

A Study of Renal Outcomes in Obese Living Kidney Donors

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Background. Little is known about the long-term outcomes of obese living kidney donors (OLKDs). We undertook this study to describe renal outcomes of OLKDs several years after donation.

Methods. We invited 101 OLKDs for follow-up health evaluation.

Results. Thirty-six subjects (35.6%) completed evaluation at 6.8 ± 1.5 years postdonation. The mean estimated glomerular filtration rate (eGFR) using the abbreviated modification of diet in renal disease (MDRD) equation (MDRD-eGFR) at follow-up was 72.1 ± 16.3 (range: 42–106) mL/min per 1.73 m^2 , and 47.2% of subjects had an MDRD-eGFR of 30 to 59. The absolute decrease in MDRD-eGFR from the time of donation to follow-up was 27.2 ± 13.1 mL/min per 1.73 m^2 ($P < 0.001$ on paired t test), which represents a 29.2% drop in the serial MDRD-eGFRs. Seven subjects (19.4%) had microalbuminuria (30–300 $\mu\text{g}/\text{mg}$ creatinine). Subjects with microalbuminuria were more likely to have MDRD-eGFR of less than 60 mL/min per 1.73 m^2 ($P = 0.021$). Subjects whose body mass index was greater than or equal to $35 \text{ kg}/\text{m}^2$ ($n = 14$) were found to have an absolute decrement in MDRD-eGFR similar to those with body mass index less than $35 \text{ kg}/\text{m}^2$ (31.5 ± 15.6 and 24.7 ± 11.0 mL/min/ 1.73 m^2 , respectively; $P = \text{not significant}$). Fifteen (41.6%) were hypertensive at follow-up.

Conclusions. On medium-term follow-up, a large proportion of OLKDs will have a MDRD-eGFR of less than 60 mL/min per 1.73 m^2 , and the likelihood increases markedly among those who develop microalbuminuria. This raises concern for hyperfiltration injury. Furthermore, OLKDs experience a substantial incidence of hypertension. Caution is advised in selecting OLKDs pending further data on long-term outcomes.

Keywords: Living donor, Kidney transplantation, Obesity.

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Living donor kidney transplantation has been embraced as a treatment of end-stage renal disease based on the favorable balance of benefit afforded to the recipient and risk borne by the donor. The risk of donating a kidney seems to be min-

imal in a carefully selected individual, with multiple individual studies (1–5) and a meta-analysis (6) demonstrating lack of long-term adverse health effects of unilateral nephrectomy performed on a healthy individual.

However, the strong demand for live kidney donors has put pressure on the transplant community to allow willing donors to bear more risk and “push the envelope” of acceptability for donation. In the absence of data to indicate an excessive risk, many centers have accepted donor candidates who are theoretically less than ideal. The long-term safety of unilateral nephrectomy in such individuals with a more-than-minimal risk for development of chronic kidney disease (CKD) is not clear, because studies that have established the safety of the procedure were largely performed in an undifferentiated population.

Obesity has been found to be a common and strong risk factor for CKD (7–10), focal glomerulosclerosis (8), and end-stage renal disease (11). Hyperfiltration injury has been hypothesized to be pathogenic in obesity-related kidney disease (8). Therefore, it would seem plausible that a 50% reduction in renal mass in an obese individual could put this person at risk for adverse renal complications after donation. Experimentally, it has been shown that unilateral nephrectomy caused more renal injury in obese hyperlipidemic versus lean normolipemic Zucker rats (12). Clinical studies have also

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raised concern for outcomes of the solitary kidney state in obese individuals. Praga et al. reported on renal outcomes on 73 patients who had undergone unilateral nephrectomy for pathologic reasons with 13.6 ± 13.6 years follow-up. They found the proteinuria-free and chronic renal failure-free 10-year survival was only 40% and 70%, respectively, among the 14 obese patients (body mass index [BMI] >30 kg/m²), and this was substantially worse than the respective 93% and 98% 10-year survivals in nonobese patients ($P < 0.001$) (13). Although short-term follow-up (up to 1 year) studies of obese living kidney donors (OLKDs) have not revealed differences in glomerular filtration rate (GFR) compared with nonobese donors (14–16), the renal functional reserve capacity was lower in obese donors (16), and obesity was predictive of having GFR less than 60 mL/min per 1.73 m² during the first few months postdonation (15). Unfortunately, the long-term data on renal outcomes in obese donors are sparse (17–19). Among a cohort of 39 African American donors with a mean follow-up of 7.1 ± 1.6 years postdonation, we found that subjects whose BMI was greater than or equal to 35 kg/m² ($n=8$) experienced a greater decrement in estimated GFR (eGFR) than those with BMI less than 35 kg (20). A recent study did not find a higher incidence in long-term reduced renal in obese donors compared with nonobese donors, but their cohort included only 16 obese donors (BMI ≥ 30 kg/m²) and only 4% African Americans (21).

Given that the prevalence of obesity in the U.S. population is currently approximately 25% and projected to increase (22) and given that a substantial proportion of current live donors are obese, the lack of knowledge of specific risks for obese donors is an important public health issue. Further studies that examine the long-term safety of live kidney donation from obese individuals are greatly needed to help recipients, donors, and transplant teams weigh the risk of donation from such candidates. We undertook this study to describe the renal outcomes in a cohort of OLKDs several years after donation.

RESULTS

Table 1 summarizes the results of recruitment, which took place between December 2004 and December 2007. At the time of donation, 22 subjects had class I obesity, 12 sub-

jects had class II obesity, and two subjects (with BMIs of 41.2 and 41.7 kg/m²) had class III obesity. At the time of follow-up in the General Clinical Research Center (GCRC), five subjects were overweight (with BMIs of 25.7–29.6 kg/m²), 11 had class I obesity, 14 had class II obesity, and six (with BMIs of 40.4, 41.1, 43.1, 44.9, 46.4, and 49.1 kg/m²) had class III obesity. The subjects' mean BMI increased 1.6 ± 4.0 kg/m², with range -4.9 to 11.96 kg/m². Five subjects were no longer obese at follow-up. Among those who remained obese, two dropped by one category of severity, 19 remained in the same category of severity, eight increased by one category of severity, and two increased by two categories of severity.

Table 2 provides details of various baseline parameters that were available in our database for the study group (group 1), when compared with the group of OLKDs who were invited to participate but did not accept (group 2) and to the group of OLKDs who were not invited because they did not reside locally (group 3). As can be seen, the demographic, survival, and baseline clinical parameters at the time of donation were mostly similar in the study group and the other OLKD groups. The few notable exceptions were more advanced age and a higher proportion of individuals living in high-poverty zip code in the study participants versus group 2 and fewer males and more African Americans in the study group versus group 3.

Table 3 details the demographics and outcomes of interest in the group of subjects who completed the evaluation in the GCRC. It shows that the estimations of renal function and, therefore, the proportion of subjects with reduced renal clearance (eGFR or creatinine clearance <60 mL/min) vary dramatically depending on the estimation equation used. To assist in the interpretation of the results, in this table, we included data from the studies by Ibrahim et al. (5, 23) on similar outcomes in their cohorts of living donors who were not selected based on high BMI and who had long-term follow-up at the University of Minnesota GCRC. As can be seen, the BMI was, of course, much higher in our cohort. Although the mean blood pressures (BPs) at follow-up are similar, the OLKD cohort seemed to have higher rate of hypertension. Also, the OLKD cohort seemed to have a slightly higher proportion of subjects with renal clearances (eGFR or creatinine clearance) less than 60 mL/min by various estimation equations.

The follow-up modification of diet in renal disease (MDRD)-eGFR was 27.2 ± 13.1 mL/min per 1.73 m² less than the predonation value (P value < 0.001 on paired t test), which represents a 29.2% drop in the serial MDRD-eGFRs. Figure 1 plots the BMI at the time of donation and the absolute change in MDRD-eGFRs for the subjects. It shows a statistically nonsignificant trend for greater absolute loss of MDRD-eGFR with increasing BMI at the time of donation. Using linear regression, the slope estimate for β is -0.74 (95% confidence interval: -2.13 to 0.65) mL/min per 1.73 m² per 1 kg/m² ($P = \text{not significant [NS]}$), with correlation coefficient (r) = 0.185.

Subjects whose BMI was greater than or equal to 35 kg/m² ($n=14$) were found to have an absolute decrement in MDRD-eGFR similar to those with BMI less than 35 kg/m² (31.5 ± 15.6 and 24.7 ± 11.0 mL/min/1.73 m², respectively; $P = \text{NS}$) and a similar relative decrement of this parameter

TABLE 1. Recruitment results

Obese live kidney donors who donated during study period	199
Locally residing obese live kidney donors to whom letters were sent=invited subjects	101
Replies obtained	77
Refused to participate	26 (25.7% of those invited)
Agreed to participate	54 (53.5% of those invited)
Consented	39
Evaluated in GCRC	36 (35.6% of those invited and 18.1% of all OLKDs)

OLKD, obese live kidney donors; GCRC, General Clinical Research Center.

TABLE 2. Baseline characteristics and early renal function in study group, recruited OLKDs who did not participate, and nonrecruited OLKDs (nonlocally residing)

Characteristics	Group 1: study participants	Group 2: invited OLKDs who did not participate	Group 3: nonrecruited OLKDs (nonlocally residing)	P, group 1 vs. group 2	P, group 1 vs. group 3
Number of subjects	36	65	98	N/A	N/A
Age (yr) at donation	45.1±10.8	37.7±11.2	39.9±10.8	0.002	NS
Male	22.9%	37.7%	46.9%	NS	0.013
African American	45.7%	40.0%	23.5%	NS	0.013
BMI	34.2±3.38	34.9±4.2	35.4±5.6	NS	NS
Predonation serum creatinine	0.88±0.19	0.86±0.19	1.00±0.96	NS	NS
Predonation MDRD-eGFR	91±20.3	94.2±19.6	94.0±22.6	NS	NS
Unrelated to recipient	31.4%	24.6%	34.7%	NS	NS
Delayed or slow graft function in recipient	22.9%	12.7%	24.7%	NS	NS
Donor deaths	0	1	0	N/A	N/A
Donor residence in high-poverty zip code at donation	27.6%	8.9%	15.4%	0.033	NS
Median family annual income in donor zip code of residence at time of donation (in thousands of dollars)	\$50.5±\$19.3	\$46.7±\$14.7	49.1±17.5	NS	NS

Continuous values presented as mean±standard deviation.

BMI, body mass index; MDRD-eGFR, estimated glomerular filtration rate calculated using modification of diet in renal disease equation; OLKD, obese live kidney donors; GCRC, General Clinical Research Center; NA, not applicable; NS, not significant.

(32.2% and 27.5%, respectively; $P=NS$), similar proportion of subjects with MDRD-eGFR of less than 60 mL/min per 1.73 m² at follow-up (50.0% and 45.5%, respectively; $P=NS$), similar proportion of subjects with hypertension (35.7% and 45.5%, respectively; $P=NS$), and a similar proportion of subjects with microalbuminuria at follow-up (21.4% and 18.2%, respectively; $P=NS$).

The absolute drop in MDRD-eGFR was greater in African American subjects, when compared with non-African American subjects (33.3±9.6 and 22.7±12.7 mL/min/1.73 m², respectively; $P=0.016$). We found no difference in absolute decrement in MDRD-eGFR in male donors, when compared with female donors (27.2±12.3 and 27.2±13.6 mL/min/1.73 m², respectively; $P=NS$); in donors younger than 35 years, when compared with those aged 35 years or older (30.8±14.1 and 26.2±12.9 mL/min/1.73 m², respectively; $P=NS$); or in hypertensive, when compared with non-hypertensive subjects (30.7±11.1 and 24.9±14.1 mL/min/1.73 m², respectively; $P=NS$). Microalbuminuria was not associated with a greater drop in MDRD-eGFR from predonation to follow-up (21.2±13.3 vs. 28.4±13.0 mL/min/1.73 m², $p=NS$), although subjects with microalbuminuria were more likely to have an MDRD-eGFR below 60 mL/min per 1.73 m², when compared with those without microalbuminuria (85.7% vs. 37%, respectively; $P=0.021$). We found no association of magnitude of weight gain from predonation to the time of follow-up with absolute change in MDRD-eGFR ($r=0.109$ with $P=NS$). The absolute decline in MDRD-eGFR was similar among the subjects whose BMI increased by 10% or more from predonation to follow-up ($n=6$), when compared with those whose BMI did not increase to this degree (26.8±7.3 vs. 27.3±14.1 mL/min/1.73 m², $P=NS$).

Figure 2 plots the duration of time from pre to postdonation measurement of MDRD-eGFRs and the absolute change in MDRD-eGFRs for the subjects. It shows that the longer intervals between measurements were not associated with greater absolute loss of MDRD-eGFR. Using linear regression, the slope estimate for β is 0.64 (95% confidence interval: -2.47 to 3.74) mL/min per 1.73 m² per year between donation and follow-up ($P=NS$), with $r=0.072$.

DISCUSSION

This study provides descriptive data on medium-term renal outcomes of OLKDs. The study demonstrates that OLKDs demonstrate a modest drop in MDRD-eGFR in the years after kidney donation, with a large proportion being left with MDRD-eGFRs less than 60 mL/min per 1.73 m². Although we found that only a minority of the obese donors have microalbuminuria at follow-up, the presence of microalbuminuria was strongly associated with reduced renal clearance at follow-up. As can be seen in Table 2, the proportion of subjects with eGFR or creatinine clearance less than 60 mL/min and, therefore, conclusions about renal risk in the groups varied dramatically depending on which equation was used to calculate GFR or creatinine clearance. Still, it is somewhat reassuring that we found no evidence that higher BMIs or longer duration of follow-ups were associated with worse outcomes in this cohort.

A concerning finding of the study is that a large proportion of OLKDs are left with MDRD-eGFRs that are substantially less than 60 mL/min per 1.73 m². Although this level of renal clearance would be classified as stage 3 CKD (24) in nondonors, the significance of such MDRD-eGFRs in previ-

TABLE 3. Demographics and outcomes of interest at the time of follow-up evaluation in GCRC

	OLKDs in this study	University of Minnesota cohort of 255 live kidney donors (5)
Length of follow-up from donation to GCRC visit (yr)	6.8±1.5 (3.9–10.2)	12.2±9.2
Age at time of follow-up (yr)	52.6±10.9 (31.4–73.7)	52.9±9.9
Mean BMI (kg/m ²) at time of follow-up visit	35.8±5.3 (25.7–49.1)	29.3
Average SBP during GCRC visit (mm Hg)	122.0±13. (92–144)	121.8±14.6
Average DBP during GCRC visit (mm Hg)	77.3±7.4 (62–95)	73±8.9
SBP ≥140 or DBP ≥90 at GCRC visit	6 (16.7%)	14.4%
Diagnosed with hypertension (using antihypertensive drugs) before GCRC visit	11 (30.6%)	24.7%
Current diagnosis of hypertension (defined as use of antihypertensive medications or BP >140/90 at time of follow-up visit)	15 (41.6%)	
Undiagnosed hypertension	4 (11.1%)	
Urine albumin-to-creatinine ratio (μg/mg creatinine)	21.7±40.7 (0–192)	
Microalbuminuria	7 (19.4%) 6 of these subjects had MDRD-eGFR of less than 60 mL/min per 1.73 m ²	
Macroalbuminuria	0	
Serum creatinine (mg/dL)	1.17±0.26 (0.7–1.7)	1.1±0.2
Diagnosed with diabetes mellitus	2 (5.6%)	3.1%
Diagnosed with stroke	1 (2.8%)	
Diagnosed with myocardial infarction or coronary artery disease	0	
Diagnosed with atherosclerosis or arterial narrowing	2 (5.6%)	
Diagnosed with cardiovascular disease (myocardial infarction, coronary artery disease, stroke, atherosclerosis, or arterial narrowing)	3 (8.3%)	
MDRD-eGFR (mL/min/1.73 m ²)	63.0±15.3 Range, 42–103 7 (47.2%)<60	63.7±11.3
		University of Minnesota cohort of 112 live kidney donors (23)
MDRD-eGFR (mL/min/1.73 m ²)	63.0±15.3 Range, 42–103 7 (47.2%)<60	65±13 39.3%<60
MC-eGFR (mL/min/1.73 m ²)	77.0±18.5 Range, 43–115 7 (17.9%)<60	86±17 6.2%<60
Actual CG-Cl _{Cr} (mL/min/1.73 m ²)	76.7±21.5 Range, 43–133 9 (25%)<60	75±17 22.3%<60
Lean CG-Cl _{Cr} (mL/min/1.73 m ²)	45.6±12.9 Range, 25–90 32 (88.9%)<60, 4 (11.1%)<30	

Continuous values presented as mean±standard deviation (range from lowest to highest). Proportions presented as total number (percent of total number of subjects evaluated in GCRC). For comparison, we included similar outcomes at approximately 12-yr postdonation in two series of donors done at the University of Minnesota and reported by Ibrahim et al. (5, 23).

OLKD, obese live kidney donors; GCRC, General Clinical Research Center; BMI, body mass index; eGFR(MDRD), estimated glomerular filtration rate calculated using modification of diet in renal disease equation; CG-Cl_{Cr}, Cockcroft-Gault creatinine clearance; MC, Mayo Clinic; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.

ous kidney donors is less clear, considering reports indicating that the GFR after uninephrectomy should settle at approximately 75% of the two-kidney baseline (1, 2, 6, 23, 25). Thus, the relative loss of GFR from predonation to follow-up of 29.2% in our group of OLKDs does not seem to be excessive. However, we found the association of microalbuminuria

with MDRD-eGFR less than 60 mL/min per 1.73 m² to be concerning, because one would expect the pathophysiology to involve hyperfiltration injury and would, thus, expect it to be accompanied by urinary albumin excretion. On the other hand, arguing against this scenario, no subjects had macroalbuminuria, and microalbuminuria was not associated

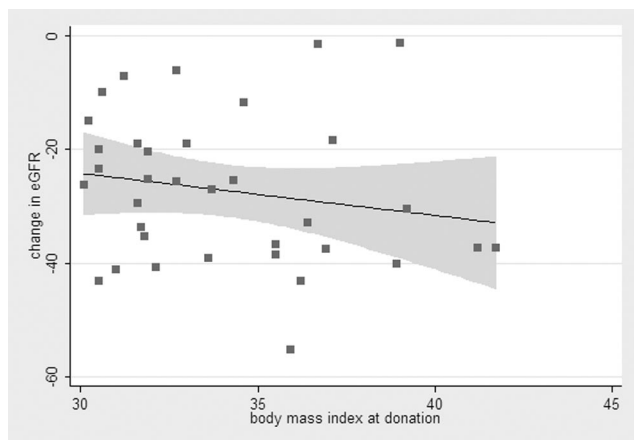


FIGURE 1. Change in MDRD-eGFR predonation to follow-up in GCRC plotted against body mass index at time of donation (small solid boxes), with linear regression line (solid black line) and 95% confidence intervals (gray area). eGFR: estimated glomerular filtration rate calculated using modification of diet in renal disease equation. MDRD, modification of diet in renal disease; eGFR, estimated glomerular filtration rate; GCRC, General Clinical Research Center.

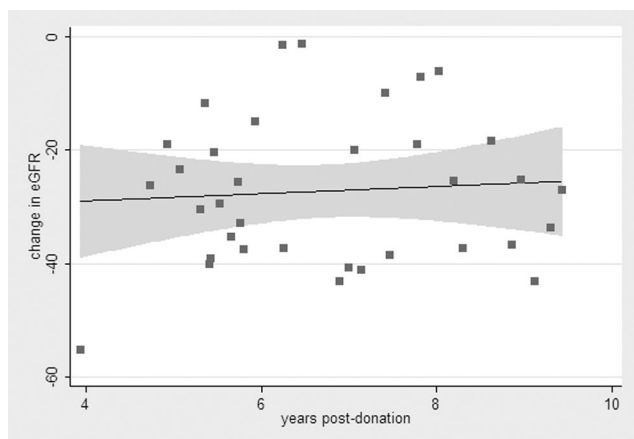


FIGURE 2. Change in MDRD-eGFR predonation to follow-up in GCRC plotted against years between measurements for individual study subjects (small solid boxes), with linear regression line (solid black line) and 95% confidence intervals (gray area). eGFR: estimated glomerular filtration rate calculated using modification of diet in renal disease equation. MDRD, modification of diet in renal disease; eGFR, estimated glomerular filtration rate; GCRC, General Clinical Research Center.

with a greater drop in MDRD-eGFR. In addition, the finding that longer intervals between measurements were not associated with greater absolute loss of MDRD-eGFR also argues against progressive CKD in this cohort. Thus, it remains unclear whether these relatively low renal clearances may simply be due to reduced renal mass or due to inaccuracies in using serum creatinine to identify individuals with CKD, or whether a reduction of MDRD-eGFR to this level may indicate threatening renal pathologic condition.

From the cardiovascular perspective, obesity has been linked to an increased risk for diabetes mellitus, hyperlipid-

emia and hypertension, and cardiovascular disease (26, 27). Given the clear associations of cardiovascular disease and any degree of kidney dysfunction (28–39) (including microalbuminuria), the development of renal dysfunction after nephrectomy would be especially concerning in relationship to cardiovascular risk in this population. The finding that nearly half of the donors had developed hypertension in the several years since donation is concerning with respect to their cardiovascular disease risk. Although no subjects reported the development of heart disease, there was a nonnegligible incidence of diabetes and vascular disease (stroke and atherosclerosis/arterial narrowing) in the cohort. This study, certainly, does not adequately address this important issue of cardiovascular risk in OLKDs, and further studies on whether kidney donation increases cardiovascular risk in OLKDs are clearly needed.

It is important to appreciate the limitations of our study. First, our assessment of renal function and our ability to reliably identify individuals with CKD was limited by our reliance on serum creatinine, because the inaccuracies of using the commonly used serum creatinine-based estimation equations in individuals without known CKD has been well described (23, 40). Clearly, all the renal function estimation techniques that we used have important limitations in this population. The wide fluctuations in the rate of the outcome of renal clearances below 60 mL/min—from 17.9% to 88.9%—and the differing conclusions that would, thus, be made about the risk of reduced renal function in this cohort further demonstrate the vagaries of estimating renal function using serum creatinine in this population. Second, the lack of an internal control group requires us to use data in the literature on cohorts of live donors who were not selected based on high BMI, and this limits the interpretation of the findings. Because of funding limitations and because of the substantial expenditure of resources that was generally needed to recruit a donor to come to the GCRC and complete the study procedure, we opted to concentrate our efforts on getting as many obese donors as possible. Given our finite resources, we believed that a descriptive study on a larger cohort of obese donors was more valuable than a comparative study on a smaller group of obese donors and their controls. Finally, with only 35.6% of invited subjects completing the evaluation in the GCRC, the broader applicability of our findings to the larger OLKD population is uncertain, even though our comparison of the baseline parameters of those OLKDs who participated versus those who did not participate did not reveal major differences. It should be noted that this critical limitation has affected nearly all long-term donor follow-up studies, including the recent landmark study by Ibrahim et al. (5) that achieved a 14.3% participation rate of follow-up in their GCRC with iohexol GFR measurements.

In conclusion, this study demonstrates that a large proportion of OLKDs will be left with an MDRD-eGFR of less than 60 mL/min per 1.73 m² and that the likelihood increases markedly among those who develop microalbuminuria, thus raising concern for hyperfiltration injury. We conclude that live kidney donation from obese individuals should be undertaken with great caution, because such hyperfiltration injury could put donors at risk for progressive CKD. The finding that a substantial percentage of OLKDs will develop hypertension within several years of donation further heightens

concern for their outcomes. However, given that the majority of OLKD donors do not suffer dramatic drops in GFR and do not develop microalbuminuria, there is clearly a need for further study to guide the selection and counseling of potential OLKD donors. The study also suggests that OLKD donors should be closely monitored for hypertension and CKD. Currently, our center considers a BMI of 35 kg/m² or higher to be a strong relative contraindication to donation and a BMI of 40 kg/m² or higher to be an absolute contraindication to donation. We strongly believe that living kidney donation from an obese individual should be permitted only after careful informed consent, which must include a frank discussion of the uncertain long-term risk of donation in obese individuals along with counseling to control weight and maintain appropriate medical follow-up over the years and decades after donation.

MATERIALS AND METHODS

After obtaining approval from the University of Maryland Institutional Review Board, locally residing OLKD donors who donated at University of Maryland Medical System between September 11, 1996, and March 15, 2002, inclusive, were recruited to come to the University of Maryland GCRC for a health questionnaire and measurement of height, weight, three BPs (using a standardized measurement technique [41]), urine albumin/microalbumin, urine creatinine, and serum creatinine. We defined OLKD as having a BMI of at least 30 kg/m². It is important to note that the study procedures involved prospective data collection on a cohort of individuals who had already donated a kidney. Thus, the institutional review board approval applied only to the recruitment and data collection on prior kidney donors. The selection and acceptance of kidney donors were not part of the study procedures, but these were clinical and ethical decisions that were made by the transplant team (individual clinicians before November 7, 2001, and a donor ethics committee since this date) based on their understanding of the prevailing standard of care at that time. During the years that the subjects donated their kidney, our center did not have a firm rule regarding what degree of obesity would be an absolute contraindication for donation. Although our team's evaluation of such individuals evolved over the years that the subjects donated, we generally demanded that all such individuals should have a 2-hr glucose with oral glucose tolerance test as part of the predonation evaluation; and we generally considered candidates with a fasting blood glucose of 126 mg/dL or more on at least two occasions or with an oral glucose tolerance test 2-hr glucose of 200 mg/dL or more not to be acceptable for donation. In general, if the CrCl was greater than or equal to 80 mL/min, the urine protein-to-creatinine ratio was less than 200 mg/g, and the urinary sediment examination was normal, then the donor candidate passed the test for absence of evidence of CKD. However, we often permitted donation in individuals with lower clearances if they were older than 50 years and if their estimated GFR fell within one standard deviation of the mean for the donor's age group. We did not routinely measure predonation urine albumin levels.

A letter of introduction was mailed to the potential subjects, and it included a preaddressed, postage-paid reply form that allowed them to decline participation. If we did not receive the reply form within 2 weeks, a study coordinator then contacted the subjects by phone to invite donors to participate in the study. Predonation serum creatinine and early postdonation serum creatinine values were obtained from a computerized database.

We estimated renal function at the time of follow-up using four different equations:

1. The abbreviated MDRD equation estimated GFR (MDRD-eGFR)

$$\text{MDRD-eGFR} = 186 \times \text{SCr}^{-1.54} \times \text{age}^{0.203} \times 0.742 \text{ (if female)}$$

$$\times 1.210 \text{ (if black) (42).}$$

2. Mayo Clinic quadratic formula as described by Rule et al. (40) to estimate GFR (Mayo Clinic-eGFR)

$$\text{GFR} = \exp \left(1.911 + \frac{5.249}{\text{SCr}} - \frac{2.114}{\text{SCr}^2} - 0.00686 \times \text{age} - 0.205 \text{ [if female]} \right).$$

If SCr was less than 0.8 mg/dL, then a value of 0.8 was used.

3. The body surface area (BSA)-adjusted Cockcroft-Gault formula for creatinine clearance using actual body weight (actualCG-Cl_{cr}): $([140 - \text{age}] \times \text{actual body weight} / [72 \times \text{SCr}]) \times (0.85, \text{ if female})$. We adjusted the creatinine clearance estimate for BSA by multiplying by 1.73 m²/BSA in m².
4. The BSA-adjusted Cockcroft-Gault formula for creatinine clearance using calculated lean body weight than actual body weight (leanCG-Cl_{cr}).

Daily albumin excretion rate was estimated using the urine albumin-to-creatinine ratio, defined as the ratio of urine albumin concentration to creatinine concentration expressed as microgram of albumin per milligram of creatinine. Microalbuminuria was defined as urine albumin-to-creatinine ratio of 30 to 300 μg/mg creatinine and macroalbuminuria as more than 300 μg/mg creatinine. Hypertension was defined as treatment with hypertensive drugs for an indication of hypertension or the average systolic BP at the GCRC of 140 mm Hg or more, or the average diastolic BP at the GCRC of 90 mm Hg or more. Categories of severity of obesity based on BMI are as follows: class I obesity, 30 to 34.99 kg/m²; class II obesity, 35 to 39.99 kg/m²; and class III obesity, 40 kg/m² or more. Overweight was defined as BMI of 25 to 29.99 kg/m². Diagnoses of diabetes mellitus and cardiovascular outcomes were based strictly on self-report by subjects. We obtained donor survival status and median household family annual income (in 1999 dollars) and poverty level for a donor's zip code at the time of donation as described previously (20).

Statistical Methods

Continuous variables were reported as mean ± standard deviation and were compared using Student *t* tests. Categorical variables were reported as absolute numbers or percentages and will be compared using 2 × 2 contingency tables and χ² tests. Correlation between two continuous values was estimated with Pearson correlation coefficient (*r*), and slopes were calculated using linear regression. *P* values less than 0.05 were considered statistically significant.

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