Received: 6 June 2017 | Revised: 30 August 2017 | Accepted: 16 September 2017
DOI: 10.1111/ajt.14519

ORIGINAL ARTICLE

AJT

Temporal trends, center-level variation, and the impact of prevalent state obesity rates on acceptance of obese living kidney donors

Abhijit S. Naik[1] | Diane M. Cibrik[1] | Ankit Sakhuja[2] | Milagros Samaniego[1] | Yee Lu[1] | Vahakn Shahinian[1] | Silas P. Norman[1] | Mark A. Schnitzler[3] | Bertram L. Kasiske[4,5] | Dorry L. Segev[6] | Krista L. Lentine[3]

[1]Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA
[2]Division of Pulmonary and Critical Care, Mayo Clinic, Rochester, MN, USA
[3]Saint Louis University Center for Abdominal Transplantation, St. Louis, MO, USA
[4]Hennepin County Medical Center, Minneapolis, MN, USA
[5]Scientific Registry of Transplant Recipients, Minneapolis Medical Research Foundation, Minneapolis, MN, USA
[6]Abdominal Transplantation, Johns Hopkins University, Baltimore, MD, USA

Correspondence
Abhijit S. Naik
Email: abhinaik@med.umich.edu

Funding information
US Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation, Grant/Award Number: HHSH250201500009C

The impact of pre-donation obesity on long-term outcomes of living kidney donors remains controversial. Published guidelines offer varying recommendations regarding BMI (kg/m^2) thresholds for donor acceptance. We examined temporal and center-level variation in BMI of accepted donors across US transplant centers. Using national transplant registry data, we performed multivariate hierarchical logistic regression modeling using pairwise comparisons (overweight, BMI: 25-29.9; mildly obese, BMI: 30-34.9; very obese, BMI: ≥35; versus normal BMI: 18.5-24.9). Metrics of heterogeneity, including median odds ratio (MOR), were calculated. Among 90 013 living kidney donors, 2001-2016, proportions who were very obese decreased and proportions who were mildly obese or overweight increased. Significant center-level heterogeneity was noted in BMI of accepted donors; the MOR varied from 1.10 for overweight to 1.93 for very obese donors. At centers located in the 10 states with the highest general population obesity rates, adjusted odds of very obese donor status were 185% higher (reference: normal BMI) than in states with the lowest obesity rates. Although there is a declining trend in acceptance of very obese living kidney donors, variation across centers is significant. Furthermore, local population obesity rates may affect the decision to accept obese individuals as donors.

KEYWORDS
clinical research, kidney transplantation, kidney transplantation: living donor, nephrology, obesity, practice

1 | INTRODUCTION

Living donor kidney transplantation provides the best long-term outcomes for patients with end-stage renal disease (ESRD).[1] However, debate has been increasing regarding the long-term risks of living donation, including relative donation-related increase in risk of ESRD.[2-4] Understanding the impact of baseline clinical factors on long-term post-donation outcomes is especially important given the changing composition of the donor population. Recent years show an increasing trend toward accepting donors who are older, obese, or members of nonwhite racial and ethnic groups.[5]

Obesity is a growing epidemic in the United States, although regional variation in its prevalence is substantial.[6] In 2015, the prevalence of obesity among adults in nearly half of US states (24 states) was >30%, compared with 12 states in 2010 and none in 2005.[7] Because the pool of potential living donors reflects the community at large, it is perhaps not surprising that the prevalence of obesity among living donors has also increased over time. In the early 2000s, >25%

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; ICC, intraclass correlation; MOR, median odds ratio; OPTN, Organ Procurement and Transplantation Network; SRTR, Scientific Registry of Transplant Recipients; WHO, World Health Organization.

of all living kidney donors were obese at the time of donation, compared with <8% in the 1970s.[5] Living donor recovery programs define criteria for donor exclusion, including BMI thresholds due to concern about associations of obesity with chronic kidney disease (CKD),[8] ESRD, and CKD risk factors (hypertension, diabetes) observed in the general population.[9] However, these thresholds are variable, given the uncertainty regarding the outcome implications among actual donors, resulting in variation in clinical practice guidelines. For example, the European Best Practices, UK Guidelines for Living Donor Kidney Transplantation and the Amsterdam Forum recommend that a BMI >35 kg/m^2 be considered a contraindication to donation, whereas the British Transplantation Society recommends that individuals with BMI >35 kg/m^2 be "discouraged from donating."[10-12] In contrast, the Caring for Australasians with Renal Impairment Guidelines recommend that a BMI >30 kg/m^2 be considered a relative contraindication to donation.[13] Based on uncertainty, Organ Procurement and Transplantation Network (OPTN) Standard Transplant Policy requires measurement of BMI during the living donor evaluation but does not specify thresholds for donor exclusion.[14]

Two recent studies examined possible implications of obesity for living donors. A study performed to develop an ESRD risk projection tool to support donor evaluation found a modest 16% increase in ESRD risk for every 5 kg/m^2 increase in BMI above 30 kg/m^2 among healthy nondonors.[4] A subsequent study[15] found that ESRD risk among living donors increased by 7% (adjusted hazard ratio,1.07; 95% confidence interval [CI] 1.02-1.12) for every 1 kg/m^2 increase above 27 kg/m^2. An older study of postnephrectomy outcomes among nondonors found that obesity was associated with increased risk of proteinuria and chronic renal failure,[16] supporting the possibility that obesity and nephrectomy may pose synergistic "hits" in a pathway to renal injury and CKD.

Given the lack of consensus regarding the appropriate BMI threshold for living donor acceptance, we examined and quantified the variation in BMI among accepted donors across the United States. We also investigated trends over time, demographic and clinical characteristics of very obese living donors, and possible association of state-level obesity prevalence with acceptance of obese donors.

2 | METHODS

2.1 | Study design, data source, and sampling

We conducted a retrospective cohort study of living donors in the United States. Living donor data were obtained from the Scientific Registry of Transplant Recipients (SRTR), which includes data on all donors, waitlisted candidates, and transplant recipients in the United States submitted by the members of OPTN. The Health Resources and Services Administration, US Department of Health and Human Services, provides oversight to the activities of the OPTN and SRTR contractors.

We included living kidney donors, 2001-2016, who were aged 18-84 years at the time of donation (n = 96 261). Because this study used donor BMI as the dependent variable, we excluded donors with missing BMI information (n = 6100; 6.34%), BMI <12 kg/m^2 or ≥60 kg/m^2 (n = 148, 0.002%) to reach our final sample of 90 013 patients (Figure 1). Sensitivity analysis before exclusion revealed no clinically relevant differences between the excluded and final cohorts.

2.2 | Variables

Donors were initially classified according World Health Organization (WHO) BMI categories based on calculated BMI (kg/m^2) at the time of transplantation. Given very few individuals with BMI ≥40 kg/m^2 , we regrouped donors as follows: BMI <18.5, underweight; 18.5 to <25, normal; 25 to <30, overweight; 30 to <35, mildly obese (WHO class 1); ≥35, very obese (WHO class 2 and 3).[17] Age was stratified into 4 groups, 18-30, 30-45, 45-60, and >60 years. Race was categorized as white, black, Hispanic, other (Asian, American Indian, Alaskan Native, Native Hawaiian, other Pacific Islander, multiracial, etc.) as reported by centers to OPTN. Biological relatedness between donor and recipient was defined as related or unrelated. Estimated glomerular filtration rate (eGFR) was calculated using serum creatinine values based on the CKD-EPI equation.[18] Year of donation was categorized into 4 eras: era 1 (2001-2004), era 2 (2005-2008), era 3 (2008-2012), era 4 (2013-2016).

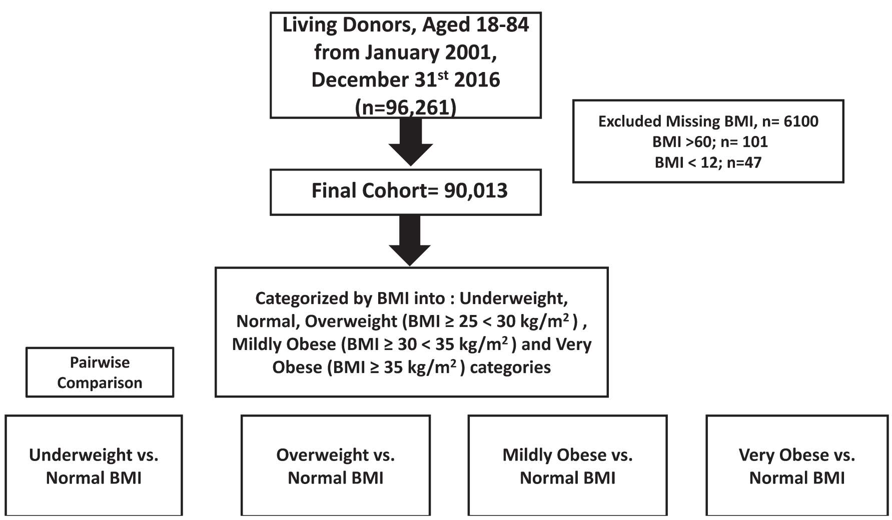

FIGURE 1 Cohort creation from the Scientific Registry of Transplant Recipients dataset, including generation of pairwise comparison

TABLE 1 Recipient and demographic factors by BMI group

BMI group	Underweight n = 590	Normal n = 31 582	Overweight n = 37 078	Class I obesity n = 17 262	Class II & III n = 3501	*P*-value
Age (y)	37.8 ± 12.4	40.5 ± 11.9	42.0 ± 11.4	41.3 ± 10.9	39.5 ± 10.5	<.0001[a]
Donor BMI, kg/m^2	16.8 ± 1.4	22.6 ± 1.7	27.4 ± 1.4	32.0 ± 1.4	37.6 ± 3.2	.0001
Sex (male)	144 (24.4)	9566 (30.3)	17 076 (46.1)	7437 (43.1)	1252 (35.8)	<.0001[b]
Race						
White	398 (67.5)	23 012 (72.9)	25 852 (69.7)	11 516 (66.7)	2179 (62.2)	<.0001[b]
Black	77 (13.1)	2968 (9.4)	4451 (12.0)	2599 (15.1)	701 (20.0)	
Hispanic	67 (11.4)	3487 (11.0)	5230 (14.1)	2645 (15.3)	534 (15.3)	
Other	48 (8.1)	2115 (6.7)	1545 (4.2)	502 (2.9)	87 (2.5)	
eGFR, mL/min/1.73 m^2	101.1 ± 27.4	97.2 ± 22.0	95.5 ± 21.2	96.1 ± 21.2	97.8 ± 22.6	.0001
Era of nephrectomy						
Era 1 (2001-04)	158 (26.8)	7887 (25.0)	8584 (23.2)	3846 (3.22)	1240 (35.4)	<.0001[b]
Era 2 (2005-08)	179 (30.3)	8253 (26.1)	9505 (25.6)	4444 (25.7)	1002 (28.6)	
Era 3 (2009-12)	150 (25.4)	8159 (25.8)	9844 (26.6)	4627 (26.8)	695 (19.9)	
Era 4 (2013-16)	103 (17.5)	7283 (23.1)	9145 (24.7)	4345 (25.2)	564 (16.1)	

[a]By Kruskal-Wallis test.
[b]Chi-square test.

2.3 | Statistical analyses

For descriptive statistics, we used the Kruskal-Wallis test for comparison of 2 or more continuous variables and the chi-square test for categorical variables. We performed multivariate hierarchical logistic regression modeling using pairwise comparison in which each BMI group was compared with normal BMI as the reference. To minimize bias, we adjusted models for donor age, race/ethnicity, sex, era of donation, biological relationship to recipient, eGFR at time of donation, and center volume. We allowed for clustering at the center level to allow assessment of center variation. Metrics of heterogeneity included intraclass correlation (ICC), the ratio of cluster variance (center impact) to total observed variance by BMI group. The median odds ratio (MOR) was used to estimate the average odds that patients with identical characteristics would undergo donor nephrectomy when 2 centers were drawn at random from among all centers.

As a secondary analysis, we assessed whether obesity prevalence rates in the state of the living donor recovery center were associated with BMIs of accepted donors. We first analyzed state obesity rates in 2015.[7] We identified 10 top-ranking states according to population-level obesity prevalence with living kidney donor recovery centers. Louisiana, Alabama, West Virginia, Mississippi, Kentucky, Arkansas, Kansas, Oklahoma, Tennessee, Texas, and Missouri had the highest prevalent obesity rates (high prevalence). As a reference, we used transplant centers located in the 10 states with the lowest population-level obesity prevalence (low prevalence): New Jersey, Connecticut, Vermont, New York, Utah, Massachusetts, California, Hawaii, District of Columbia, and Colorado (Montana was excluded since it had no transplant centers). The living donor recovery centers in the remaining states formed the third group (intermediate prevalence). For this analysis, we restricted the cohort to era 4, 2012- 2016, the donation era closest to the year of prevalent obesity rates (2015).

3 | RESULTS

3.1 | Characteristics of the study cohort

Among 90 013 US living kidney donors, mean age at donation was 41.2 ± 11.5 years and ranged from 18 to 84 years; 60.6% of donors were women. Race/ethnicity distribution was 69.9% white, 12.0% black, 13.3% Hispanic, and 4.8% other. Mean BMI of the entire cohort was 26.9 ± 4.4 kg/m^2. Mean BMIs within BMI categories were 27.4 ± 1.4 kg/m^2, overweight; 32.0 ± 1.4 kg/m^2, mildly obese; and 37.7 ± 3.2 kg/m^2, very obese. The eGFR at donation was highest in underweight donors, at 101.1 ± 27.4 mL/min/1.73 m^2, and lowest (95.5 ± 21.2 mL/min/1.73 m^2) in overweight donors, P = .0001 (Table 1).

3.2 | Temporal trends in BMI

Since 2001, BMI among accepted living kidney donors has not changed significantly; mean BMI was 26.8 ± 4.7 kg/m^2 in 2001 and 26.9 ± 4.1 kg/m^2 in 2016. The proportion of donors with BMI ≥40 kg/m^2 declined from 1.11% in 2001 to 0.26% in 2016, whereas the proportion of very obese donors declined from 5.8% in 2001 to 2.5% in 2016 (Figure 2). However, proportions of mildly obese donors increased from 17.0% in 2001 to 20.6% in 2016, and of overweight donors from 38.7% to 42.9%. Collectively, the proportion of overweight and obese donors (BMI ≥30 kg/m^2) increased from 61.5% in 2001 to 66% in 2016.

In a hierarchical model (Table 2), using pairwise comparison of BMI groups (versus normal BMI), the adjusted odds of very obese compared

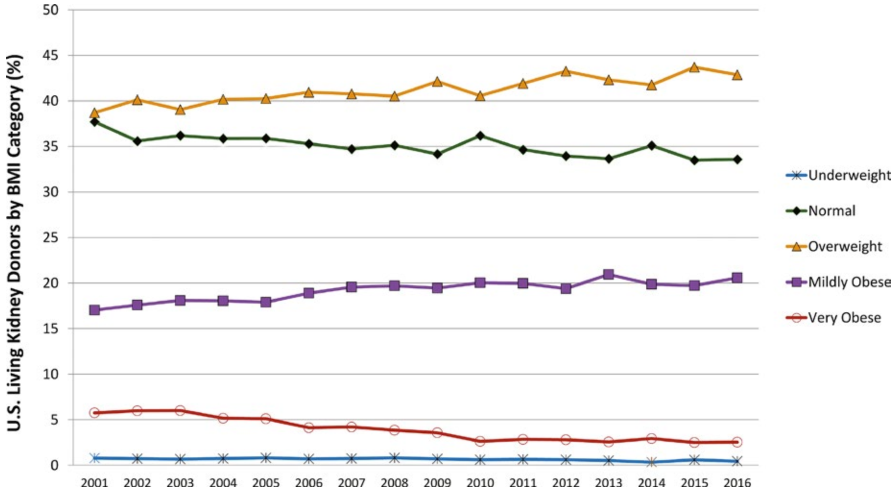

FIGURE 2 Temporal trends by BMI categories (2001-2016) [Color figure can be viewed at wileyonlinelibrary.com]

with normal BMI status among accepted donors decreased by 40% (adjusted odds ratio [aOR] 0.60; 95% CI 0.54-0.68) in era 4 (compared with era 1); by era 4, the odds of mildly obese status increased by 32% (aOR 1.32; 95% CI 1.24-1.40 and of overweight status by 21% (aOR 1.21; 95% CI 1.16-1.27) compared with era 1.

3.3 | Associations of patient-level factors with BMI group

The likelihood of very obese versus normal BMI status among accepted donors was 40% lower in donors aged younger than 30 or older than 60 years (compared with ages 30-45 years). Women (compared with men) and donors of nonwhite race/ethnicity (compared with white race) were more likely to be very obese versus normal weight. These patterns were consistent in comparisons of mildly obese and overweight status with normal BMI status, except that accepted overweight donors were more likely to be older (Table 2).

3.4 | Center-level variation by BMI thresholds

Center clustering explained only 0.3% and 2% of all variance for overweight and mildly obese donors, respectively (Table 3). However, 13% of the variance among very obese donors was driven by center. The MOR varied from 1.10 for overweight donors to 1.93 for very obese donors (Figure 3). Thus if 2 donors with identical characteristics who underwent nephrectomy were drawn randomly across centers, the odds of being very obese (compared with normal BMI) were almost 93% higher at one center than at the other. In a subgroup analysis to assess temporal trends in variation across centers, we found that when the cohort was restricted to era 4, 2012-2016, 32% of the variance (ICC = 0.32) in acceptance of very obese donors was driven by center, with a MOR of 3.23.

3.5 | Association of donor BMI with state obesity rates

To understand whether prevalent obesity rates in the states in which centers were located may influence the acceptance of obese living donors, we performed additional secondary analysis. We noted that compared with accepted donors with normal BMI, very obese BMI status was 185% more likely (aOR 2.85; 95% CI 1.30-6.23) in states with high prevalent population obesity rates compared with states with low prevalent obesity. We also noted higher likelihood of mildly obese and overweight donor status in states with high prevalent obesity rates compared with states with low prevalent obesity rates (Table 4).

4 | DISCUSSION

In a large living donor cohort spanning the past decade and a half, we noted several significant findings. First, proportions of very obese living donors declined, whereas proportions of mildly obese and overweight donors increased. Collectively, overweight and obese donors now account for two thirds of all accepted living donors. Second, despite the overall decline in very obese donors, center variation in acceptance of such donors is significant. Third, we found that often demographic characteristics of very obese donors were associated with higher ESRD risk (such as black race) among donors and nondonors.[2,19] Finally, we noted that compared with normal BMI donor status, overweight, mildly obese, and very obese status were 22%-185% more likely in states with high prevalent obesity rates compared with states with low prevalent obesity rates.

Obesity is a risk factor for ESRD in the general population.[20] Among incident ESRD patients in the general population, one study found an incremental relationship between BMI and ESRD. In patients with a BMI of 30.0-34.9 kg/m^2, risk of ESRD was increased 3.5-fold, compared with individuals with normal BMI, and this risk increased to 6- to 7-fold among those with BMI ≥35.0 kg/m^2. This elevated risk persisted even after adjustment for multiple clinical and demographic factors including diabetes and hypertension, both of which are on the ESRD causal pathway and strongly associated with obesity.[21] It would thus be expected that obese donors would face the same or elevated risk of ESRD after living donation. However, until recently, no detailed, long-term studies had been undertaken to investigate this specific question. In a large registry-based study, Locke et al. demonstrated

TABLE 2 Associations of donor characteristics by BMI group (compared with normal BMI) among donors who underwent nephrectomy

	Very obese		Mildly obese		Overweight	
	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Age (y)						
18-30	0.62	0.55-0.69	0.59	0.56-0.63	0.64	0.61-0.67
31-45	Ref		Ref		Ref	
46-60	0.84	0.76-0.92	0.97	0.93-1.02	1.12	1.08-1.16
>60	0.56	0.45-0.69	0.80	0.73-0.88	1.10	1.03-1.18
Sex	1.32	1.22-1.44	1.81	1.74-1.88	2.07	2.00-2.14
Race						
White	Ref		Ref		Ref	
Black	2.37	2.12-2.66	1.87	1.76-2.00	1.48	1.40-1.56
Hispanic	1.77	1.56-2.00	1.67	1.57-1.78	1.49	1.42-1.57
Other	0.55	0.43-0.69	0.52	0.47-0.58	0.68	0.63-0.73
Era						
2001-2004	Ref		Ref		Ref	
2005-2008	0.8	0.72-0.89	1.13	1.07-1.19	1.07	1.02-1.11
2009-2012	0.62	0.55-0.69	1.22	1.16-1.29	1.15	1.10-1.21
2013-2016	0.6	0.54-0.68	1.32	1.24-1.40	1.21	1.16-1.27
Donor type						
Unrelated	0.95	0.87-1.03	0.95	0.91-0.99	0.98	0.95-1.01
eGFR	0.99	0.99-1.00	0.996	0.995-0.997	0.997	0.996-0.998

Hierarchical models were also adjusted for center living donor volume. *P* for all <.05.
eGFR, estimated glomerular filtration rate.

TABLE 3 Heterogeneity across adjusted models[a]

BMI group (reference: normal BMI)	Proportion of variance in hierarchical model explained by center alone	MOR unadjusted	Proportion of variance in hierarchical model explained by center, adjusted for donor factors	MOR adjusted
Very obese	0.13	1.95	0.13	1.93
Mildly obese	0.02	1.26	0.02	1.26
Overweight	0.003	1.09	0.003	1.10

ICC, intraclass correlation coefficient; MOR, median odds ratio.
[a]Proportion of variance in hierarchical model is equal to the ICC.

a small absolute increased risk of ESRD among obese living donors (94 per 10 000 in donors vs. 30 per 10 000 in nondonors). On further stratification, they noted a small increase in ESRD risk for every 1 kg/m^2 increase in BMI over 27 kg/m^2. These data would suggest that, in addition to obesity, even overweight status may confer an elevated ESRD risk (compared with normal BMI); overweight donors now make up for 43% of all living donors.

Despite a reduction in proportions of very obese living donors (from 5.8% in 2001 to 2.5% in 2016), proportions of mildly obese donors increased (from 17.0% to 20.6%); thus the proportion of obese (≥30 kg/m^2) living donors remained essentially unchanged from 2001 to 2016. Furthermore, the proportion of overweight donors increased from 38.7% to 42.9%, the largest group of current living donors. Taken together, obese and overweight living donors made up approximately 66% of all living donors in 2016, a proportion that has been steadily increasing since 2001. In an adjusted analysis accounting for multiple clinical and demographic donor factors, we noted that compared with era 1, the adjusted odds of very obese donor status (compared with normal BMI status) had decreased by almost 40% in era 4. However, at the same time, the odds of overweight and mildly obese status increased by 21% and 32%, respectively. These trends likely reflect increased concern about long-term risk of living donation for very obese individuals, and a relatively lower concern for overweight and mildly obese individuals, who, as recent data suggest, might also be at increased ESRD risk.[15]

In addition to accepting fewer very obese donors, centers may be increasingly selective regarding such donors. Our data suggest that accepted very obese donors were less likely to be aged younger than 30 or older than 60 years. This likely reflects increased concern

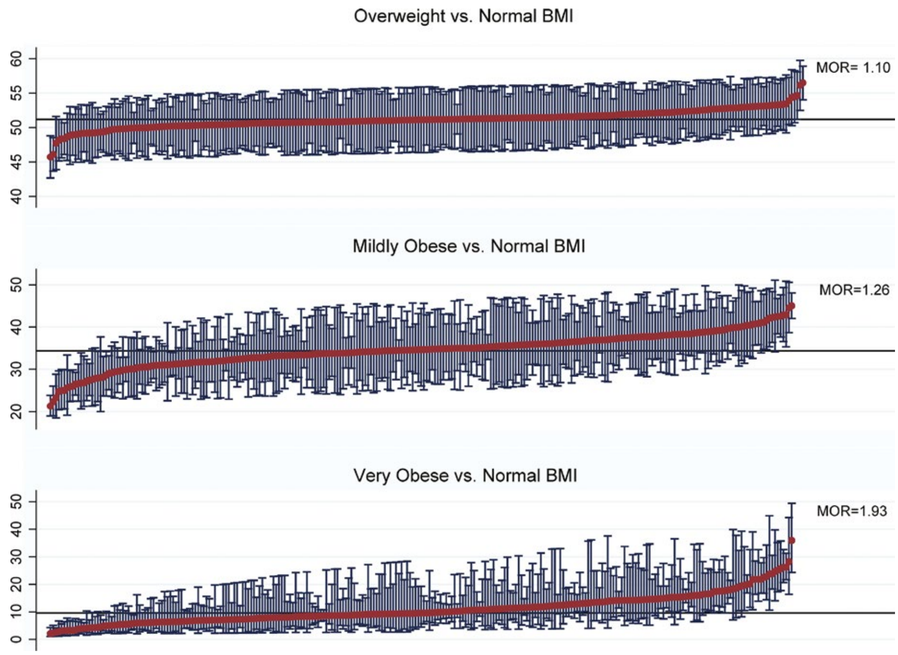

FIGURE 3 Pairwise comparison of BMI group versus normal BMI (reference regimen). The *Y*-axis represents the proportion of BMI group by normal BMI (accepted donors). On the *X*-axis, each vertical line parallel to the *Y*-axis represents an individual center. The horizontal dark solid line represents the "expected" national average adjusted for donor characteristics [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 4 Associations of donor characteristics by BMI group (compared with normal BMI) among donors who underwent nephrectomy in 2012-2016 with state obesity rates

	Very obese		Mildly obese		Overweight	
	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Age (y)						
18-30	0.42	0.32-0.56	0.59	0.52-0.66	0.67	0.61-0.74
31-45	Ref		Ref		Ref	
46-60	0.81	0.65-1.02	0.97	0.88-1.06	1.08	1.00-1.17
>60	0.60	0.39-0.91	0.71	0.60-0.83	1.09	0.97-1.23
Sex	1.58	1.29-1.93	1.83	1.69-1.99	1.97	1.84-2.11
Race						
White	Ref		Ref		Ref	
Black	2.56	1.90-3.46	2.07	1.80-2.38	1.74	1.54-1.95
Hispanic	2.24	1.69-3.00	1.79	1.58-2.03	1.63	1.47-1.80
Other	0.52	0.29-0.91	0.50	0.41-0.61	0.73	0.64-0.83
State-level obesity						
Low prevalence	Ref	Ref	Ref	Ref	Ref	
Intermediate	2.14	1.10-4.13	1.12	0.94-1.33	1.05	0.96-1.15
High prevalence	2.85	1.30-6.23	1.39	1.11-1.72	1.22	1.09-1.38
Donor type						
Unrelated	0.94	0.77-1.13	0.97	0.90-1.06	1.02	0.96-1.08
eGFR	1.002	0.996-1.008	0.992	0.989-0.995	0.994	0.992-0.997

Hierarchical models were also adjusted for center living donor volume. *P* for all <.05.
eGFR, estimated glomerular filtration rate.

about lifetime ESRD risk among younger donors and about the higher comorbidity burden associated with increasing age among older donors.[22] However, despite this selectivity in age, very obese donors were more likely to be biologically related to the recipient, a group shown to constitute almost all donors who develop ESRD among predominantly white donors.[3,23] In addition, very obese status was more likely in black donors, a racial group that already has a high baseline risk of ESRD[19] in the general population and among donors.[2]

When comparing proportions of accepted very obese donors with normal-BMI donors at an individual center, measured across all centers, we noted that at many centers, proportions of very obese donors were higher than the national average. The MOR, across all eras, for very obese donor status was 1.93, and approximately 13% (ICC = 0.13) of the variance in the model was explained by center effect. However, a subgroup analysis assessing temporal trends in variance showed that by era 4, the MOR had increased to 3.23 and approximately 32% (ICC = 0.32) of the variance in the model was now due to center effect. These findings illustrate that although use of very obese donors has declined, the BMI acceptance thresholds for centers vary widely, especially in the last era of our analysis. This point can be further illustrated by the observation that in era 1, proportions of donors with very obese BMI status at 46 procuring centers were above the national average; this number had increased to 96 centers by era 4 (2012-2016; Table S1). This wide variation in later eras is likely driven by the lack of strong long-term data on long-term risk among very obese donors, or perhaps it reflects the local available living donor pool.

As the worldwide obesity epidemic continues, it will be reflected in the medical fitness of the overall living donor pool. A survey of 3 US transplant centers previously showed that center thresholds for various clinical characteristics have evolved over time and may reflect changing clinical and demographic characteristics of the population, suggesting that local population characteristics may affect decisions regarding donor candidacy.[5] We noted that very obese donor status was 185% more likely in states with high obesity rates compared with states with lowest obesity rates. Whether these findings reflect the changing population demographics or a "lowering of the bar" by transplant centers in areas of high obesity prevalence cannot be established with the current data and warrants future study.

Despite the increased risk of ESRD among obese living donors, it is important to note that the absolute risk remains small.[15] Furthermore, it remains unclear whether the elevated risk of ESRD among overweight and obese living donors is attributable to the nephrectomy itself, or to the increased likelihood of developing diabetes or hypertension, both of which are strongly associated with obesity and ESRD.[21,24] Preliminary data presented at the American Transplant Congress 2017 describing a linkage of living donor data to pharmaceutical claims data showed increased use of both insulin and noninsulin pharmacological agents among overweight and obese donors, compared with donors with normal BMI.[25] This would suggest that, like the rest of the population, obese and overweight donors remain at risk for development of diabetes after donation. Because in a large proportion of living donors who develop ESRD, the condition is attributed to diabetes or hypertension, the significance of these findings should be further investigated, and closer scrutiny of overweight and obese living donors is necessary.

Despite the strengths and findings of our study, as with any retrospective analysis, it has several limitations. First, our study included only donors who were cleared for donation and underwent nephrectomy. Thus all comparisons were in the context of accepted donors and not all donors who underwent evaluation. Second, our initial sampled cohort included approximately 6.5% of donors with missing BMI data, who had to be excluded. However, sensitivity analysis before exclusion revealed no meaningful differences in clinical or demographic characteristics between the excluded group and the final cohort.

In conclusion, we have shown that consistent with concerns about an elevated risk of ESRD among obese living donors, there appears to be a nationwide decline in the use of very obese living donors. Although this is reassuring, significant variation in the use of such donors remains, especially in the last era of our analysis. This variation likely stems from lack of robust evidence regarding the impact of nephrectomy on obese donors, and possibly from local prevalence of obesity. With the increasing obesity epidemic in the United States, significant concern remains regarding the future pool of living donors. Further quality studies in animal models and humans are necessary to understand the impact of nephrectomy on rates of CKD progression among obese individuals. In addition, studies assessing the impact of the rapid demographic changes on the future pool of living donors are needed.

ACKNOWLEDGMENTS

This work was conducted under the auspices of the Minneapolis Medical Research Foundation, contractor for SRTR, as a deliverable under contract number HHSH250201500009C (US Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation). The authors thank SRTR colleague Nan Booth, MSW, MPH, ELS, for manuscript editing.

DISCLAIMER

 The views expressed herein are those of the authors and not necessarily those of the US Government.

DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

REFERENCES

1. United States Renal Data System. *2014 USRDS annual data report: An overview of the epidemiology of kidney disease in the United States*. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2014. https://www.usrds.org/2014/view/v2_06.aspx. Accessed May 10, 2017.
2. Muzaale AD, Massie AB, Wang M-C, et al. Risk of end-stage renal disease following live kidney donation. *JAMA*. 2014;311:579-586.
3. Mjøen G, Hallan S, Hartmann A, et al. Long-term risks for kidney donors. *Kidney Int*. 2014;86:162-167.
4. Grams ME, Sang Y, Levey AS, et al. Kidney-failure risk projection for the living kidney-donor candidate. *N Engl J Med*. 2016;374:411-421.
5. Taler SJ, Messersmith E, Leichtman A, et al. Demographic, metabolic, and blood pressure characteristics of living kidney donors spanning five decades. *Am J Transplant*. 2013;13:390-398.
6. Ogden CL, Carroll MD, Kit BK, Flegal KM. PRevalence of childhood and adult obesity in the united states, 2011-2012. *JAMA*. 2014;311:806-814.
7. The State of Obesity. http://stateofobesity.org/adult-obesity/. Accessed March 21, 2017.
8. Foster MC, Hwang S-J, 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.

9. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: third National Health and Nutrition Examination Survey. *Am J Kidney Dis*. 2003;41:1-12.
10. European Renal Best Practice Guideline on the Management and Evaluation of the Living Kidney Donor and Recipient. NDT. 28;S2:ii1-ii71. http://ndt.oxfordjournals.org. Accessed May 8, 2017.
11. Delmonico F. A report of the Amsterdam Forum on the care of the live kidney donor: data and medical guidelines. *Transplantation*. 2005;79(2S):S53-S66.
12. Andrews PA, Burnapp L, Manas D, Bradley JA, Dudley C. Summary of the British Transplantation Society/Renal Association UK guidelines for living donor kidney transplantation. *Transplantation*. 2012;93(7):666-673.
13. Isbel N. Donors at risk: obesity. *Nephrology*. 2010;15(s1).
14. Organ Procurement and Transplantation Network. http://optn.transplant.hrsa.gov/ContentDocuments/OPTN_Policies.pdf. Accessed May 10, 2017.
15. 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.
16. 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.
17. Organization WH, Organization WH. *Obesity: Preventing and Managing the Global Epidemic*. Report of a WHO consulation (WHO Technical Report Series 894). Geneva: WHO; 2015.
18. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150:604-612.
19. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Stamler J. End-stage renal disease in African-American and white men: 16-year MRFIT findings. *JAMA*. 1997;277:1293-1298.
20. Hsu C-Y, McCulloch CE, Iribarren C, Darbinian J, Go AS. Body mass index and risk for end-stage renal disease. *Ann Intern Med*. 2006;144:21-28.
21. Hall JE, Kuo JJ, da Silva AA, de Paula RB, Liu J, Tallam L. Obesity-associated hypertension and kidney disease. *Curr Opin Nephrol Hypertens*. 2003;12:195-200.
22. Steiner R. 'Normal for now'or 'at future risk': a double standard for selecting young and older living kidney donors. *Am J Transplant*. 2010;10:737-741.
23. Ibrahim HN, Foley RN, Reule SA, et al. Renal function profile in white kidney donors: the first 4 decades. *J Am Soc Nephrol*. 2016;27:2885-2893.
24. Mokdad AH, Ford ES, Bowman BA, et al. Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. *JAMA*. 2003;289:76-79.
25. Lentine K, Naik A, Lam N, et al. Obesity predicts new-onset diabetes after live kidney donation. [abstract]. *Am J Transplant*. 2017;3(suppl 3). http://atcmeetingabstracts.com/abstract/obesity-predicts-new-onset-diabetes-after-live-kidney-donation/. Accessed May 8, 2017.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

How to cite this article: Naik AS, Cibrik DM, Sakhuja A, et al. Temporal trends, center-level variation, and the impact of prevalent state obesity rates on acceptance of obese living kidney donors. *Am J Transplant*. 2018;18:642–649. https://doi.org/10.1111/ajt.14519