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

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**DISCLOSURES**

- **JEL** – NIH/NIDDK (K23-DK103918); AST Faculty Development Grant; Member, UNOS Living Donor Committee; Member, AST KPCOP Executive Committee
- **RSG** – None
- **KLL** – Member, AST LCOP Executive Cmte; Chair, UNOS Living Donor Committee; Co-Chair, KDIGO ‘Guideline for the Evaluation & Care of Living Donors’; NIH/NIDDK R01: ‘Long-Term Health Outcomes After Live Kidney Donation’; Steering Cmte, SRTR ‘Living Donor Collective’

Conflicts of Interest: None

**WHY DO WE ACCEPT LIVING DONORS?**

Need for donated kidneys increasingly outpaces supply

*OPTN/SRTR Annual Data Report 2015; Am J Transpl 2017; 15*  

- *Active*
- *Inactive*
- *All*

Consensus Conference on Best Practices in Live Kidney Donation: Recommendations to Optimize Education, Access, and Care

Meeting Report  

*[AST COP, Am J Transplant 2015; 10:1656]*

“Live donor kidney transplantation is the **best treatment option** for most patients with late-stage chronic kidney disease”
"The only remaining problem was the ethical decision concerning the removal of a healthy organ from a normal person for the benefit of someone else."
Joseph Murray, Nobel Lecture, December 1990

**BALANCING ACT**

Living donation raises complex considerations

**DONOR RISKS**

- Short-term
- Long-term
- Medical
- Psychosocial / financial

**BENEFITS**

- Improved recipient health
- Psychosocial benefits of altruism

**LDKT HAS DECLINED DESPITE GROWING NEED**

Reasons for decline likely multi-factorial, but may include uncertainty about donor risks

**Moving from Intuition to Data: Building the Evidence to Support and Increase Living Donor Kidney Transplantation**


Focal points for future research to define effective strategies for increasing access to living donor kidney transplantation

Further Commentary: www.medpagetoday.com/nephrology/kidneytransplantation/67351
VARIATION IN ACCEPTABLE BMI_THRESHOLDS

Prior Guidelines

“Patients with a BMI 35 kg/m² should be discouraged from donating, especially when other comorbid conditions are present.”
  • Amsterdam Forum, Transplantation 2005; 79:S53

“We recommend that patients with BMI>30 kg/m² reduce weight before donation…”
  • RBP, Nephrol Dial Transplant 2015; 30:1790

VARIATION IN U.S. CENTER PRACTICE

2017 KDIGO GUIDELINE

Obesity
11.2: Body mass index (BMI) should be computed based on weight and height measured before donation, and classified based on World Health Organization (WHO) criteria for the general population or race-specific categories.
11.3: The decision to approve donor candidates with obesity and BMI >30 kg/m² should be individualized based on demographic and health profile in relation to the transplant program’s acceptable risk threshold.

Basis: 1) systematic review (ERT); 2) de novo evidence generation

Projected ESRD by BMI, Healthy Persons

[The KDIGO WG, Lentine et al. Transplantation 2017; 101:S1-S109]

[Naik/Lentine Am J Transpl 2017; In Press]

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

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University of Alabama at Birmingham School of Medicine, Comprehensive Transplant Institute, Birmingham, Alabama; CUA; Johns Hopkins University School of Medicine, Baltimore, Maryland, USA and University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA

Determining candidacy for live kidney donation among obese individuals remains challenging. Among healthy non-donors, body mass index (BMI) >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. In this US study, we studied the risk of ESRD associated with obesity at the time of donation among 119,769 live kidney donors (LKDs) (1987-2013). Maximum follow-up was 20 years (IQR:6.0-16.0). Obese (BMI>30) LKDs 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 and 39.7 per 10 000 for non-obese LKDs (p < 0.001). Adjusted for age, sex, ethnicity, blood pressure, baseline estimated glomerular filtration rate (eGFR), and relationship to recipient, obese LKDs had an 86% increased risk of ESRD compared to their non-obese counterparts (aHR:1.86; 95%CI:1.05-3.30, p=0.04). For each unit increase in BMI >27kg/m², there was an associated 7% increase in ESRD risk (aHR:1.07, 95%CI:1.02-1.12, p=0.004). The impact of obesity on ESRD risk was similar for male and female donors, African American and Caucasian donors, and across the baseline eGFR spectrum. These findings may help to inform selection criteria and discussions with persons considering living kidney donation.

STUDY METHODS

• Scientific Registry of Transplant Recipients (SRTR) – 10/1/87 to 6/30/2013
  • 119,769 previous living kidney donors were identified
  • Median follow-up 10.7 years (IQR: 6.0-16.0 years; max 26.8 years)

• Missing data: the probability of a particular set of variables missing for an individual was assumed to not depend on the values themselves, conditional on the observed values of other variables
  • Utilized chained equations
  • 20 imputation run, each with 20 burn-in periods, and trace file plots used to assess convergence of the imputations

• Donors were defined as obese at the time of donation if their BMI was ≥30kg/m²

STUDY METHODS

• Linkage to Medical Evidence Form (CMS 2728) permitted ascertainment of ESRD
  • Defined as earliest initiation of maintenance dialysis, placement on the renal transplant waiting list, or receipt of a living or deceased donor kidney transplant

• Survival analyses were performed among the complete cases and the imputed data (estimating parameters from all imputed datasets and adjusting coefficients and standard errors for variability between imputations
  • Adjusted for donor age, sex, race, blood pressure, eGFR, relationship

• Cumulative incidence of ESRD was estimated using KM methods

DEMOGRAPHICS

<table>
<thead>
<tr>
<th>Donor characteristic</th>
<th>Obese (BMI ≥ 30 kg/m²)</th>
<th>Non-obese (BMI &lt; 30 kg/m²)</th>
<th>Missing BMI (N=41,177)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>40.7 (10.7)</td>
<td>40.8 (11.4)</td>
<td>38.5 (10.9)</td>
</tr>
<tr>
<td>Sex, %()</td>
<td>8,864 (43.1)</td>
<td>22,763 (39.2)</td>
<td>17,744 (39.1)</td>
</tr>
<tr>
<td>Male</td>
<td>11,274 (56.9)</td>
<td>35,241 (60.8)</td>
<td>23,433 (60.9)</td>
</tr>
<tr>
<td>African American</td>
<td>3,374 (16.4)</td>
<td>6,450 (11.1)</td>
<td>5,485 (13.3)</td>
</tr>
<tr>
<td>Female</td>
<td>17,214 (83.6)</td>
<td>51,554 (88.9)</td>
<td>35,692 (86.7)</td>
</tr>
<tr>
<td>BMI, kg/m², mean (SD)*</td>
<td>32.7 (9.2)</td>
<td>24.8 (2.9)</td>
<td>24.8 (2.9)</td>
</tr>
<tr>
<td>Systolic BP, mean (SD)*</td>
<td>124.1 (13.1)</td>
<td>119.9 (13.3)</td>
<td>119.9 (13.3)</td>
</tr>
<tr>
<td>Diastolic BP, mean (SD)*</td>
<td>75.6 (9.3)</td>
<td>72.9 (9.4)</td>
<td>72.9 (9.4)</td>
</tr>
<tr>
<td>eGFR-mL/min/1.73m², mean (SD)*</td>
<td>96.8 (18.8)</td>
<td>97.2 (18.9)</td>
<td>97.2 (18.9)</td>
</tr>
<tr>
<td>Ever smoked cigarettes*</td>
<td>3,192 (15.5)</td>
<td>8,926 (15.4)</td>
<td>278 (0.7)</td>
</tr>
<tr>
<td>Insured*</td>
<td>8,981 (43.7)</td>
<td>35,482 (61.2)</td>
<td>1,360 (3.3)</td>
</tr>
<tr>
<td>Related to recipient*</td>
<td>12,953 (62.9)</td>
<td>35,482 (61.2)</td>
<td>34,124 (82.3)</td>
</tr>
</tbody>
</table>
**Study Summary**

- Approximately 40 non-obese and 94 obese living donors per 10,000 developed ESRD within 20 years of kidney donation.
- While the absolute risk for post-donation ESRD was low, donor obesity was independently associated with increased risk for ESRD 20 years after donation.
- Compared to non-obese living donors, obese donors had a 1.9-fold increased risk for post-donation ESRD.
- For each 1 unit increase in pre-donation BMI >27 kg/m² there was an associated 7% increased risk of ESRD post-donation.

**Acknowledgements**

**Study Co-Authors**

- Dorry L. Segev, Rhiannon D. Reed, Allan Massie, Paul A. MacLennan, Deirdre Sawinski, Vineeta Kumar, Shikha Mehta, Roslyn B. Mannon, Robert Gaston, Cora E. Lewis.
CANDIDACY FOR LD TRANSPLANTATION

Table 2. Criteria for Transplantation

<table>
<thead>
<tr>
<th>Donor:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Two normal kidneys</td>
<td></td>
</tr>
<tr>
<td>(2) Normal lower urinary tract</td>
<td></td>
</tr>
<tr>
<td>(3) Absence of infection</td>
<td></td>
</tr>
<tr>
<td>(4) Sufficient understanding</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recipient:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Irreversible terminal disease</td>
<td></td>
</tr>
<tr>
<td>(2) Normal lower urinary tract</td>
<td></td>
</tr>
<tr>
<td>(3) Infection, if present, minimal or controllable</td>
<td></td>
</tr>
<tr>
<td>(4) Inactive primary renal disease</td>
<td></td>
</tr>
</tbody>
</table>

*Mortality risk is not greater than:
- General population over decades
- Matched healthy controls over 10-15 years*

*Renal risk likely increases after donation
- Greatest in donors already at increased risk
- Risk increases with time post donation
- Risk is affected by events that occur after donation
- Overall risk reflects the interrelationships of multiple variables

WHAT DO WE ALREADY KNOW ABOUT LD RISK?

A LOT

ESRD RISK IN LIVING KIDNEY DONORS

Table 2. Risk factors for ESRD in living kidney donors

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>aHR*</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (at age 40)</td>
<td>1.88 (95% CI, 1.50 to 2.35)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Black race (at age 40)</td>
<td>2.94 (95% CI, 2.25 to 3.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age per 10 yr: nonblack</td>
<td>1.40 (95% CI, 1.23 to 1.59)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age per 10 yr: black</td>
<td>0.88 (95% CI, 0.72 to 1.09)</td>
<td>0.3</td>
</tr>
<tr>
<td>BMI per 5 kg/m²</td>
<td>1.61 (95% CI, 1.29 to 2.00)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>First-degree biologically related to recipient</td>
<td>1.70 (95% CI, 1.24 to 2.34)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

*Male sex and greater BMI were associated with higher risk of ESRD both (P=0.001). Older age was associated with higher risk of ESRD in nonblack male donors (P=0.001), but the association between age and risk was not statistically significant in black donors (P=0.1). Donors who were closely related to their recipient had higher risk of ESRD (P<0.01).


ESRD RISK IN LIVING KIDNEY DONORS

Distribution of predicted ESRD in live donors

CONTEXT IN UNDERSTANDING LD OUTCOMES

- A significant amount of information, potentially available at the time of listing, was not reported to the OPTN.
- Of 441 kidney donors listed for transplant:
  - 169 had information allowing determination of interval from donation to listing.
  - 99 (22% of the total) had information on the donor-recipient relationship and ESRD etiology.
  - 87 were related to their recipient.
  - Among the 87, only a minority (23%) of donor-recipient pairs shared ESRD etiology (mostly HTN).

QUALITY OF DATA FROM WHICH TO BUILD PREDICTIVE MODELS?

- Systematic review of 8 donor nephrectomy studies – no association of BMI and perioperative complications
- Linkage of OPTN registry and administrative data from a US academic consortium – BMI >30 kg/m² associated with 55% increase in risk of severe (Clavien 4/5) complications (aHR 1.55, 95% CI 1.21–1.98)

A GROWING CONCERN

OTHER CONSIDERATIONS?

- Perioperative Complications
  - Systematic review of 8 donor nephrectomy studies – no association of BMI and perioperative complications
  - Linkage of OPTN registry and administrative data from a US academic consortium – BMI >30 kg/m² associated with 55% increase in risk of severe (Clavien 4/5) complications (aHR 1.55, 95% CI 1.21–1.98)
**Approach to the Obese Donor Candidate**

- Comprehensive assessment of full demographic and health profile (e.g. age, sex, race, BP, GFR, albuminuria, smoking, etc)
- Surgeon/clinician assessment of body habitus (weight distribution, waist-to-hip ratio) -> judgement on technical & perioperative risks
- Pending creation of an updated tool for integrated, tailored pre- and post-donation ESRD risk
  - Predonation ESRD risk tool prediction
  - Consider comparing Postdonation risk tool (recognizing: limited covariates)

![ESRD Risk Tool for Kidney Donor Candidates](transplantmodels.com)