



## Transplantation

Presented at the Academic Surgical Congress 2019

## Donation approval among obese living kidney donor candidates: The impact of metabolic syndrome



Margaux N. Mustian, MD, MSPH<sup>a</sup>, Vineeta Kumar, MD<sup>b</sup>, Michael Hanaway, MD<sup>a</sup>, Paul A. MacLennan, PhD<sup>a</sup>, Brittany A. Shelton, MPH<sup>a</sup>, Rhiannon D. Reed, MPH, DrPH<sup>a</sup>, Tanya Correya<sup>a</sup>, Raynesha Grant, BS, MS<sup>a</sup>, Alexis Carter, BS<sup>a</sup>, Gavin Baker<sup>a</sup>, Jelecia Patterson<sup>a</sup>, Markayla Peoples, BS<sup>a</sup>, Semaj Holden<sup>a</sup>, Babak J. Orandi, MD, PhD<sup>a</sup>, Jayme E. Locke, MD, MPH, FACS, FAST<sup>a,\*</sup>

<sup>a</sup> Department of Surgery, Division of Transplantation, University of Alabama at Birmingham, AL

<sup>b</sup> Department of Medicine, Division of Transplant Nephrology, University of Alabama at Birmingham, AL

## ARTICLE INFO

## Article history:

Accepted 7 July 2019

Available online 20 August 2019

## ABSTRACT

**Background:** The scarcity of organs available for transplantation has increased attempts to augment transplantation by utilizing obese living kidney donors. The literature has suggested that these donors have increased risks postdonation. Not surprising, the threshold for living kidney donor approval among obese persons is typically higher and the process more costly. Therefore, a screening tool to predict the likelihood of approval among obese living kidney donor candidates was created.

**Methods:** A single-center retrospective study was performed among obese (body mass index  $\geq 30$  kg/m<sup>2</sup>) living kidney donor candidates evaluated in clinic (January 1, 2012, to December 31, 2017). Approved candidates were compared with those not approved using multivariable logistic regression, and a prediction tool was generated.

**Results:** Among 389 obese living kidney donor candidates, there were no significant differences in sex or race and ethnicity by approval status. However, nonapproved candidates had a higher prevalence of metabolic syndrome. In the prediction model, glucose impairment and hypertension were most predictive of nonapproval.

**Conclusion:** Among obese living kidney donor candidates, several metabolic syndrome components were associated with decreased odds of approval. This tool may serve as a useful initial screening for obese living kidney donor candidates, permitting more cost-effective evaluation processes. The tool could also be used to promote expeditious interventions in the preclinical setting, including weight management programs, to improve the likelihood of donation and postdonation outcomes.

© 2019 Elsevier Inc. All rights reserved.

## Introduction

Although kidney transplantation is the standard of care for patients with end-stage renal disease,<sup>1</sup> access to transplantation is limited. Nearly 100,000 candidates are on the kidney transplant waitlist in the United States, with fewer than 20,000 transplants performed annually.<sup>2</sup> Because of the scarcity of organs available for transplantation, there has been a motivation to expand living donor kidney (LKD) transplantation through the utilization of medically

complex LKDs, including LKDs with isolated medical abnormalities such as obesity (body mass index [BMI]  $\geq 30$  kg/m<sup>2</sup>), hypertension, or glucose impairment.<sup>3</sup> Consequently, there has been a rise in the prevalence of obesity among LKDs over time.<sup>4</sup>

Despite the increased utilization of medically complex living donors, donation in the setting of medical abnormalities has higher associated risks compared with standard criteria donation. The literature has demonstrated that obese LKDs have elevated risks of adverse outcomes postdonation, including perioperative complications such as multi-organ failure or intensive care requirements.<sup>5</sup> In the general population, there is an association between obesity and the development of chronic kidney disease,<sup>6</sup> and studies have also revealed an increased risk of end-stage renal disease postdonation among obese LKDs.<sup>7</sup> Praga et al<sup>8</sup> demonstrated that, after

Presented at the 2019 Academic Surgical Congress.

\* Reprint requests: Jayme E. Locke, MD, MPH, FACS, FAST, Associate Professor of Surgery, 1720 2nd Ave. South, LHRB 780, Birmingham, AL 35294-0007.

E-mail address: [jllocke@uabmc.edu](mailto:jllocke@uabmc.edu) (J.E. Locke).

<https://doi.org/10.1016/j.surg.2019.07.008>

0039-6060/© 2019 Elsevier Inc. All rights reserved.

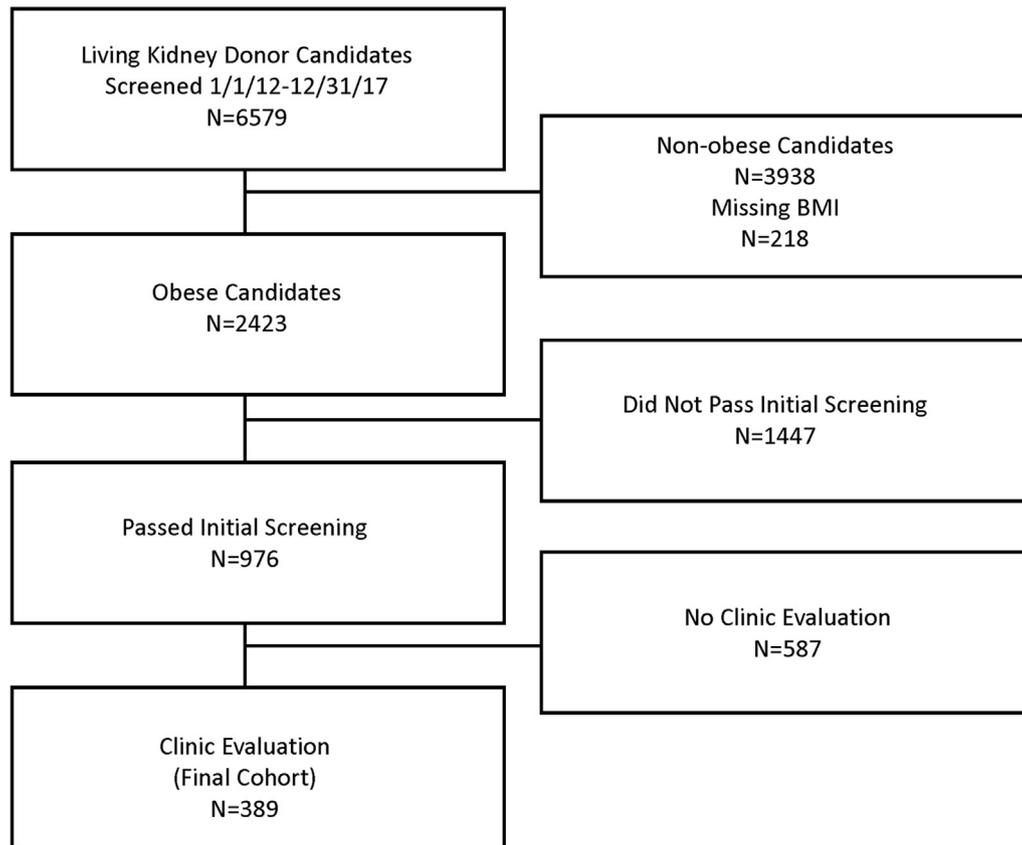


Fig 1. Cohort construction.

uni-nephrectomy, obese patients had increased proteinuria. Furthermore, medical comorbidities commonly found among obese patients, such as metabolic syndrome (MetS), have also been shown to be associated with poor outcomes post-nephrectomy,<sup>9</sup> which may compound the donation risks among obese LKDs.

Given the increased perioperative and long-term risks for medically complex donors, an elevated BMI can still serve as a barrier to living kidney donation.<sup>10–12</sup> Although there is no standard criteria for BMI within the field, transplant centers use various thresholds for donation, with many ranging from 30 to 35 kg/m<sup>2</sup>.<sup>12</sup> Moreover, the donor evaluation process is costly, time-consuming, and inconvenient for the potential donor.<sup>13</sup> At a minimum, the evaluation process includes imaging with computed tomography angiography; blood-typing and crossmatch run with the intended recipient; electrocardiogram; chest x-ray; urinalysis; 24-h urine collection; and consultations with surgeons, nephrologists, and social workers. Because of the costliness of in-clinic evaluation for potential LKDs, particularly for donor candidates who are unlikely to be approved for donation, there is a need to refine the workup of obese potential LKDs before formal clinical evaluation at the transplant center. Therefore, the goal of this study was to create a screening tool capable of predicting the likelihood of approval among obese donor candidates to aid in a reduction of costs. Likewise, such a screening tool would also allow for earlier referral for directed interventions aimed at modifiable risk factors before formal evaluation and could also serve to better inform potential donor expectations. We hypothesized that the presence of MetS, or the components thereof, may be associated with a decreased likelihood of donation approval among obese LKD candidates and could potentially be targeted for improvement before formal evaluation.

## Methods

### Data source

This study used data from the University of Alabama at Birmingham Transplant registry, and all potential LKD candidates who entered the evaluation process from January 1, 2012, through December 31, 2017, were identified. Data were supplemented from the electronic medical records and abstracted by 2 independent analysts. Data integrity was then confirmed by auditing 20% of the charts. The study was approved by the Institutional Review Board at the University of Alabama at Birmingham.

### Study population

Within our study population ( $n = 6,579$ ), we excluded all potential LKD candidates with missing BMI information ( $n = 218$ ). Of those with non-missing BMI ( $n = 6,361$ ), 3,938 candidates with BMI  $< 30$  kg/m<sup>2</sup> were excluded, leaving 2,423 (38.1%) obese (BMI  $\geq 30$  kg/m<sup>2</sup>) LKD candidates (Fig 1). Among the obese donor candidates, 976 (40.3%) passed the initial screening and were invited for formal medical/surgical/psychosocial evaluation. Among those, a final cohort of 389 (39.9%) obese LKD candidates who completed formal in-person evaluation in our clinic were identified. Of note, within our institution, we typically require a BMI  $\leq 38$  kg/m<sup>2</sup> to begin the formal evaluation process.

### Statistical analyses

A retrospective case control study was performed among obese LKD candidates who underwent formal evaluation in the clinic.

**Table 1**  
Demographics and laboratory values for obese LKD candidates

Characteristic	Approved (n = 127)	Not approved (n = 262)	P value
Age (y) <sup>*</sup>	44 (35–54)	44 (35–53)	.77
Male <sup>†</sup>	43.3 (55)	45.0 (118)	.75
African American <sup>†</sup>	33.1 (42)	40.1 (105)	.18
History of HTN <sup>†</sup>	3.2 (4)	11.9 (31)	.01
Metabolic syndrome <sup>†,‡,§</sup>	19.7 (25)	40.8 (107)	< .001
Smoking history <sup>†</sup>	35.4 (45)	37.8 (99)	.65
Family history DM <sup>†</sup>	49.6 (63)	50.6 (132)	.19
Family history HTN <sup>†</sup>	73.2 (93)	67.1 (175)	.06
BMI <sup>†</sup>	33.3 (32.0–35.2)	34.2 (32.6–36.2)	< .001
SBP measured in clinic <sup>*</sup>	128.9 ± 14.4	135.2 ± 15.7	< .001
DBP measured in clinic <sup>*</sup>	75.6 ± 8.4	76.5 ± 11.0	.38
SBP from outpatient log <sup>*,‡</sup>	125.7 ± 8.3	131.0 ± 10.6	< .001
DBP from outpatient log <sup>*,‡</sup>	78.5 ± 6.1	81.2 ± 7.9	< .01
Blood type <sup>†</sup>			.16
A	29.4 (37)	27.6 (72)	
AB	–	3.5 (9)	
B	11.1 (14)	13.8 (36)	
O	59.5 (75)	55.2 (144)	
Serum creatinine <sup>*</sup>	0.9 ± 0.2	0.9 ± 0.2	.29
Serum fasting glucose <sup>*</sup>	96.6 ± 15.2	100.7 ± 23.4	.04
Serum fasting glucose ≥ 100 <sup>†</sup>	28.4 (36)	45.4 (119)	.001
Serum albumin <sup>*</sup>	4.15 ± 0.32	4.07 ± 0.32	.01
Cholesterol <sup>*,‡</sup>	175.4 ± 35.2	184.1 ± 41.7	.11
LDL <sup>*,‡</sup>	110.4 ± 30.9	116.8 ± 34.3	.17
HDL <sup>*,‡</sup>	46.2 ± 10.8	45.3 ± 13.5	.59
Triglycerides <sup>*,‡</sup>	113.5 ± 69.2	131.0 ± 84.8	.08
Creatinine clearance <sup>*</sup>	154.2 ± 42.9	150.6 ± 54.2	.50
HBA1c <sup>*</sup>	5.46 ± 0.60	5.54 ± 0.68	.39
2-h glucose tolerance test ordered <sup>†</sup>	17.3 (22)	19.1 (50)	.67

Evaluated in the clinic from January 1, 2012, to December 31, 2017, stratified by approval status for donation (n = 389).

BMI, body mass index; DM, diabetes mellitus; HTN, hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL, low-density lipoprotein; HDL, high-density lipoprotein; HBA1c, hemoglobin A1c.

\* Mean ± SD or median (interquartile range).

† % (N).

‡ Missing for 20%–30%.

§ Metabolic syndrome defined as ≥ 2 of the following: elevated blood pressure, hypertriglyceridemia, decreased high-density lipoprotein, impaired fasting glucose.

Cases were defined as obese living donor candidates who were approved for kidney donation (including those who were approved for kidney paired donation), and all other obese potential donors evaluated in the clinic served as controls. Other covariates of interest included age, race or ethnicity, sex, BMI, year of donor evaluation, smoking history, blood pressure recorded in clinic, personal and family history of diabetes mellitus, personal and family history of hypertension, and MetS. MetS was defined using the Adult Treatment Panel III definition—a BMI of 30kg/m<sup>2</sup> or greater as a surrogate for abdominal obesity. Patients were considered to have MetS if, in addition to obesity, they had 2 of the following components: elevated serum triglycerides (triglycerides 150 mg/dL or greater), decreased high-density lipoprotein (HDL) < 40 mg/dL for males or < 50 mg/dL for females), abnormal blood pressure (systolic blood pressure greater than 130, diastolic blood pressure greater than 85, or documented history of hypertension), and impaired fasting glucose (fasting serum glucose greater than 100 mg/dl or documented history of diabetes).<sup>14</sup> Each component of MetS was also assessed separately. Patient characteristics were compared using the Student's *t*-tests or the Wilcoxon rank test for continuous variables, depending on distribution, and  $\chi^2$  tests for dichotomous or categorical variables.

#### Risk-prediction tool development and validation

Multivariable logistic regression was utilized to generate a risk-prediction tool to estimate the odds of nonapproval among obese

donor candidates. The following characteristics were included in the models, including those selected a priori based on established clinical associations or those chosen on the basis of statistical significance in univariate analyses ( $P < .1$ ): age (< 60 y or ≥ 60 y), BMI, gender, race (African American [AA] versus non-AA), smoking status (prior or current smoker versus never smoker), and components of MetS as defined earlier in this report (including glucose impairment, elevated triglycerides, decreased HDL, and abnormal blood pressure).

Because lipid panels were not routinely obtained in the donor evaluation process at our institution until 2014, values for the lipids were largely missing before that time, which led to 30% missing for those covariates. Therefore, multiple imputation was used, with 40 imputations to generate plausible values drawn from a predicted distribution on the basis of other observed variables.<sup>15–17</sup> All predictor variables, the outcome variable, and several other covariates were included in the multiple imputations using a discriminant fully conditional specification method for categorical variables and fully conditional specification regression method for continuous variables.<sup>15</sup> The results of the imputed data sets were then combined using Rubin's rules to generate  $\beta$  coefficients for the covariates, accounting for the uncertainty attributable to missing data.<sup>16</sup> A risk score for non-approval was calculated using weighted points that were proportional to the generated  $\beta$  coefficients.<sup>18–20</sup> Model performance of the risk score was assessed for both discrimination (concordance index [c-statistic]) and calibration within the pooled

imputed data sets.<sup>15</sup> The model performance was also assessed through k-fold cross-validation.

### Sensitivity analyses

As sensitivity analyses, the risk prediction tool was also generated within a complete case and within a bootstrapped (200 repetitions) complete case cohort. We then applied those risk prediction tools to the pooled imputed data sets for validation. Additionally, we also assessed MetS within the model as a dichotomous variable rather than including the individual components of MetS. In all models, our results were similar and inferences unchanged. Finally, interactions were assessed between components of MetS and race by including cross-product terms in our adjusted models, and we found no statistically significant multiplicative interactions.

All analyses were performed using SAS 9.4 (SAS Institute Inc, Cary, NC).

## Results

### Study population

The cohort consisted of 389 obese LKD candidates evaluated at our institution from January 1, 2012, to December 31, 2017. Of those donor candidates, 32.6% ( $n = 127$ ) were approved for donation, but 67.4% ( $n = 262$ ) were not approved. We observed no statistically significant differences on the basis of age, gender, or race between those who were approved and not approved (Table I). Prior diagnosis of hypertension was more common among those who were not approved (11.9%) compared with 3.2% of approved donors ( $P = .01$ ). We observed no difference between the 2 groups on the basis of smoking history, with roughly 35%–38% of the LKD candidates reporting being a current smoker or having a history of smoking ( $P = .65$ ). Approximately half of the candidates had a family history of diabetes mellitus, irrespective of donation approval (Table I). Of note, family history of hypertension was more commonly reported among approved donors (73.2%) compared with nonapproved donor candidates (67.1%); however, this difference did not reach statistical significance ( $P = .06$ ).

Median BMI for the approved LKD candidates was 33.3 kg/m<sup>2</sup> (interquartile range: 32.0–35.2), compared with median BMI of 34.2 kg/m<sup>2</sup> (interquartile range: 32.6–36.2) for LKD candidates who were not approved ( $P < .001$ ). We observed no statistically significant differences on the basis of blood type, serum creatinine, cholesterol, low-density lipoprotein, high-density lipoprotein, or triglycerides between the 2 groups (Table I). Obese LKD candidates who were approved for donation had a lower mean serum fasting glucose and were less likely to have impaired ( $\geq 100$  g/dL) fasting glucose (28.4% compared with 45.4%,  $P \leq .01$ ). Approved LKD candidates also had a higher serum albumin (4.2 g/dL) compared with their nonapproved counterparts (4.1 g/dL,  $P = .01$ ). We also observed no significant differences in creatinine clearance, hemoglobin A1c, and whether a 2-h glucose tolerance test was ordered between the 2 groups (Table I).

We did observe changes in the donor candidate population over time. During the first year of the study (2012), the obese donor candidates had a lower prevalence of metabolic syndrome (only 15.7%) compared with later years where the prevalence of metabolic syndrome increased to a minimum of 30% (ranging from 29.9% in 2013 to 41.1% in 2017).

### Odds of nonapproval for donation in univariate analyses

In univariate analyses, we found that increasing BMI was associated with increased odds of nonapproval, such that for every

**Table II**

Unadjusted ORs for donation nonapproval among obese LKD candidates ( $n = 389$ )

Characteristic	OR	95% Confidence interval	P value
Age $\geq 60$ y	1.45	0.76–2.78	.26
Male	1.07	0.70–1.64	.74
Race			
Non-African American	Ref	Ref	
African American	1.35	0.87–2.11	.18
BMI	1.18	1.08–1.30	<.01
History of hypertension	4.16	1.44–12.05	.01
Metabolic syndrome <sup>†</sup>	1.47	1.14–1.91	.01
Family history DM	1.00	0.65–1.53	.13
Family history HTN	.69	0.42–1.11	.26
SBP	1.03	1.01–1.04	<.01
DBP	1.01	0.99–1.03	.43
Blood type			
A	1.01	0.62–1.65	.96
AB	—	—	
B	1.34	0.68–2.64	.96
O	REF	REF	
Serum creatinine	1.82	0.60–5.53	.29
Serum fasting glucose	1.02	1.00–1.04	.07
Serum fasting glucose $\geq 100$	2.10	1.33–3.32	.001
Serum albumin	0.43	0.22–0.84	.01
HDL <sup>‡</sup>	1.00	0.98–1.02	.63
Low HDL <sup>‡</sup>	1.12	0.87–1.46	.37
Triglycerides <sup>‡</sup>	1.00	1.00–1.01	.11
Elevated triglycerides <sup>‡</sup>	1.19	0.87–1.63	.29
HBA1c	1.24	0.75–2.04	.40
Creatinine clearance	1.00	0.99–1.00	.53
2H GTT ordered	1.13	0.65–1.96	.68
Evaluation year			
2012	Ref	Ref	
2013	3.30	1.73–6.28	.05
2014	2.80	1.35–5.81	.33
2015	1.54	0.73–3.21	.19
2016	2.12	0.97–4.61	.93
2017	3.50	1.61–7.62	.09
History of or current smoking	1.11	0.71–1.72	.65

OR, odds ratio; BMI, body mass index; DM, diabetes mellitus; HTN, hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoprotein; HBA1c, hemoglobin A1c.

<sup>†</sup> Metabolic syndrome defined as  $\geq 2$  of the following: elevated blood pressure, hypertriglyceridemia, decreased high-density lipoprotein, impaired fasting glucose.

<sup>‡</sup> Derived within imputed data sets (40 MI).

1 kg/m<sup>2</sup> increase in BMI, donor candidates had an 18% increased odds of nonapproval (OR 1.18; 95% CI: 1.08–1.30). Likewise, earlier diagnosis of hypertension was a significant predictor for donation approval status, with a greater than fourfold increased odds of nonapproval (OR 4.16; 95%CI: 1.44–12.05; Table II). Similarly, the presence of MetS was associated with a nearly 50% increased odds

**Table III**

Adjusted odds ratios for donation nonapproval among obese LKD candidates<sup>\*</sup>

Characteristic	aOR (95% confidence interval)	$\beta$ estimate	Points
Age $\geq 60$ y	1.69 (0.83–3.44)	0.5267	14
Female	1.04 (0.65–1.67)	0.0386	1
African American race	1.57 (0.95–2.59)	0.4505	12
BMI (for each increase of 1 kg/m <sup>2</sup> over 30)	1.19 (1.08–1.31)	0.1702	4
Prior/current smoking history	1.23 (0.76–2.00)	0.2077	5
Metabolic syndrome components			
Glucose impairment	1.83 (1.11–3.03)	0.6048	16
Low HDL	1.40 (0.78–2.51)	0.3379	9
Elevated TG	1.25 (0.61–2.57)	0.2259	6
Abnormal BP	1.96 (1.07–3.60)	0.6747	17

aOR, adjusted odds ratio; BMI, body mass index; TG, triglycerides; BP, blood pressure.

<sup>\*</sup> Derived within imputed datasets (40 MI), with a median c-statistic of 0.6714 from pooled imputed data sets.

### Obese LKD Candidate Nonapproval Prediction

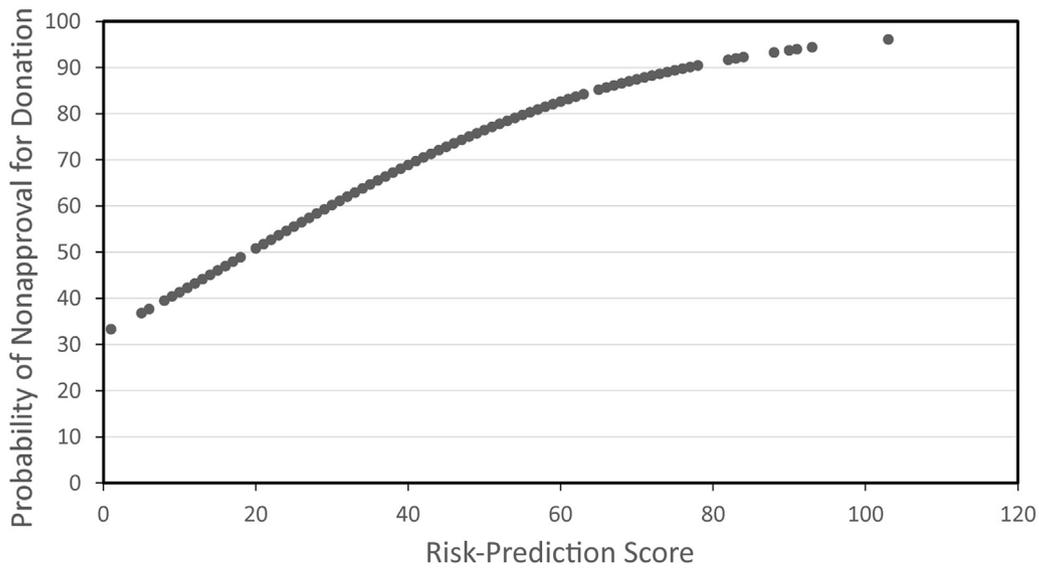


Fig 2. Predicted probability of nonapproval for donation, by risk prediction score, among a cohort of obese LKD candidates.

of nonapproval (OR 1.47; 95% CI: 1.14–1.91). Impaired fasting glucose was also associated with twofold increased odds of non-approval (OR 2.10; 95% CI: 1.33–3.32). For each increase in systolic blood pressure of 10 mmHg, the odds of nonapproval increased by 30% (OR 1.03; 95% CI: 1.10–1.04). Although not typically used clinically as a determinant for donation approval among otherwise healthy LKD candidates, increased serum albumin was also associated with a decreased odds of donation nonapproval (OR 0.43; 95% CI: 0.22–0.84). In addition, the odds of nonapproval among obese donors changed over time throughout the study period (Table II). Of note, the donor candidate population also changed over time.

#### Risk prediction tool for donation non-approval

After controlling for several demographic and health characteristics in our multivariate model, impaired fasting glucose (adjusted odds ratio [aOR] 1.83; 95%CI: 1.11–3.03) and abnormal blood pressure (aOR 1.96; 95% CI: 1.07–3.60) remained significant covariates for donation nonapproval (Table III). Likewise, among our cohort of obese LKD candidates, for each increase in BMI of 1 kg/m<sup>2</sup> there was an associated 19% increase in the odds of nonapproval (aOR 1.19; 95%CI: 1.08–1.31). The remaining components of MetS were not statistically significant predictors of donation non-approval (Table III). However, to assess the odds of donation approval, the weighted points were calculated from the β coefficients for each covariate and summed to generate a risk score, with increasing risk scores correlating with decreased odds of donation approval (Fig 2). The model calibration is presented in Figure 3. Within the pooled imputed data sets, discrimination was assessed, and the c-statistic was 0.6714. Then, using tenfold cross-validation, the c-statistic was 0.6711.

#### Individualized risk prediction of nonapproval

For candidates with BMI of 30 kg/m<sup>2</sup> and no other identified risk factors, the probability of nonapproval was close to 30%, indicating that, with a risk score of 0, obese LKD candidates were not universally approved (Fig 2). In addition, the probability of approval varied by race and gender such that a non-AA female candidate with a BMI of 30 kg/m<sup>2</sup> and no other risk factors (such as MetS components, smoking history, or advanced age) had a 33.3% projected estimate of nonapproval for donation. However, an AA male candidate with a BMI of 30 kg/m<sup>2</sup> and no other risk factors had a 43.2% projected risk of nonapproval.

Likewise, the predicted probability of nonapproval increased among elderly candidates (age >60 y), AAs, those with increasing components of MetS, and current or past smokers. Example combinations of donor candidate demographics and clinical characteristics are presented in Tables IV and V, along with the corresponding projected estimates for candidates with a BMI of 30 kg/m<sup>2</sup> (Table IV) or 35 kg/m<sup>2</sup> (Table V). For example, an elderly

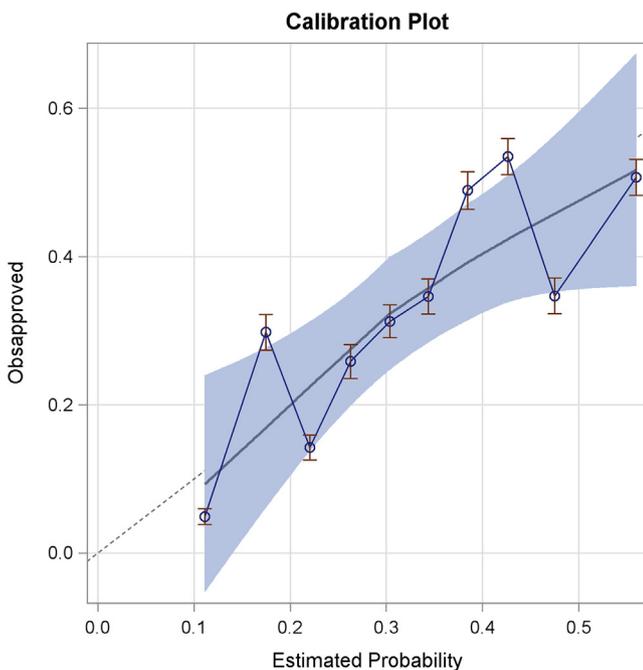


Fig 3. Model calibration plot, comparing observed and expected donation approval based on the risk-prediction score.

**Table IV**  
Estimated probability of donation nonapproval among obese LKD candidates with BMI of 30

Score	Age ≥ 60 y	Sex	Race	Smoking history	Glucose impairment	Low HDL	Elevated TG	Abnormal BP	Probability of nonapproval (95% CI)
1	No	F	Non-AA	No	No	No	No	No	33.3 (31.5–35.2)
30	No	M	Non-AA	Yes	Yes	Yes	No	No	60.2 (59.3–61.1)
52	Yes	M	AA	No	Yes	No	No	No	77.8 (76.9–78.6)
54	Yes	F	Non-AA	No	Yes	No	Yes	Yes	79.1 (78.2–79.9)
30	No	F	AA	No	No	No	No	Yes	60.2 (59.3–61.1)
49	Yes	F	AA	Yes	No	No	No	Yes	75.8 (74.9–76.6)
75	Yes	F	AA	No	Yes	Yes	Yes	Yes	89.4 (88.5–90.2)

BMI, body mass index; HDL, high-density lipoprotein; TG, triglycerides; BP, blood pressure; AA, African American; Non-AA, non-African American.

female AA candidate with a BMI of 35 kg/m<sup>2</sup>, impaired fasting glucose, hypertension, abnormal HDL and elevated triglycerides, and a history of smoking had a projected probability for non-approval of 95.6% (Table V).

## Discussion

This study of nearly 400 obese LKD candidates at a single institution demonstrated that several clinical factors were predictive of nonapproval, including many components of MetS. Obese LKD candidates who were approved for donation less commonly had an earlier diagnosis of hypertension. Likewise, approved candidates had a lower prevalence of impaired fasting glucose and abnormal blood pressure. These findings demonstrated that not all obese LKD candidates presented with the same odds of donation approval, and therefore BMI in isolation may not necessarily be the best marker for determining donation criteria. Other patient characteristics, which can be identified in the preclinical setting, such as components of MetS, specifically fasting glucose and blood pressure measurements, may consequently be useful as screening tools before costly evaluation in an LKD clinic. Moreover, the increasing prevalence of metabolic syndrome among our donor candidates at our institution over time, which likely corresponded with the temporal changes in odds of approval, suggests that preclinical screening tools may be critical because of the increasing medical complexity of donor candidates over time. Therefore, this risk-prediction model may also be used to identify obese LKD candidates who would benefit from risk modification interventions before formal evaluation, including dietary or exercise programs.

The literature has suggested that, among LKDs, components of MetS have been associated with delayed renal recovery and an increased risk of chronic kidney disease post-donation.<sup>9</sup> Moreover, aside from the important adverse risks for donors with metabolic abnormalities, MetS among donors has also been identified as a risk factor for the development of graft failure among kidney transplant recipients as well.<sup>21</sup> As such, preclinical evaluation for MetS would be valuable to not only permit a more efficient donor evaluation process for obese candidates, but could also serve to improve post-transplant outcomes for recipients. Through the use of this screening tool, an improved donor selection process has the potential to lead to improved graft survival among kidney transplant

recipients and post-donation outcomes among obese LKDs. Likewise, because MetS, and components thereof, are modifiable risk factors, expeditious identification of these barriers to donation is therefore important to allow for earlier directed interventions aimed at behavioral modifications, such as referral for diet and exercise programs.

To our knowledge, this is the first donor approval tool created among obese donor candidates, although studies<sup>22–24</sup> have demonstrated that glucose impairment, obesity, and hypertension serve as significant exclusion criteria for living kidney donation approval. After instituting a protocol to screen for MetS at the time of clinical evaluation, Marcusa et al<sup>25</sup> found that there was a decrease in the percentage of obese donors accepted for donation (46.3% vs 56.3% before the policy). However, it should be emphasized that the intention of preclinical screening for MetS should not be to decrease access to living kidney donation by diminishing the utilization of obese LKDs. Instead, these efforts should only serve to aid in selecting the most appropriate candidates for donation in an efficient manner and also to identify LKD candidates who would benefit from strategic lifestyle modifications before formal evaluation.

The strengths of this study include the granular information that was available from a large single-transplant registry with a diverse patient population. However, this study is not without limitations. Although the model performance was assessed through cross-validation, we were unable to examine external validation because no readily available data exist on obese LKDs evaluated at other centers. As such, attributable to the single-site study, small sample size of the cohort, and temporal changes in the cohort population, there may be a lack of generalizability of our results. Consequently, because of our center-specific criteria or acceptance practices, the predictive value of this model in other institutions may vary, as some centers may be more stringent in their donor candidate evaluations than others. In addition, the model also did not account for psychosocial issues, which can serve as significant barriers to donor candidate evaluation, workup, and approval. Moreover, there were some missing data for values obtained from lipid panels, but this was handled with multiple imputation and complete case sensitivity analyses. Also, the model was developed and validated among obese LKD candidates and therefore may not be applicable to LKD candidates with BMI of less than 30 kg/m<sup>2</sup>.

**Table V**  
Estimated probability of donation nonapproval among obese LKD candidates with BMI of 35

Score	Age ≥ 60 y	Sex	Race	Smoking history	Glucose impairment	Low HDL	Elevated TG	Abnormal BP	Probability of nonapproval (95% CI)
21	No	F	Non-AA	No	No	No	No	No	51.8 (50.5–53.0)
50	No	M	Non-AA	Yes	Yes	Yes	No	No	76.4 (75.6–77.3)
72	Yes	M	AA	No	Yes	No	No	No	88.3 (87.3–89.1)
74	Yes	F	Non-AA	No	Yes	No	Yes	Yes	89.0 (88.1–89.9)
50	No	F	AA	No	No	No	No	Yes	76.4 (75.6–77.3)
69	Yes	F	AA	Yes	No	No	No	Yes	87.0 (86.1–87.9)
100	Yes	F	AA	Yes	Yes	Yes	Yes	Yes	95.6 (95.0–96.2)

BMI, body mass index; HDL, high-density lipoprotein; TG, triglycerides; BP, blood pressure; AA, African American; Non-AA, non-African American.

Finally, the c-statistic for the model was not extremely robust but was similar to those of other models in the transplant literature.<sup>26</sup> Therefore, the results should be interpreted with caution in determining candidacy for donation among obese donor candidates. Instead, the risk-prediction tool should be utilized to more readily identify those who would benefit from earlier behavioral interventions before formal evaluation.

In summary, within a risk-prediction model created among obese LKD candidates, components of MetS (specifically impaired fasting glucose, increasing BMI, and abnormal blood pressure), were predictive of nonapproval for living kidney donation. These findings highlight the role for MetS screening in the pre-clinical setting to improve the donor selection process, decrease the costliness of LKD candidate in-clinic evaluations, and to identify LKD candidates who would benefit from behavioral modifications and interventions before formal evaluation. Optimizing living kidney donation remains a critical task because of the magnitude of the organ shortage; however, efforts to improve the cost-effectiveness of donor evaluation and to maintain post-donation safety for obese LKDs are imperative.

### Funding/Support

This project was supported by the National Institutes of Health (NIH)- National Research Service Award, through Grant Award Number T32 DK007545 (P.I. Mustian, mentored), and the National Institute of Diabetes and Digestive and Kidney Diseases – R01 DK113980 (P.I. Locke) and K23 DK103918 (P.I. Locke, mentored). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

### Conflict of interest/Disclosure

The authors declare no conflicts of interest related to this project.

### References

1. Wolfe RA, Ashby VB, Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med.* 1999;341:1725–1730.
2. United States Renal Data System. *2018 USRDS annual data report: Epidemiology of kidney disease in the United States.* Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2018.
3. Reese PP, Feldman HI, McBride MA, Anderson K, Asch DA, Bloom RD. Substantial variation in the acceptance of medically complex live kidney donors across US renal transplant centers. *Am J Transplant.* 2008;8:2062–2070.
4. Sachdeva M, Rosen LM, Varghese J, Fishbane S, Molmenti EP. Weight trends in United States living kidney donors: Analysis of the UNOS database. *World J Transplant.* 2015;5:137–144.
5. Lentine KL, Lam NN, Axelrod D, et al. Perioperative complications after living kidney donation: A national study. *Am J Transplant.* 2016;16:1848–1857.
6. Foster MC, Hwang SJ, Larson MG, et al. Overweight, obesity, and the development of stage 3 CKD: The Framingham heart study. *Am J Kidney Dis.* 2008;52:39–48.
7. Locke JE, Reed RD, Massie A, et al. Obesity increases the risk of end-stage renal disease among living kidney donors. *Kidney Int.* 2017;91:699–703.
8. Praga M, Hernandez E, Herrero JC, et al. Influence of obesity on the appearance of proteinuria and renal insufficiency after unilateral nephrectomy. *Kidney Int.* 2000;58:2111–2118.
9. Yoon YE, Choi KH, Lee KS, Kim KH, Yang SC, Han WK. Impact of metabolic syndrome on postdonation renal function in living kidney donors. *Transplant Proc.* 2015;47:290–294.
10. Bailey PK, Tomson CRV, MacNeill S, et al. A multicenter cohort study of potential living kidney donors provides predictors of living kidney donation and non-donation. *Kidney Int.* 2017;92:1249–1260.
11. Sachdeva M, Sunday S, Israel E, et al. Obesity as a barrier to living kidney donation: A center-based analysis. *Clin Transplant.* 2013;27:882–887.
12. Mandelbrot DA, Pavlakis M, Danovitch GM, et al. The medical evaluation of living kidney donors: A survey of US transplant centers. *Am J Transplant.* 2007;7:2333–2343.
13. Rodrigue JR, Schold JD, Morrissey P, et al. Predonation direct and indirect costs incurred by adults who donated a kidney: Findings from the KDOC study. *Am J Transplant.* 2015;15:2387–2393.
14. Grundy SM, Cleeman Jr, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation.* 2005;112:2735–2752.
15. Steffen A, MacInnis RJ, Joshy G, Giles GG, Banks E, Roder D. Development and validation of a risk score predicting risk of colorectal cancer. *Cancer Epidemiol Biomarkers Prev.* 2014;23:2543–2552.
16. Sterne JA, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: Potential and pitfalls. *BMJ.* 2009;338:b2393.
17. Wood AM, Royston P, White IR. The estimation and use of predictions for the assessment of model performance using large samples with multiply imputed data. *Biom J.* 2015;57:614–632.
18. Sullivan LM, Massaro JM, D'Agostino Sr RB. Presentation of multivariate data for clinical use: The Framingham study risk score functions. *Stat Med.* 2004;23:1631–1660.
19. Rassi Jr A, Rassi A, Little WC, et al. Development and validation of a risk score for predicting death in Chagas' heart disease. *N Engl J Med.* 2006;355:799–808.
20. Locke JE, Sawinski D, Reed RD, et al. Apolipoprotein L1 and chronic kidney disease risk in young potential living kidney donors. *Ann Surg.* 2018;267:1161–1168.
21. Ozdemir FN, Karakan S, Akgul A, Haberal M. Metabolic syndrome is related to long-term graft function in renal transplant recipients. *Transplant Proc.* 2009;41:2808–2810.
22. Mejia-Vilet JM, Cordova-Sanchez BM, Arreola-Guerra JM, Alberu J, Morales-Buenrostro LE. Facing the metabolic syndrome epidemic in living kidney donor programs. *Ann Transplant.* 2016;21:456–462.
23. Lapasia JB, Kong SY, Busque S, Scandling JD, Chertow GM, Tan JC. Living donor evaluation and exclusion: The Stanford experience. *Clin Transplant.* 2011;25:697–704.
24. Guthoff M, Nadalin S, Fritsche A, Konigsrainer A, Haring HU, Heyne N. The medically complex living kidney donor: Glucose metabolism as principal cause of donor decline. *Ann Transplant.* 2016;21:39–45.
25. Marcusa DP, Schaubel DE, Woodside KJ, Sung RS. Impact of screening for metabolic syndrome on the evaluation of obese living kidney donors. *Am J Surg.* 2018;215:144–150.
26. Rao PS, Schaubel DE, Guidinger MK, et al. A comprehensive risk quantification score for deceased donor kidneys: The kidney donor risk index. *Transplantation.* 2009;88:231–236.