Obesity increases the risk of end-stage renal disease among living kidney donors

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Determining candidacy for live kidney donation among obese individuals remains challenging. Among healthy non-donors, body mass index (BMI) above 30 is associated with a 16% increase in risk of end-stage renal disease (ESRD). However, the impact on the ESRD risk attributable to donation and living with only one kidney remains unknown. Here we studied the risk of ESRD associated with obesity at the time of donation among 119 769 live kidney donors in the United States. Maximum follow-up was 20 years. Obese (BMI above 30) live kidney donors were more likely male, African American, and had higher blood pressure. Estimated risk of ESRD 20 years after donation was 93.9 per 10 000 for obese; significantly greater than the 39.7 per 10 000 for non-obese live kidney donors. Adjusted for age, sex, ethnicity, blood pressure, baseline estimated glomerular filtration rate, and relationship to recipient, obese live kidney donors had a significant 86% increased risk of ESRD compared to their non-obese counterparts (adjusted hazard ratio 1.86; 95% confidence interval 1.05–3.30). For each unit increase in BMI above 27 kg/m^2 there was an associated significant 7% increase in ESRD risk (1.07, 1.02–1.12). The impact of obesity on ESRD risk was similar for male and female donors, African American and Caucasian donors, and across the baseline estimated glomerular filtration rate spectrum. These findings may help to inform selection criteria and discussions with persons considering living kidney donation.

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The demand for transplantable kidneys remains high, and living kidney donors (LKDs) continue to be a critical source of organs, facilitating both timely transplantation and excellent outcomes.[1] Historically, LKDs were free of isolated medical abnormalities (IMAs) at the time of donation. However, in response to the organ shortage and changes in the general population, transplantation centers now commonly approve donors with IMAs such as obesity.[2–7] Currently, >25% of all LKDs are considered obese at the time of donation compared with <8% in the 1970s.[6] Relaxation of selection criteria to include obese LKDs has occurred despite a paucity of supporting safety data.

The National Institutes of Health defines obesity as a body mass index (BMI) of >30 kg/m^2.[8] According to data from the National Health and Nutrition Examination Survey, the prevalence of obesity has increased in the United States from 27.5% in 1999 to 36.5% in 2011 to 2014,[9] and in parallel with these general trends, the mean BMI of LKDs in the United States has increased over time, from 24.3 kg/m^2 in the 1970s to 27.3 kg/m^2 in the 2000s.[6] Obesity is strongly correlated with increased risk for cardiovascular disease, diabetes mellitus, and chronic kidney disease (CKD).[10–14] Data from a population-based, case−control study conducted in Sweden and 2 US studies (The Framingham Offspring cohort and the Hypertension Detection and Follow-up Program) have shown that higher weight for height is associated with an increased risk of new-onset CKD.[15–17]

Beyond CKD, obesity has been linked with increased risk for end-stage renal disease (ESRD). In the general population, Hsu *et al.* found that compared with persons considered normal weight (BMI: 18.5−24.9 kg/m^2), obese individuals (BMI ≥30 kg/m^2) were at 3.57-fold higher risk of developing ESRD (adjusted risk ratio [RR]: 3.57; 95% confidence interval [CI]: 3.05−4.18).[18] However, donors are not drawn from the general population, but are very carefully screened, and the impact of obesity might be different in these healthier individuals. In a multi-cohort study of individuals healthy enough to be potential donors (healthy nondonors), the adjusted risk of ESRD associated with obesity was only 1.16 (95% CI: 1.04−1.29).[19] The true risk among living donors likely falls somewhere in between these estimates; living donors are healthy at baseline, but then they lose half of their nephron mass, and the impact of obesity in this context remains unclear.

Unfortunately, the 4 recent major studies of LKDs that establish the existing evidence of living donor risk for ESRD were done in the context of standard selection criteria, healthy and IMA-free, and did not address the impact of obesity, highlighting a remaining gap in our knowledge of living donor outcomes.[20–23] To better understand ESRD risk in obese LKDs, and to better inform selection criteria for potential obese kidney donors, we performed a national study of the association between BMI and postdonation risk of ESRD among LKDs, adjusting for potential confounders and exploring the potential effect modifiers of this association.

RESULTS

The mean BMI among obese donors was 32.7 kg/m^2 compared with 24.8 kg/m^2 among nonobese donors. At the time of donation, obese and nonobese living donors were similar with regard to age, baseline estimated glomerular filtration rate (eGFR), smoking history, insurance status, and relationship to the recipient. However, compared with their nonobese counterparts, obese living donors were more commonly men (43.1% vs. 39.2%), African American (16.4% vs. 11.1%), and had higher mean systolic (124.1 mm Hg vs. 119.9 mm Hg) and diastolic (75.6 mm Hg vs. 72.9 mm Hg) blood pressures (Table 1).

The cumulative incidence of ESRD per 10,000 living donors was 3-fold greater among LKDs who were obese at the time of donation compared with their nonobese counterparts. At 20-years postdonation, obese LKDs had a cumulative incidence of ESRD of 93.9 per 10,000 compared with 39.7 per 10,000 among their nonobese living donor counterparts (Table 2 and Figure 1; Supplementary Table S1 for absolute numbers).

After controlling for multiple risk factors, including age at donation, ethnicity, sex, baseline eGFR and blood pressure, and relationship to the recipient, the only potentially modifiable factor that remained independently associated with an increased risk for development of ESRD postdonation was obesity. Compared with nonobese LKDs, obese LKDs had a 1.9-fold increased risk of ESRD postdonation (adjusted hazard ratio [aHR]: 1.86; 95% CI: 1.05−3.30; $P = 0.04$) (Table 3). This finding was consistent with the results seen with analyses performed only among donors who had complete data available (Table 4). On stratified analyses, for each 1-U increase in BMI >27 kg/m^2, there was an associated 7% increase in the risk of ESRD (aHR: 1.07; 95% CI: 1.02−1.12; $P = 0.004$). This same effect was not observed for those with a BMI ≤27 kg/m^2. The potential for effect modification was explored using interaction term analyses. No significant interactions were observed between obesity and sex (aHR: 1.09, 95% CI: 0.51−2.34; $P = 0.82$), African American ethnicity (aHR: 0.89; 95% CI: 0.41−1.92; $P = 0.75$), relationship to the recipient (aHR: 1.15; 95% CI: 0.45−2.93; $P = 0.76$), or eGFR (aHR: 1.00; 95% CI: 0.98−1.02; $P = 0.99$).

DISCUSSION

In this national study of 119,769 LKDs linked to Centers for Medicare and Medicaid Services (CMS) data for ascertainment of ESRD, we estimated that approximately 40 nonobese and 94 obese living donors per 10,000 developed ESRD within 20 years of kidney donation. Although the absolute risk for postdonation ESRD was low, donor obesity was independently associated with an increased risk for ESRD 20 years after kidney donation. Compared with nonobese living donors, obese donors had a 1.9-fold increased risk for postdonation ESRD, and for each 1-U increase in predonation BMI >27 kg/m^2 there was an associated 7% increased risk of ESRD postdonation.

Studies from the general US population have demonstrated the relationship between excess weight or obesity and risk of ESRD. However, these cohorts included individuals with baseline comorbidities such as diabetes and hypertension, which are conditions known to be along the CKD and/or ESRD causal pathway.[18,24] Although our cohort of LKDs was free of diabetes and hypertension at the time of donation,

Table 1 | Demographics of living kidney donors by obesity status at time of donation*

Donor characteristic	Obese (BMI ≥30 kg/m^2) (n = 20,588)	Nonobese (BMI <30 kg/m^2) (n = 58,004)	Missing BMI (n = 41,177)
Age, yrs, mean ± SD	40.7 ± 10.7	40.8 ± 11.4	38.5 ± 10.9
Sex, no. (%)			
Male	8,864 (43.1)	22,763 (39.2)	17,744 (43.1)
Female	11,724 (56.9)	35,241 (60.8)	23,433 (56.9)
Ethnicity			
African American	3,374 (16.4)	6,450 (11.1)	5,485 (13.3)
Non-African American	17,214 (83.6)	51,554 (88.9)	35,692 (86.7)
BMI,† kg/m^2, mean ± SD	32.7 ± 3.2	24.8 ± 2.9	-
Systolic BP,† mean ± SD	124.1 ± 13.1	119.9 ± 13.3	121.2 ± 14.0
Diastolic BP,† mean ± SD	75.6 ± 9.3	72.9 ± 9.4	74.1 ± 9.3
eGFR,† ml/min/1.73 m^2, mean ± SD	96.8 ± 18.9	97.2 ± 18.5	95.5 ± 20.0
Ever smoked cigarettes†	3,192 (15.5)	8,926 (15.4)	278 (0.7)
Insured†	8,981 (43.7)	25,996 (44.8)	1,360 (3.3)
Related to recipient†	12,953 (62.9)	35,482 (61.2)	34,124 (82.9)

BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate.
*From October 1, 1987 to June 30, 2013.
†Not collected for the entire cohort.

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