ORIGINAL ARTICLE

The temporal and long-term impact of donor body mass index on recipient outcomes after kidney transplantation – a retrospective study

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SUMMARY

The impact of increasing body mass index (BMI) on development and progression of chronic kidney disease is established. Even implantation kidney biopsies from obese living donors demonstrate subtle histologic changes despite normal function. We hypothesized that kidneys from obese living (LD) and deceased donors (DD) would have inferior long-term allograft outcomes. In a study utilizing US transplant registry, we studied adult kidney transplant recipients from 2000 to 2014. Donors were categorized as BMI <20 (underweight), 20–25 (normal), 25–30 (overweight), 30–35 (mildly obese), and >35 kg/m^2 (very obese). Our outcome of interest was death censored graft failure (DCGF). Cox proportional hazards model were fitted separately for recipients of DD and LD kidneys, and adjusted for donor, recipient, and transplant characteristics, including donor and recipient size mismatch ratio. Among 118 734 DD and 84 377 LD transplants recipients, we observed a significant and graded increase in DCGF risk among the overweight (LD:HR = 1.06, DD:HR = 1.04), mildly obese (LD:HR = 1.16, DD:HR = 1.10), and very obese (LD:HR = 1.22, DD:HR = 1.22) compared to normal BMI ($P < 0.05$). The graded effect of donor BMI on outcomes begins early and persists throughout the post-transplant period. Donor obesity status is an independent risk factor for inferior long-term renal allograft outcome despite adjusting for donor and recipient size mismatch and other donor, recipient, and transplant factors.

Transplant International 2020; 33: 59–67

Key words
donor BMI, graft failure

Received: 19 November 2018; Revision requested: 19 December 2018; Accepted: 25 August 2019; Published online: 7 October 2019

Introduction

The obesity epidemic has reached alarming proportions and has been linked to the increasing burden of chronic kidney disease (CKD) in the United States and worldwide [1,2]. Obesity causes various structural, hemodynamic, and metabolic alterations in the kidney. Kidneys from obese individuals have been noted to have glomerulomegaly (glomerular hypertrophy), focal segmental glomerulosclerosis, and focal podocyte foot process effacement together being distinctly named as "obesity-related glomerulopathy" (ORG) [3,4]. It has been demonstrated that patients diagnosed with ORG have an increased risk of progression to end-stage renal

doi:10.1111/tri.13505

disease (ESRD) [3,5–7]. The impact of obesity also extends into the arena of transplantation where obese kidney transplant recipients have been noted to have inferior allograft outcomes even after accounting for the increased risk of all-cause death among the obese [8]. However, the impact of donor body mass index (BMI) on both living and deceased donor kidney transplant (KT) outcomes has not been studied systematically.

The exact mechanism(s) behind how obesity leads to CKD or the observed structural changes in the kidney remains unknown. Brenner *et al.* [9] have hypothesized that a kidney that is small for the metabolic needs of an individual is likely to experience a triad of glomerular hypertension, hypertrophy, and hyperfiltration that eventually leads to progressive glomerulosclerosis, proteinuria, and loss of function. This hypothesis explains not only the increased risk of ESRD among obese individuals, but also in kidney transplantation where worse outcomes have been observed in larger recipients of smaller donor kidneys. In contrast, smaller recipients of larger donor kidneys have been associated with better long-term outcomes [10–12].

However, a number of "larger" kidney donors are overweight and obese and are likely to have underlying structural changes in the kidney that would be consistent with ORG. Indeed, implantation biopsies from living donors has revealed the presence of increased glomerular planar surface area (GPSA) and tubular dilatation in obese versus nonobese donors despite no significant difference in serum creatinine or iothalamate clearance [13]. However, whether these structural changes affect long-term allograft outcomes in recipients remain unclear. Previous studies evaluating the role of donor BMI on transplantation outcomes are limited and do not account for the important role that donor and recipient size mismatch play in allograft outcomes [10–12,14–,17]. Given the observed structural changes in the kidneys of obese individuals, we hypothesized that kidneys procured from such donors are likely to have worse outcomes in recipients, independent of the recipient's BMI and even after accounting for the donor and recipient size mismatch, both of which have been independently shown to affect long-term allograft outcomes.

Methods

Data source/demographics

The Scientific Registry of Transplant Recipients (SRTR) database was used for the purpose of this study. The SRTR data system includes data on all donors, waitlisted candidates, and transplant recipients in the United States, as submitted by the members of the Organ Procurement and Transplantation Network (OPTN), and has been described elsewhere. The Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors.

The study population consisted of first-time kidney-only transplants between January 01, 2000 and December 31, 2014. All recipients and donors younger than 18 years of age were excluded from the study. The natural age cutoff to adulthood was chosen with the rationale that kidneys from younger donors might be more immunogenic, have higher rates of delayed graft function (DGF), hyperfiltration injury and increased risk of vascular and ureteral complications [18–24]. Donors were initially classified based on their calculated BMI (kg/m^2) at the time of donation. Since there were few donors with BMI <18.5 kg/m^2 or >40 kg/m^2, we grouped all donors as follows: BMI <20 kg/m^2 (Underweight), 20–24.9 kg/m^2 (Normal BMI), 25–29.9 kg/m^2 (Overweight), 30–35 kg/m^2 (Mildly Obese), and >35 kg/m^2 (Very Obese). Race was categorized as White, Black, Hispanic, and Other (Asian, American Indian, Alaskan Native, Native Hawaiian, other Pacific Islander, Multiracial etc.) as reported by centers to the OPTN.

The primary outcome of interest, death censored graft failure (DCGF), was defined as the earlier of retransplant or return to dialysis with death as a censoring event. Patients were followed from the date of KT until the date of graft failure, date of death, or the end of the observation period (December 31, 2014). Because of the intrinsic differences between deceased and living organ donations, we conducted separate but parallel analyses for the two groups. In addition, as a secondary objective, we assessed the impact of donor obesity on all-cause graft failure (where deaths are treated as events, instead of being censored).

Statistical methods

Our primary objective was to determine if recipients who received kidneys from obese donors experienced worse outcomes compared to recipients who received kidneys from donors of normal BMI. To gain a clearer understanding of the effect of donor BMI on KT outcomes, we adjusted for the following standard donor covariates in addition to donor BMI category for deceased donors: race, gender, 20 pack-year smoking history, diabetes status, hypertension status, cerebrovascular cause of death, donation after cardiac death,

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hepatitis C status, age, and serum creatinine at the time of death. Transplant and recipient factors include the following: cold ischemia time, transplant date, recipient age, race, gender, height, weight, most recent PRA, presence of peripheral vascular disease and chronic obstructive pulmonary disease, hepatitis C status, diabetes status, previous diagnoses (polycystic kidney disease, diabetes, hypertension, etc.), length of dialysis, ABO blood type, medical condition (ICU/hospitalized/reference), previous malignancy, and HLA mismatches. Recipient transplant centers were adjusted using indicator variables (i.e., fixed effects model).

With one exception, the degree of missing data was low (<10%) across all variables of our data set, including variables pertinent to the calculation of donor BMI (0.003% for deceased donor transplants; 7.3% for living donors). Given the low level of missingness, we singly imputed the covariate sample median. One outlier in terms of missingness is that 27.5% of living donations was missing cold ischemic time (CIT). Upon closer look, however, we observe that CIT, for those observed, is highly skewed. Over 50% had a cold ischemic time of less than 1 h and over 75% had a value of less than or equal to 2 h. Because most directed donor or in-center transplants will realistically have a CIT of less than 3 h, it is plausible that the missingness is largely due to clerical oversight (i.e., missing completely at random). Under these conditions, we imputed with the median value (1 h).

For living donations, all standard transplant and recipient factors were the same as those for deceased donations. However, due to the stringent selection criteria for living donors, information on donor smoking, diabetes, hypertension, cerebrovascular cause of death, and hepatitis C status were considered irrelevant. Hence, the adjusted donor factors only include race, gender, age, and creatinine.

In addition to the above-mentioned covariates, we also adjusted our model with a donor to recipient Mosteller body surface area difference [25]. This is in essence an interaction term to account for donor and recipient body surface area mismatch that have previously been shown to be independently related to allograft outcomes [10]. Functional form of the Mosteller body surface area difference was used to visualize and confirm the general linear trend of the covariate (data not shown).

To obtain the functional form of donor BMI, we fit a model with quadratic spline terms (with knots at 25, 27.5, and 30 for deceased donors, and knots at 25 and 30 for living donors) that adjusted for the same confounders as the model to derive the HR comparing the categorized BMI. We then plotted the log HR as a function of donor BMI including 95% confidence intervals, with the reference (log HR of 0) set to a patient with BMI of 25.

Proportional hazards models were fitted separately to deceased and living-donor recipients, adjusting for the afore-listed covariates [26]. Our main covariate of interest, donor BMI, was separated into five categories as listed above. The reference group was selected to be the normal weight group (BMI 20–25 kg/m^2), and hazard ratios (HRs) were computed for all other groups compared to the reference group.

We quantified the effect on DCGF of donor BMI using two metrics. The first was the hazard ratio (HR), estimated using the Cox models described in the preceding paragraph. For example, the HR for the donor BMI 26–30 equals the DCGF hazard (rate) divided by the DCGF rate of the BMI 20–25 category (i.e., the reference), considering two hypothetical transplants where all covariates (aside from donor BMI) are equal. The second metric was the cumulative hazard ratio, which we plotted against time since transplant [27]. Unlike the HR, the cumulative hazard ratio is not assumed to be constant and, instead, is computed as a process over follow-up time. Cumulative hazard ratios were estimated through models that adjusted for the same covariates listed above, but stratified by donor BMI category. The two metrics are related in the sense that the cumulative hazard ratio equals the HR when the former is constant over time.

Donor and recipient BMI are associated with delayed graft function (DGF) which, in turn, has been shown to be associated with allograft survival [28]. Hence, in a second analysis, we excluded patients that experienced DGF or had graft losses in the first 7 days, then fitted a Cox model in this cohort.

All analyses were performed using R version 3.5.1 and SAS version 9.4.

Results

A total of 118 734 deceased-donor and 84 377 living-donor KT were included in our analysis. Of these, 21 996 (18.5%) of deceased-donor and 11 497 (13.6%) of living-donor KT recipients experienced graft failure. For deceased donations, 21 655 graft failures were attributed to return to dialysis and 637 to repeat transplantation. These numbers include 296 same-day events between return to dialysis and re-transplants. Similarly, for living organ transplants, there were 10 998 and 840 graft failures attributed to returns to dialysis and re-transplants, with 341 same-day events.

Demographics of study cohort

Table 1 shows the donor factors of the study population for both deceased and living donor KT. Deceased donors had a mean BMI of 27.3 (SD 5.76), while living donors had a mean BMI of 26.9 (SD 4.49) (Fig. 1). Compared to deceased donors, living donors tended to be more overweight (43.7% vs. 34.0%) and obese (18.0% vs. 16.9%). The mean serum creatinine among living donors was 0.87 mg/dl (SD 0.26) vs. 1.13 mg/dl (SD 0.66) among deceased donors at the time of donation. Delayed graft function was reported in 26.2% of deceased donor recipients and 3.96% of living kidney donor recipients.

Differential survival based on donor BMI categories

To determine the overall effect of donor BMI categories on graft failure, we fitted a Cox regression model adjusting for standard covariates. Table 2 shows the subset of cox regression results for donor BMI categories using the reference category of donor BMI 20–25. There is a clear stepwise increase in death censored allograft failure with increasing BMI. Notably, even a BMI <20 kg/m^2 in recipients of cadaveric donors was associated with increased risk of death censored allograft failure.

Figure 2 shows the functional form of donor BMI in both deceased and living data sets. We can see that for deceased donors, BMI roughly follows a U-shape, where the parameter estimates (equivalently, hazard ratios) are highest at the two ends of the BMI. On the other hand, the functional form of BMI for living donors is roughly linear, indicating that higher donor BMI leads to a higher prediction of risk.

To visualize the effect of donor BMI across time we plotted the cumulative hazard ratio against times since transplant (Fig. 3). Figure 3a demonstrates that recipients of kidneys from overweight, mildly obese and very obese deceased donors have a progressive increase in the risk of death censored allograft failure that begins immediately after transplantation and remains elevated over the life of the transplant compared to the donor in the reference BMI category.

Similar patterns emerge for recipients of allografts from overweight, obese and very obese living donors except when donor BMI was <20 kg/m^2 (Fig. 3b). In kidneys from underweight donors, the hazard rate was lower compared to reference after 2.5 years post-transplant despite the initial increased risk of allograft failure. One thing to note is that because Mosteller BSA difference has been included in the model and predictions are done for donor–recipient pairs with no Mosteller BSA difference, workload discrepancies between donor and recipient kidney systems alone cannot account for this discrepancy in the cumulative hazard. Figures S1 and S2 demonstrate effect of donor BMI across time on all cause graft failure and patterns remain similar to DCGF models.

When DGF and graft failure within the first 7 days after kidney transplant were excluded, there was no significant difference in our hazard estimates thereby suggesting that the effect of BMI on death censored allograft survival is likely to be independent of its effect on DGF (Table 3).

Table 1. Clinical characteristics by donor type

Donor parameters	DeceasedMean (SD) or percent	LivingMean (SD) or percent
Age	41.98 (14.05)	41.12 (11.38)
Race		
White race	71.3%	69.6%
African American race	12.6%	12.7%
Hispanic race	12.9%	13.0%
Asian race	2.3%	3.4%
Other race	0.9%	1.3%
Gender		
Female	40.8%	60.2%
Serum creatinine (mg/dl)	1.13 (0.66)	0.87 (0.26)
Greater than 20 pack-year smoking history	32.2%	NA
Diabetic	7.3%	NA
Hypertensive	30.3%	NA
Cause of death: cerebrovascular stroke	40.6%	NA
Donation after cardiac death	11.2%	NA
HCV positive	2.8%	NA
Mosteller BSA difference (donor–recipient)	0.0073 (0.36)	−0.0406 (0.33)
Donor BMI		
<20 (lower weight)	6.3%	3.8%
20–25 (normal)	32.5%	30.6%
25–30 (overweight)	34.0%	43.7%
30–35 (mildly obese)	16.9%	18.0%
>35 (very obese)	10.3%	3.9%

Discussion

In a large cohort of kidney donors and recipients spanning a decade and a half, we noted several key findings. First, we noted a graded, stepwise increase in the hazard

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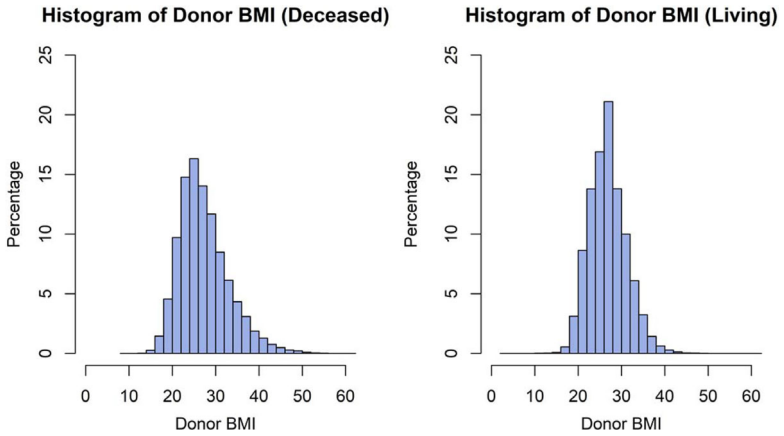

Figure 1 Distribution of body mass index by donor type

Table 2. (a) Effect of deceased donor body mass index (BMI) on death censored allograft outcomes. (b) Effect of living donor BMI on death censored allograft outcomes

Donor BMI	Coefficient	Hazard ratio	95% CI of HR	*P*-value
(a)				
<20	0.100	1.11	1.04, 1.17	0.00061***
25–30	0.036	1.04	1.00, 1.08	0.0525
30–35	0.098	1.10	1.05, 1.16	0.0002***
>35	0.201	1.22	1.14, 1.31	<0.0001***
(b)				
<20	−0.064	0.94	1.04, 1.17	0.221
25–30	0.058	1.06	1.00, 1.08	0.02*
30–35	0.147	1.16	1.05, 1.16	<0.0001***
>35	0.195	1.22	1.14, 1.31	0.0005***

Multivariable model was adjusted for:

Donor factors: race, gender, age, serum creatinine, BMI category.

Deceased only donor factors: diabetes status, hypertension status, HCV serum positivity, stroke as cause of death, donation after circulatory death, greater than 20 pack-year (smoking).

Recipient factors: age, transplant date, race, gender, height, weight, most recent PRA, comorbidities (peripheral vascular disease, chronic pulmonary obstructive disorder, diabetes, hypertension, polycystic kidney disease, other diagnoses), HCV serum positivity, dialysis length, ABO blood type, pre-transplant malignancy, working status, medical condition (ICU/hospitalized/neither).

Transplant factors: HLA mismatches, Mosteller BSA difference, cold ischemic time, transplant center (by factor).

Reference donor BMI category was 20–25 kg/m^2.

* indicates a *P*-value less than or equal to 0.05

** indicates a p-value less than or equal to 0.01.

of graft failure in kidneys procured from overweight and obese donors compared to donors with a normal body mass index. Importantly, this effect lasted even after adjustment for donor, recipient, and transplantation factors including donor and recipient size mismatch, a phenomenon known to drive long-term allograft failure. Secondly, we noted that kidneys from overweight and obese living donors experienced a high risk of graft loss early after transplantation and while this risk reduced with time, it remained elevated compared to kidneys from donors with a reference BMI. Together these data are consistent with the hypothesis that kidneys from obese (and overweight) donors, as defined by BMI, likely have underlying structural damage that affects long-term allograft survival.

Two studies have specifically investigated whether donor BMI was associated with long-term allograft outcomes. In the first study that analyzed deceased donors from the UK transplant registry, the authors noted an association between donor BMI and 12-month creatinine as well as death censored graft survival. However, this relationship was lost after multivariable adjustment [14]. While the authors did adjust for recipient BMI, they did not investigate the interaction between donor and recipient BMI on outcomes. A second US-based registry study observed no association between donor BMI and death censored allograft survival among organs procured after brain death (DBD). However, donor BMI of >45 kg/m^2 was associated with death censored allograft outcomes among recipients of organs after circulatory death (DCD) [16]. Such extremes of donor BMI are however unusual and these donors are typically excluded from donation. Additional studies evaluating the effect of recipient and donor size mismatch had not specifically tested whether donor BMI was an independent risk factor for outcomes [12,17]. In our study, after adjustments for recipient and donor body size mismatch and multiple additional donor, recipient, and transplantation factors, we were able to

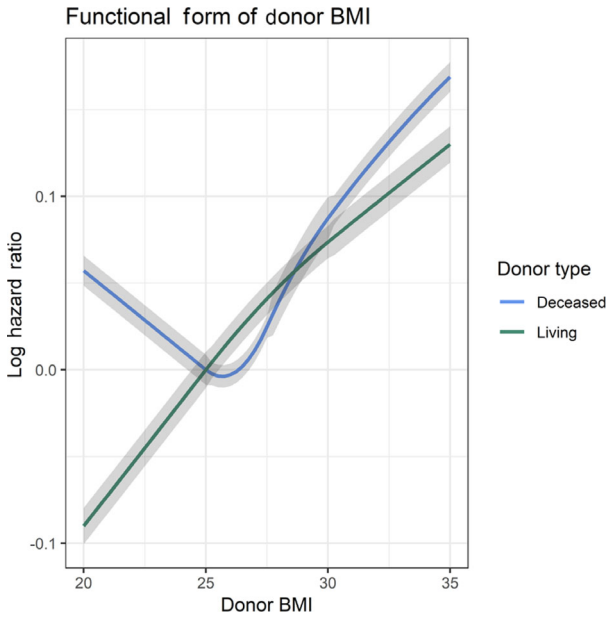

Figure 2 Functional form of donor body mass index (BMI) for deceased and living donations. Functional form of donor BMI for both deceased and living donations. Donor BMI was modeled with quadratic spline terms (with knots at 25, 27.5, and 30 for deceased donors, and knots at 25 and 30 for living donors) in a model that adjusted for confounders. Log HR was plotted against donor BMI, and 95% confidence intervals were included. The reference (log-HR of 0) was set to a patient with BMI of 25. The donor BMI functional form for deceased donations follows a U-shape, while the functional form for living donations is roughly linear.

demonstrate a clear graded increased risk of death censored and all-cause allograft failure among kidneys from donors who were overweight and obese. Further, donor DCD or DBD status did not affect this relationship.

The cause of increased risk of allograft failure among recipients of kidneys with higher donor BMI remains speculative but at least two pertinent issues are worth considering. First, it is possible that the increased risk of graft failure might be due to underlying structural injury that makes these grafts more prone to the ischemic, immune and workload insults of kidney transplantation. The second possibility is that the higher risk of delayed graft function among kidneys from obese donors might affect long-term outcomes. While a previous study did not observe an effect of donor BMI on DGF [28], a recent study of deceased donors from the British transplant registry noted a higher rate of DGF among obese donor kidneys. However, this increased rate of DGF did not translate into a higher risk of long-term allograft loss or death [14]. Despite this finding, given the known association of DGF with long-term allograft survival [29,30] we conducted additional sensitivity analysis excluding patients that had DGF or lost their grafts within the first 7 days after transplantation (to reduce the impact of DGF, technical and other organ complications on long-term outcomes). To our surprise, even after this exclusion those who received kidneys from overweight and obese donors continued to experience a stepwise higher risk of allograft failure (Table 3). This would suggest that the impact of overweight and obese donors on long-term allograft outcomes is largely independent of the effect of donor BMI on delayed graft function.

In addition, we noted that the hazard rate of graft loss over time appears to be higher in the first 1–2 years post-transplantation in the overweight and obese groups compared to reference BMI. This increased hazard rate is especially prominent among recipients of deceased donor KT, which might be related to the deleterious immune, ischemia reperfusion injury and other processes experienced during the process of transplantation in comparison to recipients of living donor kidneys. Interestingly, in recipients of a deceased donor kidney even a low donor BMI was associated with a higher risk of graft loss versus reference donor BMI. Investigations into the possible cause of graft loss in these individuals were inconclusive due to the high missing rate of cause of graft loss in our cohort for that subgroup (>90%). As we excluded donor age below 18 years of age (thus kidneys should all be of adult size) these kidney losses are unlikely to be of a technical nature. Furthermore, we would have expected any effect of technical nature to have attenuated over time. Even among kidneys from living donors, we noted an initial increase in graft losses however this effect was attenuated over time where the hazards of allograft failure appear to be lower than the reference BMI. Besides the early increase in allograft loss in recipients of kidneys from underweight deceased and living donors, the higher risk of long-term allograft loss among underweight deceased donors remains unclear but might be related to pathological weight loss in the donor prior to death and should be an area of future investigation.

Although kidneys from overweight and obese donors have inferior outcomes, we do not suggest that such kidneys not be utilized for organ transplantation. It is likely that recipients of such organs gain a significant survival benefit compared with staying on dialysis, but this hypothesis remains to be tested. It does however raise questions on potential long-term impact in overweight and obese living donors. If recipients of such kidneys have worse outcomes due to underlying structural injury to the donor kidney, the remnant kidney

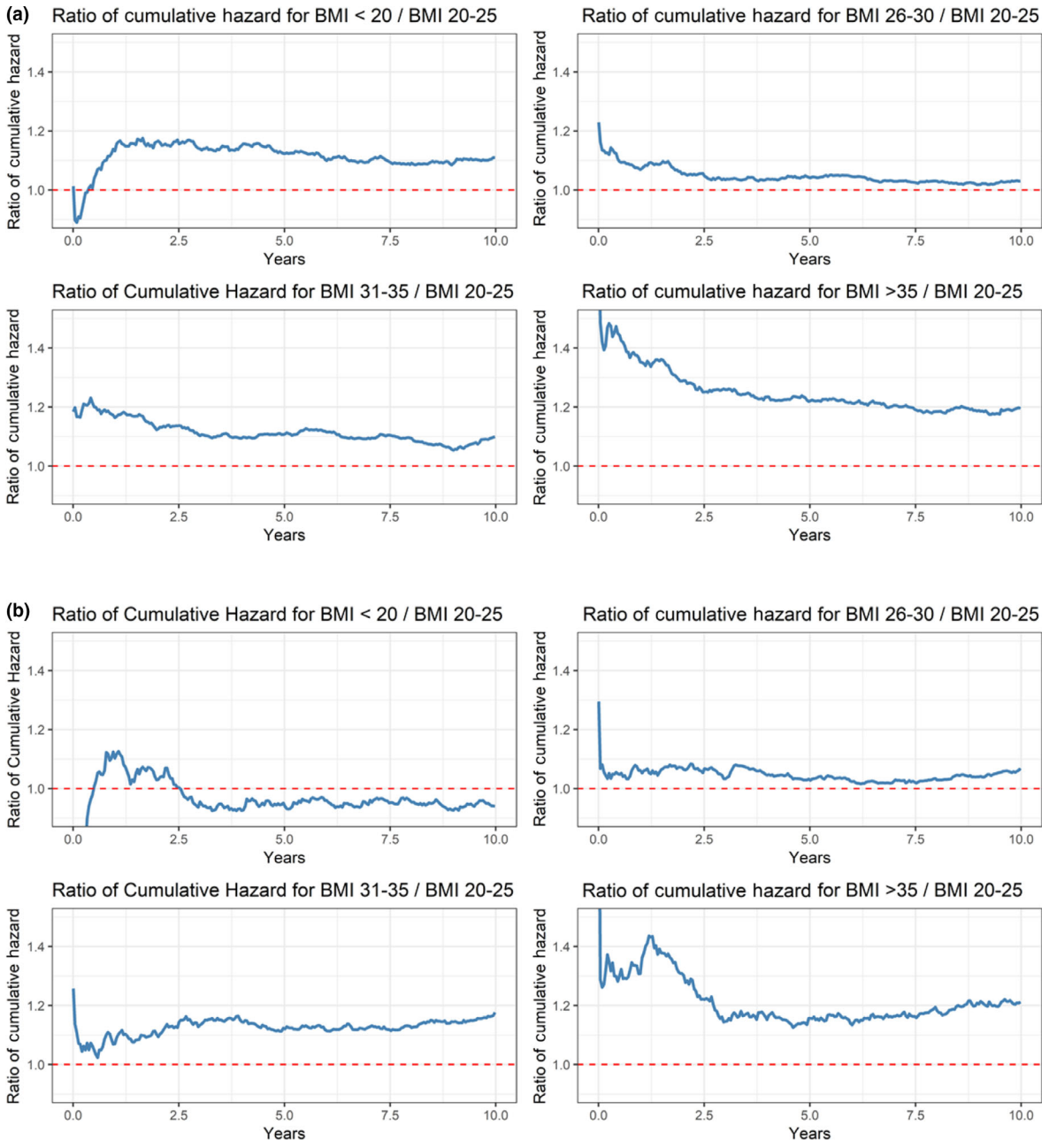

Figure 3 (a) Cumulative hazard ratio (by time since transplant) for death censored allograft failure by donor body mass index (BMI) category. Deceased donor allografts. Recipients of kidneys from overweight, obese, and very obese cadaveric donors have a graded significantly elevated risk of death censored allograft loss that begins immediately after transplant and stays elevated compared to recipients who receive kidneys from cadaveric donors with a normal BMI (solid red line as a reference). In sharp contrast, while kidneys from underweight donors do well very early after transplantation, this risk appears to increase over time for reasons that remain unclear. (b) Cumulative hazard ratio (by time since transplant) for death censored donor allograft failure by donor BMI. Living donor allografts. Recipients of kidneys from overweight, obese and very obese living donors have a graded significantly elevated risk of death censored allograft loss that begins immediately after transplant and stays elevated compared to recipients who receive kidneys from living donors with normal BMI. For recipients of underweight living donor kidney transplants, the initial risk appears low, becomes high, but falls by the end of the second post-transplantyear.#AuthorQueryReply#

in the donor will likely also experience the hypertrophic stresses of the one kidney state, minus the ischemia reperfusion injury, drug toxicity and immune insults. Further, how postdonation weight gain, development of hypertension and diabetes after donation might impact a single kidney state remains unclear due to lack of granular long-term follow-up data. As expected by this hypothesis, a recent registry-based

Table 3. (a) Effect of deceased donor body mass index (BMI) on death censored allograft outcomes when delayed graft function (DGF) patients are excluded. (b) Effect of living donor BMI on death censored allograft outcomes when DGF patients excluded

Donor BMI	Coefficient	Hazard ratio	95% CI	*P*-value
(a)				
<20	0.103	1.11	1.03, 1.19	0.004**
25–30	0.010	1.01	0.96, 1.06	0.665
30–35	0.054	1.06	0.99, 1.13	0.121
>35	0.158	1.17	1.07, 1.28	0.0007***
(b)				
<20	−0.043	0.96	0.86, 1.07	0.438
25–30	0.045	1.05	0.99, 1.10	0.100
30–35	0.141	1.15	1.07, 1.24	0.0002***
>35	0.166	1.18	1.05, 1.33	0.005**

Multivariable model was adjusted for:

Donor factors: race, gender, age, serum creatinine, BMI category.

Deceased only donor factors: diabetes status, hypertension status, HCV serum positivity, stroke as cause of death, donation after circulatory death, greater than 20 pack-year (smoking).

Recipient factors: age, transplant date, race, gender, height, weight, most recent PRA, comorbidities (peripheral vascular disease, chronic pulmonary obstructive disorder, diabetes, hypertension, polycystic kidney disease, other diagnoses), HCV serum positivity, dialysis length, ABO blood type, pre-transplant malignancy, working status, medical condition (ICU/hospitalized/neither).

Transplant factors: HLA mismatches, Mosteller BSA difference, cold ischemic time, transplant center (by factor).

In addition to DGF, any recipient with a follow-up time of <7 days was also excluded for the purpose of this analysis.

Reference Donor BMI category was 20–25 kg/m^2.

** indicates a *P*-value less than or equal to 0.05

*** indicates a p-value less than or equal to 0.01.

study demonstrated that by 15-years postdonation, obese living donors have an increased risk of progression to ESRD (93 vs. 30, for nonobese donors, per 100 000 donors) [31]. Very long-term outcomes including the risk of CKD and ESRD among overweight and obese donors are expected to be worse but studies with longer follow-up are needed.

As with any large retrospective study, our study has a specific focus and several limitations. First of all, because our primary goal was to show the relationship between donor BMI and DCGF outcomes, metrics to measure discrimination or predictive accuracy (such as the c-index) were therefore not pursued. Various adjustment measures (such as Mosteller BSA and donor BMI) were included in the model that otherwise would not be in a model that prioritized risk prediction. Secondly, the retrospective nature of our study does not allow us to adjust for unmeasured confounders that could affect allograft outcomes. Further, our dataset did not have any histologic parameters of such organs such as implant biopsy, percentage of global glomerulosclerosis, glomerular volume, or the health of the tubule-interstitium. In addition, the increased risk of graft failure among donors with higher BMI does not imply a direct causal relationship between donor BMI, abnormal histology and allograft failure. Lastly, we did not adjust for immunosuppression as linked immunosuppression data were not available. However, since most transplant centers have fixed immunosuppression protocols, we believe that adjusting for center effect should have accounted for immunosuppression effect on our outcomes of interests.

In summary, we demonstrate that kidneys from overweight and obese deceased and living donors are associated with a graded increased risk for death censored graft failure after kidney transplantation. Further, this increased risk starts early and persists throughout the entire post-transplant period. These data support the hypothesis that obesity-associated kidney disease in donors might have a detrimental impact on long-term allograft outcomes even after accounting for recipient obesity and donor and recipient size mismatch. Since the increased risk of allograft failure is also seen in kidneys procured from overweight and obese living donors, our study also offers parallel evidence to support recent studies that demonstrate increased risk of ESRD among obese living donors.

Authorship

DES: Participated in study design, acquisition of data and regulatory approvals, data analysis, and writing of the paper. ASN: Participated in study design, interpretation, and writing the first draft of the paper. RP, MD, SN, YL, ES, VS: Participated in data interpretation, and writing of the paper. YZ: Participated in data analysis, interpretation, and writing of the paper.

Funding

The authors have declared no funding.

Conflicts of interest

The authors have declared no conflicts of interest.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Cumulative Hazard Ratio (by time since transplant) for total graft failure by Donor BMI category. Deceased Donor Allografts.

Figure S2. Cumulative Hazard Ratio (by time since transplant) for total graft failure by Donor BMI.

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