology* 2009; 252: 109–116
19. Lenihan CR, Busque S, Derby G *et al*. Longitudinal study of living kidney donor glomerular dynamics after nephrectomy. *J Clin Invest* 2015; 125: 1311–1318
20. Lee JH, Won JH, Oh CK. Impact of the ratio of graft kidney volume to recipient body surface area on graft function after live donor kidney transplantation. *Clin Transplant* 2011; 25: E647–E655
21. Akoglu H, Yildirim T, Eldem G *et al*. Living donor kidney volume as a predictor of graft function: is there a role for proteinuria? *Transplant Proc* 2013; 45: 77–81
22. Song T, Fu L, Huang Z *et al*. Change in renal parenchymal volume in living kidney transplant donors. *Int Urol Nephrol* 2014; 46: 743–747
23. Taner T, Iqbal CW, Textor SC *et al*. Compensatory hypertrophy of the remaining kidney in medically complex living kidney donors over the long term. *Transplantation* 2015; 99: 555–559
24. Levey AS, Stevens LA, Schmid CH *et al*. A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009; 150: 604–612
25. DuBois D, DuBois E. Clinical calorimetry: tenth paper a formula to estimate the approximate surface area if height and weight be known. *Arch Intern Med* 1916; XVII: 863–871

26. Wang X, Vrtiska TJ, Avula RT *et al*. Age, kidney function, and risk factors associate differently with cortical and medullary volumes of the kidney. *Kidney Int* 2014; 85: 677–685
27. Davies DF, Shock NW. Age changes in glomerular filtration rate, effective renal plasma flow, and tubular excretory capacity in adult males. *J Clin Invest* 1950; 29: 496–507
28. Johnson S, Rishi R, Andone A *et al*. Determinants and functional significance of renal parenchymal volume in adults. *Clin J Am Soc Nephrol* 2011; 6: 70–76
29. Donadio C, Abdelkawy H, Grassi G. Echographic renal dimensions can predict glomerular filtration rate of potential living kidney donors. *Transplant Proc* 2010; 42: 1035–1039
30. Grassi G, Abdelkawy H, Barsotti M *et al*. Living kidney transplantation: evaluation of renal function and morphology of potential donors. *Transplant Proc* 2009; 41: 1121–1124
31. Chen CH, Shu KH, Cheng CH *et al*. Imaging evaluation of kidney using multidetector computerized tomography in living-related renal transplantation. *Transplant Proc* 2012; 44: 7–10
32. Delanaye P, Weekers L, Dubois BE *et al*. Outcome of the living kidney donor. *Nephrol Dial Transplant* 2012; 27: 41–50
33. Tan L, Tai BC, Wu F *et al*. Impact of Kidney Disease Outcomes Quality Initiative guidelines on the prevalence of chronic kidney disease after living donor nephrectomy. *J Urol* 2011; 185: 1820–1825
34. Mueller TF, Luyckx VA. The natural history of residual renal function in transplant donors. *J Am Soc Nephrol* 2012; 23: 1462–1466
35. Barri YM, Parker T III, Daoud Y *et al*. Definition of chronic kidney disease after uninephrectomy in living donors: what are the implications? *Transplantation* 2010; 90: 575–580
36. Jeon HG, Lee SR, Joo DJ *et al*. Predictors of kidney volume change and delayed kidney function recovery after donor nephrectomy. *J Urol* 2010; 184: 1057–1063
37. Halleck F, Diederichs G, Koehlitz T *et al*. Volume matters: CT-based renal cortex volume measurement in the evaluation of living kidney donors. *Transpl Int* 2013; 26: 1208–1216
38. Yakoubi R, Autorino R, Kassab A *et al*. Does preserved kidney volume predict 1 year donor renal function after laparoscopic living donor nephrectomy? *Int J Urol* 2013; 20: 931–934
39. Garg AX, Muirhead N, Knoll G *et al*. Proteinuria and reduced kidney function in living kidney donors: a systematic review, meta-analysis, and meta-regression. *Kidney Int* 2006; 70: 1801–1810
40. Young A, Storsley L, Garg AX *et al*. Health outcomes for living kidney donors with isolated medical abnormalities: A systematic review. *Am J Transplant* 2008; 8: 1878–1890
41. Boudville N, Prasad GV, Knoll G *et al*. Meta-analysis: risk for hypertension in living kidney donors. *Ann Intern Med* 2006; 145: 185–196