

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

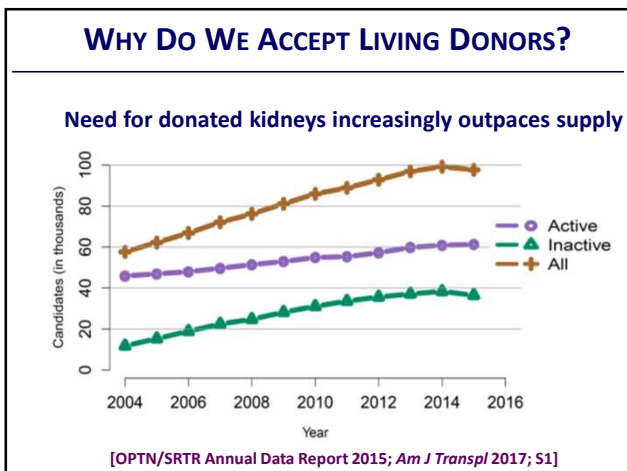
[Kidney Int.](#) 2017; 91:699-703

Jayme E. Locke, MD, MPH – University of Alabama at Birmingham
 Robert S. Gaston, MD – University of Alabama at Birmingham
 Moderator – Krista L. Lentine MD, PhD, Saint Louis University

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 LDCOP 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



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”

BALANCING ACT

“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

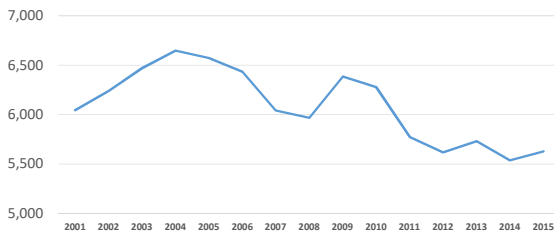
- Medical
- Psychosocial / financial



BENEFITS

- Improved recipient health
- Psychosocial benefits of altruism

LDKT HAS DECLINED DESPITE GROWING NEED

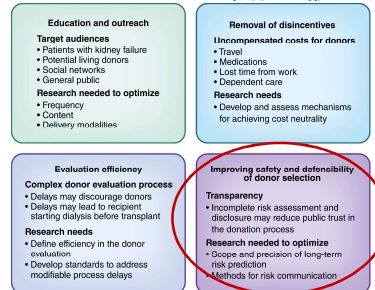


Reasons for decline likely multi-factorial, but may include **uncertainty about donor risks**

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

Further Commentary: www.medpagetoday.com/nephrology/kidneytransplantation/67351

Krista L. Lentine* and Didier Mandelbrot† Clin J Am Soc Nephrol 12: ●●●-●●●, doi: <https://doi.org/10.2215/CJN.07150717>



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

VARIATION IN ACCEPTABLE BMI THRESHOLDS

Prior Guidelines

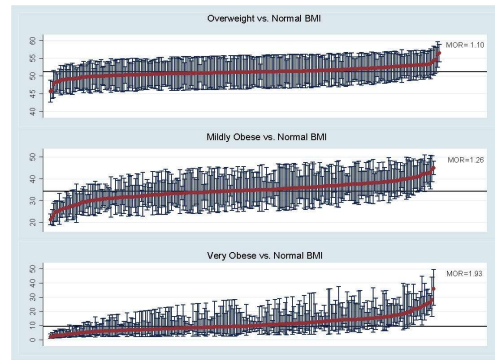
“Patients with a **BMI 35 kg/m²** should be discouraged from donating, especially when other comorbid conditions are present.”

• Amsterdam Forum, *Transplantation* 2005; 79:553

“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



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

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.

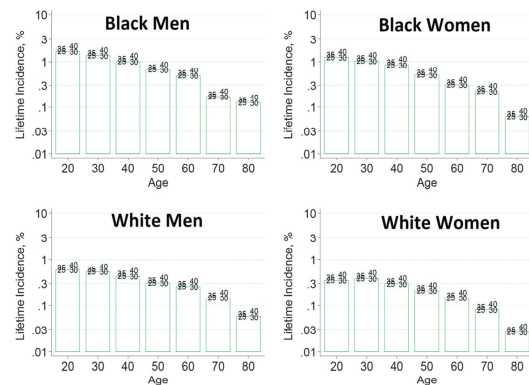
11.3: The decision to approve donor candidates with obesity and BMI >30 kg/m² should be individualized based on demographic and health profile in relation to the transplant program’s acceptable risk threshold.

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



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

PROJECTED ESRD BY BMI, HEALTHY PERSONS



[CKD-PC: Grams et al, *N Engl J Med* 2016 4; 374:411]

www.kidney-international.org clinical investigation

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

see commentary on page 534

Jayne E. Locke¹, Rhiannon D. Reed¹, Allan Massie², Paul A. MacLennan¹, Deirdre Sawinski³, Vineeta Kumar¹, Shikha Mehta¹, Roslyn B. Mannon¹, Robert Gaston¹, Cora E. Lewis¹ and Dorry L. Segev²

¹University of Alabama at Birmingham School of Medicine, Comprehensive Transplant Institute, Birmingham, Alabama, USA; ²Johns Hopkins University School of Medicine, Baltimore, Maryland, USA; and ³University 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 $>27\text{kg/m}^2$ 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.

Kidney International (2017) **91**, 699–703; <http://dx.doi.org/10.1016/j.kint.2016.10.014>

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 $\geq 30\text{kg/m}^2$

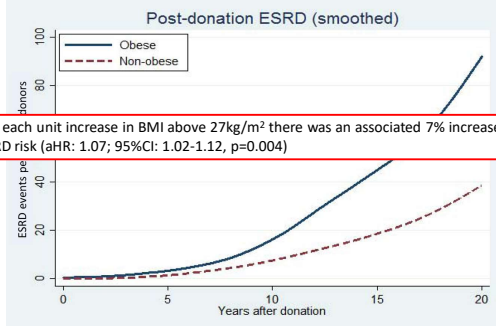
STUDY METHODS

- 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

Donor characteristic	Obese (BMI $\geq 30\text{ kg/m}^2$) (N=20 588)	Non-obese (BMI $< 30\text{ kg/m}^2$) (N=58 004)	Missing BMI (N=41 177)
Age- years, mean (SD)	40.7 (10.7)	40.8 (11.4)	38.5 (10.9)
Sex, N(%)			
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/1.73m^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)

CUMULATIVE INCIDENCE OF ESRD



Obesity status	5-years	10-years	15-years	20-years
Obese (BMI ≥ 30 kg/m ²)	3.2	15.2	42.5	93.9
Non-obese (BMI < 30 kg/m ²)	1.0	7.4	17.5	39.7

ADJUSTED RISK FOR ESRD

IMPUTED DATASET

Characteristic	HR	95% CI	p-value
Obese (ref= non-obese)	1.86	1.05-3.30	0.04
Age, per 1-year increase	0.99	0.98-1.01	0.37
Female	0.51	0.39-0.66	< 0.001
African American (ref=non-African American)	4.62	3.46-6.16	< 0.001
Systolic BP ≥ 120 or diastolic BP ≥ 80 mmHg	1.29	0.73-2.26	0.37
eGFR, per 1 mL/min/1.73m ² increase	0.97	0.95-0.98	< 0.001
Related to recipient	1.51	1.00-2.28	0.05

COMPLETE CASE DATASET

Characteristic	HR	95% CI	p-value
Obese (ref= non-obese)	2.26	1.30-3.92	0.004
Age, per 1-year increase	1.00	0.98-1.03	0.74
Female	0.56	0.32-0.98	0.04
African American (ref=non-African American)	3.17	1.72-5.86	< 0.001
Systolic BP ≥ 120 or diastolic BP ≥ 80 mmHg	1.64	0.83-3.24	0.6
eGFR, per 1 mL/min/1.73m ² increase	0.99	0.97-1.00	0.09
Related to recipient	1.27	0.67-2.41	0.47

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 >27kg/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*

Donor:	
(1)	Two normal kidneys
(2)	Normal lower urinary tract
(3)	Absence of infection
(4)	Sufficient understanding
Recipient:	
(1)	Irreversible terminal disease
(2)	Normal lower urinary tract
(3)	Infection, if present, minimal or controllable
(4)	Inactive primary renal disease

[Murray JE, Merrill JP, Harrison JH. *Ann Surg* 1958; 148: 343]

WHAT DO WE ALREADY KNOW ABOUT LD RISK? A LOT

- 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

ESRD RISK IN LIVING KIDNEY DONORS

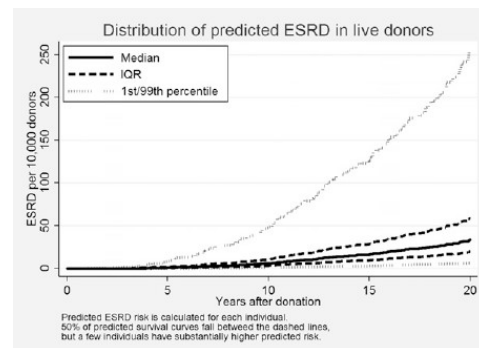
Table 2. Risk factors for ESRD in living kidney donors

Characteristic	aHR ^a	P Value
Men (at age 40)	1.88 (95% CI, 1.50 to 2.35)	<0.001
black race (at age 40)	2.96 (95% CI, 2.25 to 3.89)	<0.001
Age per 10 yr: nonblack	1.40 (95% CI, 1.23 to 1.59)	<0.001
Age per 10 yr: black	0.88 (95% CI, 0.72 to 1.09)	0.3
BMI per 5 kg/m ²	1.61 (95% CI, 1.29 to 2.00)	<0.001
First-degree biologically related to recipient	1.70 (95% CI, 1.24 to 2.34)	<0.01

^aMale 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 ($P < 0.01$).

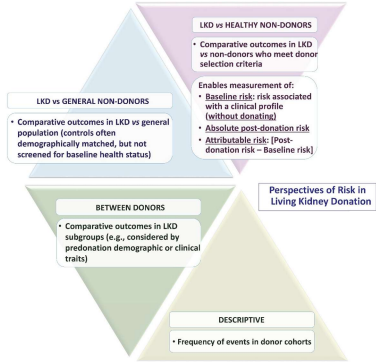
[Massie A et al, *J Am Soc Nephrol* 2017; 28: 2749]

ESRD RISK IN LIVING KIDNEY DONORS



[Massie A et al, *J Am Soc Nephrol* 2017; 28: 2749]

CONTEXT IN UNDERSTANDING LD OUTCOMES



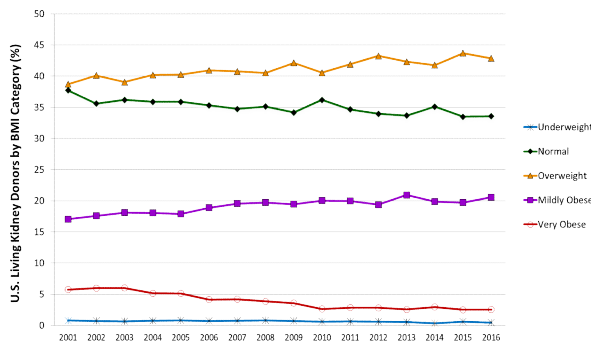
[Lentine KL & Segev DL, *J Am Soc Nephrol* 2017; 28:12]

QUALITY OF DATA FROM WHICH TO BUILD PREDICTIVE MODELS?

- 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)

[Matas AJ et al, *CJASN* 2017; 12: 663]

A GROWING CONCERN



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

OTHER CONSIDERATIONS?

- Perioperative Complications
 - Systematic review of 8 donor nephrectomy studies – *no association* of BMI and perioperative complications [Lafranca et al, *Kidney Int* 83: 931, 2013]
 - 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) [Lentine et al, *Am J Transpl* 16: 1848, 2017]

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)

