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Effects of body mass index on kidney transplant outcomes are significantly modified by patient characteristics

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Abstract

Body mass index (BMI) is a known risk factor associated with kidney transplant outcomes and is incorporated for determining transplant candidate eligibility. However, BMI is a coarse health measure and risks associated with BMI may vary by patient characteristics. We evaluated 296 807 adult (age > 17) solitary kidney transplant recipients from the Scientific Registry of Transplant Recipients (2000–2019). We examined effects of BMI using survival models and tested interactions with recipient characteristics. Overall, BMI demonstrated a "J-Shaped" risk profile with elevated risks for overall graft loss with low BMI and obesity. However, multivariable models indicated interactions between BMI with recipient age, diagnosis, gender, and race/ethnicity. Low BMI was relatively higher risk for older recipients (>60 years), people with type I diabetes, and males and demonstrated no additional risk among younger (18–39) and Hispanic recipients. High BMI was associated with elevated risk for Caucasians and attenuated risk among African Americans and people with type II diabetes. Effects of BMI had variable risks for mortality vs graft loss by recipient characteristics in competing risks models. The association of BMI with posttransplant outcomes is highly variable among kidney transplant recipients. Results are important considerations for personalized care and risk stratification. Findings suggest that transplant contraindications should not be based on absolute BMI thresholds but modified based on patient characteristics.

Keywords

clinical research/practice; diabetes: type 1; epidemiology; ethnicity/race; gender; graft survival; health services and outcomes research; kidney transplantation/nephrology

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DISCLOSURE

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

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

1 | INTRODUCTION

The association of body mass index (BMI) with mortality and other health outcomes has been extensively described in the general population.[1–3] In general, both low and high BMI levels are associated with inferior outcomes and increased disability. Average BMI levels have significantly increased over time in the United States included several states with more than one third of the population classified as obese.[4] BMI is also a significant risk factor among kidney transplant recipients. High BMI level at the time of transplantation is associated with increased risk of posttransplant mortality, graft failure, delayed graft function, and other surgical complications.[5–7] Low BMI levels have also been shown as a risk factor for diminished posttransplant outcomes, which in some cases may relate to frailty and sarcopenia.[8–11] Cumulatively, there is a well-established "J-Shaped" curve characterizing risks associated with BMI for kidney transplant recipients.

High BMI levels are commonly used as a contradiction for patient eligibility for the transplant procedure. Selected obese patients gain a survival advantage with kidney transplantation relative to maintenance dialysis in almost all subsets of the population, but specific transplant eligibility criteria based on BMI thresholds may vary between transplant centers.[12] Relative to patients with BMI classified in normal ranges, obese patients have significantly diminished access to kidney transplantation.[13–17] Transplant centers may also advise obese patients to lose weight prior to considering their eligibility for the procedure.[18,19]

Despite the robust evidence establishing the effects of BMI on access to transplantation and posttransplant outcomes, BMI is relatively coarse measure of health status. BMI may represent variable physiological states, and other measures, such as waist circumference, muscle mass, and visceral fat levels, may be more specific indicators of risks and outcomes.[20–23] The degree to which the effects of BMI may differ based on other transplant recipient characteristics are relatively unclear. For example, BMI may have different implications for certain portions of the population such as the elderly or cause of end-stage renal disease.[2,21,23,24] Despite the potential variable implication of BMI, thresholds guiding eligibility for the transplant procedure or certain interventions may be consistently applied within the population.

In the present study, we sought to further characterize the association of BMI with kidney transplant graft and patient survival. Our intent was to evaluate the potential for effect modification based on the relationships of BMI with recipient characteristics. Our specific hypotheses were that the association of obesity and underweight BMI levels had differential effects within strata of the recipient population and that these effects may be substantial enough to consider for differential clinical management and decision-making.

2 | METHODS

The data source for this study was the Scientific Registry of Transplant Recipients (SRTR). The SRTR data system includes data on all donors, waitlisted candidates, and transplant recipients in the United States, submitted by the members of the Organ Procurement

and Transplantation Network (OPTN), and has been described elsewhere.[25] The Health Resources and Services Administration (HRSA), US Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors.

We evaluated the cumulative incidence of graft loss and mortality using unadjusted competing risks models.[26] Graft loss was defined as the initial event of either repeat transplantation or return to maintenance dialysis. We evaluated the association of BMI with time to overall graft loss (death, repeat transplantation, or return to maintenance dialysis) using multivariable Cox proportional hazard models. We tested for interactions of BMI with time to graft loss and patient death among a priori selected characteristics including recipient age, race/ethnicity, gender, and primary diagnosis. For the purpose of testing interactions, we categorized recipient characteristics based on predefined clinical groups and to maintain sufficient sample size within each subgroup to test for interactions. All multivariable models were adjusted for recipient age, race/ethnicity, gender, primary diagnosis, donor type, donor age, panel reactive antibody percentage, dialysis time prior to transplant, primary vs retransplantation, year of transplant, history of malignancy, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, drug-treated chronic obstructive pulmonary disease, human leukocyte antigen matching, and primary insurance with additional interaction terms for variables previously described. We categorized missing data as a level for applicable variables and included these levels in statistical models. In order to consider nonlinear effects of BMI, we incorporated BMI as a cubic spline term in multivariable models with 5 potential knots using a truncated power function for spline expansion. This approach allowed for the effects of BMI to vary at different levels including potential accelerated risks at extreme levels. These results were also used to produce multivariable plots depicting the relative hazards for overall graft loss by BMI.

We presented stratified models by BMI group incorporating potential differential effects of covariates between BMI groups including deceased and living donor transplants as well as stratified by decade within the study period. The stratified models for deceased donor transplants incorporated adjustment for the kidney donor risk index to replace donor age alone. In addition, we estimated 10 years adjusted overall graft survival by BMI and recipient groups using Cox multivariable models. These models were generated using average transplant characteristics beyond the variables of interest (eg, BMI and recipient characteristics). The study was approved by the Cleveland Clinic Institutional Review Board (protocol #09–648). All statistical analyses were evaluated with SAS v. 9.4(SAS Institute, Cary, NC).

3 | RESULTS

The study population included 296 807 adult (age >17 years) solitary kidney transplant recipients with a transplant between 2000 and 2019. Recipients with a missing BMI or a BMI recorded as <13 or >60 kg/m^2 were excluded from the study population assuming potential miscoding (n = 580, 0.2%). The distribution of BMI is displayed in Figure 1. The median BMI in the study population was 27.2 kg/m^2 and the mean was 27.7 kg/m^2 (standard deviation = 5.5 kg/m^2). There were 6.1% of recipients with a BMI < 20 kg/m^2 and 10.5% with BMI ≥ 35 kg/m^2. The majority of transplants derived from deceased donors (63.7%)

and were male recipients (60.5%) and the proportion of patients by race/ethnicity included 51.8% non-Hispanic Caucasian, 25.7% African American, and 15.0% Hispanic. BMI levels significantly increased over time including a 48% increase in morbidly obese recipients (BMI > 35 kg/m^2) from the 2000–2004 to the 2015–2019 era. Demographic and clinical characteristics of the study population stratified by BMI level are displayed in Table 1.

3.1 | Association of body mass index with outcomes by recipient age

The distribution of BMI by recipient age at the time of transplantation is displayed in Table 1. Younger recipients were more likely to have a low BMI (14.2% with BMI < 20 kg/m^2) and morbid obesity was most common in age groups 40–49 (11.9%) and 50–59 (11.3%). In unadjusted competing risk models, there were statistically significant differences in the effects of recipient age by BMI and the cumulative incidence of graft loss and mortality. For young recipients (18–39 years), graft loss was more common than mortality and the incidence of graft loss increased with increasing BMI (Figure 2A). These results were consistent in the multivariable model, in which lower BMI was associated with the lowest relative risk for overall graft loss and the relative hazard increased with severity of obesity consistent with other recipients in the study population (Figure 3A). The estimated adjusted 10-year overall graft survival was highest for younger recipients with BMI = 18 kg/m^2 as compared to other BMI levels (Table 2).

For recipients ages 40–49, the incidence of graft loss was more frequent than mortality across BMI levels (Figure 2B). Graft loss was highest in the obese groups and mortality was lowest in the average BMI (20–29 kg/m^2) groups. In multivariable analysis with adjustment for donor and recipient characteristics, both low and high BMI levels had higher relative hazard for overall graft loss as compared to other age groups (Figure 3B). Estimated 10-year overall graft survival was highest for BMI = 25 kg/m^2 and reduced for both low BMI and increasing level of obesity (Table 2). Among recipients ages 50–59, mortality was more frequent than graft loss across all levels of BMI (Figure 2C). The incidence of mortality was highest for both low BMI and obesity and incidence of graft loss was highest associated with obesity. In multivariable analysis, low BMI and higher BMI were associated with increased hazards for overall graft loss with a similar effect size (Figure 3C). Adjusted 10-year overall graft survival was highest among recipients with a BMI = 25 kg/m^2 and reduced to a similar level among recipients with BMI = 18 and 35 kg/m^2 (Table 2).

For recipients ages >60 years, the incidence of mortality was significantly more common than graft loss. Mortality incidence was highest in the low BMI group and the incidence of graft loss was highest among obese recipients (Figure 2D). In multivariable analysis, the hazard for overall graft loss was highest for recipients with low BMI and relatively lower for obesity compared to younger recipients in the population (Figure 3D). Ten-year estimated adjusted overall graft survival was highest among recipients with BMI = 25 kg/m^2 and lower among recipients with BMI = 18 kg/m^2 as compared to recipients with BMI = 35 kg/m^2 (Table 2).

3.2 | Association of body mass index with outcomes by race/ethnicity

The distribution of BMI was variable by the race/ethnicity of transplant recipients (Table 1). African Americans had the highest proportion of morbidly obese recipients and lowest proportion of low BMI recipients. Recipients in the other race/ethnic category had the highest proportion of low BMI patients. Among non-Hispanic Caucasian recipients, the cumulative incidence of mortality was highest among obese recipients and graft loss was highest among both low BMI and obese recipients (Figure 4A). As depicted in Figure 5A, in adjusted analysis both low BMI and obesity had higher relative effects on overall graft loss as compared to other racial/ethnic groups. Among African Americans, the incidence of graft loss was higher than mortality across all BMI groups (Figure 4B). However, the incidence of graft loss and mortality was similar in each BMI group. In multivariable analysis, the relative effect of obesity was lower among African Americans than other race/ethnic groups (Figure 5B). African Americans had lower adjusted estimated 10-year overall graft survival than other racial/ethnic groups but the differences by BMI were less pronounced than other group (Table 2). For Hispanic recipients, the incidence of graft loss was higher than mortality across all BMI groups but the incidence of mortality increased by BMI (Figure 4C). In multivariable analysis, there was minimal effect of low BMI on the hazard for overall graft loss among Hispanics and a similar relative effect of obesity with increased hazards (Figure 5C). Ten-year estimated adjusted overall graft survival was highest among Hispanics relative to other race/ethnic groups and highest in low to mid BMI levels (Table 2).

3.3 | Association body mass index with outcomes by gender

Female recipients were more likely to have both low BMI and morbid obesity relative to male recipients (Table 1). Female recipients had the highest incidence of graft loss and mortality among obese recipients and relatively similar incidence between low and mid BMI levels (Figure 6A). Males had the lowest incidence of graft loss and death in the mid BMI groups (Figure 6B). In multivariable analysis, females had an attenuated effect of low BMI as compared to males and males had a higher relative effect of obesity relative to females (Figure 7). Ten-year adjusted estimated overall graft survival was higher among females than males in each BMI level but more pronounced at low and high BMI levels (Table 2).

3.4 | Association of adjusted overall graft loss by primary diagnosis

There was significant variation in the BMI distribution by patients' primary diagnoses (Table 1). Recipients with glomerulonephritis as primary diagnosis were more likely to have low BMI, and people with type II diabetes more commonly had high BMI levels. For recipients with glomerulonephritis as primary diagnosis, incidence of graft loss was more common than mortality across BMI levels and the incidence of graft loss and mortality was highest among obese recipients (Figure 8A). In multivariable analyses, low BMI had a modest association with overall graft loss, and obesity had a similar relative hazard for overall graft loss as other recipients in the study population (Figure 9A). Ten-year adjusted estimated graft survival was higher among glomerulonephritis patients relative to other diagnosis categories and relatively higher in low BMI groups (Table 2).

Among patients with type II diabetes as primary diagnosis, the incidence of mortality was higher than incidence of graft loss across all BMI groups (Figure 8B). Mortality incidence was highest among recipients with low BMI. In multivariable analyses, the effects of obesity were relatively attenuated among patients with type II diabetes as compared to other recipient groups (Figure 9B). People with type II diabetes had the lowest adjusted estimated 10-year overall graft survival rates compared to other diagnosis groups; however, the effects of BMI were relatively modest as compared to other groups (Table 2). Among recipients with hypertension as primary diagnosis, the incidence of graft loss was higher than mortality across all BMI groups and the highest rates of graft loss were among obese recipients (Figure 8C). In multivariable analysis, the estimated hazard for overall graft loss for recipients with low BMI was reduced compared to other recipients with a similar relative hazard associated with increasing obesity (Figure 9C). For recipients with type I diabetes, the incidence of mortality was higher than graft loss across all BMI groups (Figure 8D). The mortality incidence was highest among low BMI groups and the incidence of graft loss was highest among obese patients. In multivariable analyses, the effect of low BMI was significantly higher among patients with type -I diabetes compared to other diagnosis groups (Figure 9D). Adjusted estimated 10-year overall graft survival was lower among patients with low BMI = 18 kg/m^2 as compared to morbid obese levels BMI = 35 kg/m^2 among people with type I diabetes (Table 2). The association of categorized BMI levels with outcomes stratified by donor type (living or deceased donors) and transplant era (transplant years 2000–2009 and 2010–2019) are displayed in Table S1. In general, results in subsets of the population were consistent between deceased and living donors and over the 2 decades of the study period.

4 | DISCUSSION

There are several principal findings of this study of adult solitary kidney transplant recipients in the United States from 2000 to 2019. The association of BMI with outcomes following kidney transplantation demonstrated a “J-shaped” risk profile with higher risks at both low and high levels. However, the relative magnitude of these risks varied significantly within the study population including differential effects by age, race/ethnicity, gender, and primary diagnosis. The relative risks for mortality and graft loss differed by subgroups and the risks of each event were modified by BMI. Cumulatively, the results indicated that BMI has a heterogeneous effect on posttransplant graft and patient survival and the risks are modified based the combination of demographic and clinical characteristics. These results have implications for risk stratification and to inform personalized interventions. Results may also be important for assessing candidate viability for transplantation with consideration of variable BMI thresholds based on patient factors.

The differential association of posttransplant outcomes by age may be related to several factors. Certainly, underlying reasons for low BMI levels (and potentially weight loss) and the prevalence of associated comorbid conditions associated with diabetes may be different for young and older patients.[27] As depicted in the results, lower BMI was not associated with risk for younger patients, which may be more commonly reflective of healthy physiological states, whereas low BMI among older patients may be more likely to reflect various forms of frailty or comorbid conditions.[10,20,22] In addition, the relationship

between BMI and outcomes has differential effect on graft failure as compared to mortality as depicted in competing risks analysis. Not surprisingly for younger patients, mortality rates are low and incidence of overall graft loss is affected primarily by graft failure. Mortality shifts to the primary reason for overall graft loss with increasing age. For patients older than 60 years, mortality rates were notably higher at low BMI levels whereas graft loss rates incrementally increased with elevated BMI. Overall, the effects of BMI explicitly on graft loss and mortality differ as well and contribute to the modified effect of BMI by age.[21,28]

The association of BMI also varied significantly by race/ethnicity in the study population. In particular the relative effect of high BMI levels for African Americans were attenuated relative to Caucasians. African Americans had significantly higher graft failure rates than Caucasians at each BMI level but similar overall mortality.[29] Increased graft failure rates among African Americans have been attributed to numerous factors including underlying comorbid conditions, environmental and socioeconomic condition, but based on the present results, elevated BMI is less impactful as compared to other racial/ethnic populations.[30–32] Hispanic recipients had higher estimated posttransplant overall graft survival than other racial/ethnic groups which has been reported in prior studies.[33–36] This survival advantage may not be uniform as age and race/ethnic combination has been shown to modify survival among Hispanics.[33,35] The present study depicted that longer term overall graft survival is higher among Hispanics across BMI levels and interestingly, the deleterious association of low BMI was not present in this group. Evaluation of the potential differential physiological associated features of BMI between Hispanics and other racial/ethnic groups requires further study.

In another national registry study, Gill et al[14] demonstrated that BMI was a significant modifier of access to transplantation by gender with higher BMI associated with a reduced likelihood of transplant among women but increased likelihood among men. In a Japanese cohort, female transplant recipients had lower relative risks of posttransplant graft loss as compared to men.[37] The current findings indicated that females had higher estimated survival across all BMI levels as compared to men and furthermore that increased survival was more pronounced at low BMI and higher obesity levels. This suggests that low BMI may be more indicative of reduced health status and obesity portends more advanced disease and higher risk among men compared to women. Cumulatively, these results suggest that women may have greater survival benefits than men, particularly at more extreme BMI levels despite reduced access to transplantation.

For patients with glomerulonephritis, adjusted overall graft survival was highest compared to other diagnosis groups evaluated in this study across all BMI levels, and graft loss rather than mortality was the primary reason for overall graft loss. The increased risk of graft loss and risks of recurrence has been well described in the population, but based on the current results these risks are most pronounced at higher BMI levels and attenuated at low BMI levels.[38,39] For patients with type II diabetes as primary diagnosis, estimated survival was lower across all BMI subgroups than other diagnoses and mortality was a more common cause of overall graft loss than graft failure. However, the relative effect of elevated BMI was attenuated as compared to other diagnosis groups. These results suggest that the higher

rates of mortality for this group are not highly affected by BMI, whereas the impact of diabetes and associated comorbid conditions may be the primary source of risk of mortality in this population. Among patients with hypertension as primary diagnosis, graft failure was more common than mortality as a cause for overall graft loss across all BMI strata. Low BMI had a modest effect and obesity increased the relative hazard at a similar rate as other diagnoses. People with type I diabetes had a relatively high mortality rate compared to other diagnosis groups across all BMI strata. The effect of low BMI was significantly higher in other groups and obesity had a similar relative effect.

There are several important limitations of the study. Based on the retrospective design of the study, there is potential for residual confounding. In particular, there are likely additional factors associated with BMI that contribute to differential results between groups that could not be incorporated in risk adjustment for the current results. As has been demonstrated in numerous studies, BMI is not a specific indication of health relative to other factors and the degree to which the differential effects of other health measures is not known.[20–22,27,40] However, despite the lack of specificity as a health measure, BMI is still used as a clinical indicator and other specific measures may not be readily available for decision-making and patient management. It is important to note that the present study only used a single BMI measure as an indicator of risk. Certainly, changes in BMI and additional anatomical features that are not affected by acute episodes may be important and more sensitive diagnostic measures. In addition, the specific interventions that may be tailored to the differential risks associated with BMI are not clear from this study but do suggest nuanced approaches towards interpreting BMI may be effective.[15,41–44] Personalized approaches toward incorporating these results may also be challenging without risk calculators or other tools to jointly consider multiple factors and further work to develop these tools is important.

Overall, the study suggests that the implications of BMI on posttransplant outcomes vary within the kidney transplant recipient population. Assessing level of risk, viability for the transplant procedure, and type of intervention associated with BMI requires specific incorporation of other patient factors. Protocols that use BMI as an individual assessment or inclusion/exclusion criteria may not accurately capture patient-specific risks. Although the epidemiological observation of risks in the population associated with high and low levels of BMI are instructive, the current results suggest a more nuanced consideration of effects is needed. Further development of tools to depict risks among patients tailored to individual characteristics may be needed. In addition, further research describing the features and etiology associated patient BMI and applicable interventions specific to BMI-related morbidity may improve health in the kidney transplant population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the Scientific Registry of Transplant Recipients. Data are available from the authors with the permission of the SRTR.

Abbreviations:

BMI	body mass index
HRSA	Health Resources and Services Administration
OPTN	Organ Procurement and Transplantation Network
SRTR	Scientific Registry of Transplant Recipients

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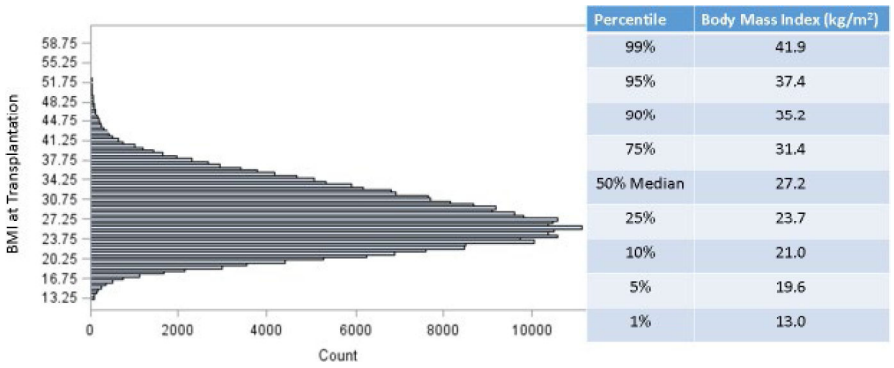

Percentile	Body Mass Index (kg/m²)
99%	41.9
95%	37.4
90%	35.2
75%	31.4
50% Median	27.2
25%	23.7
10%	21.0
5%	19.6
1%	13.0

FIGURE 1.

Distribution of body mass index among adult transplant recipients 2000–2019 (n = 296 807) [Color figure can be viewed at wileyonlinelibrary.com]

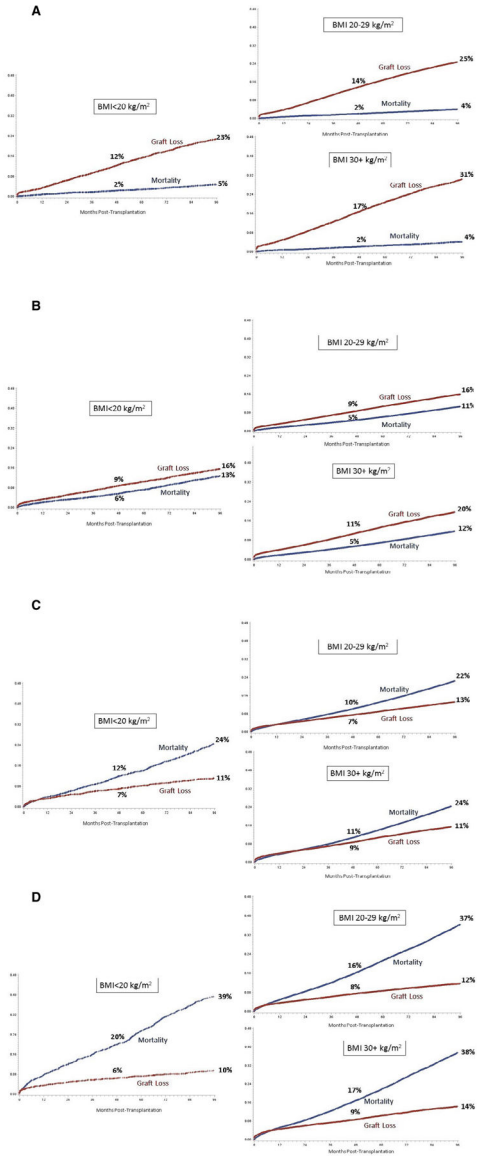

FIGURE 2.

Cumulative incidence of graft loss and mortality by recipient age from competing risks models. A, Recipients aged 18–39. Sample sizes for each body mass index (BMI) group: n = 6261, BMI < 20 kg/m^2, n = 28 393, BMI 20–29 kg/m^2, n = 9540, BMI 30+ kg/m^2. B, Recipients aged 40–49. Sample sizes for each BMI group: n = 7052, BMI < 20 kg/m^2, n = 75 696, BMI 20–29 kg/m^2, n = 42 224, BMI 30+ kg/m^2. C, Recipients aged 50–59. Sample sizes for each BMI group: n = 3137, BMI < 20 kg/m^2, n = 47 038, BMI 20–29 kg/m^2, n = 28 211, BMI 30+ kg/m^2. D, Recipients aged 60+. Sample sizes for each BMI group: n = 1772, BMI < 20 kg/m^2, n = 31 940, BMI 20–29 kg/m^2, n = 15 543, BMI 30+ kg/m^2 [Color figure can be viewed at wileyonlinelibrary.com]

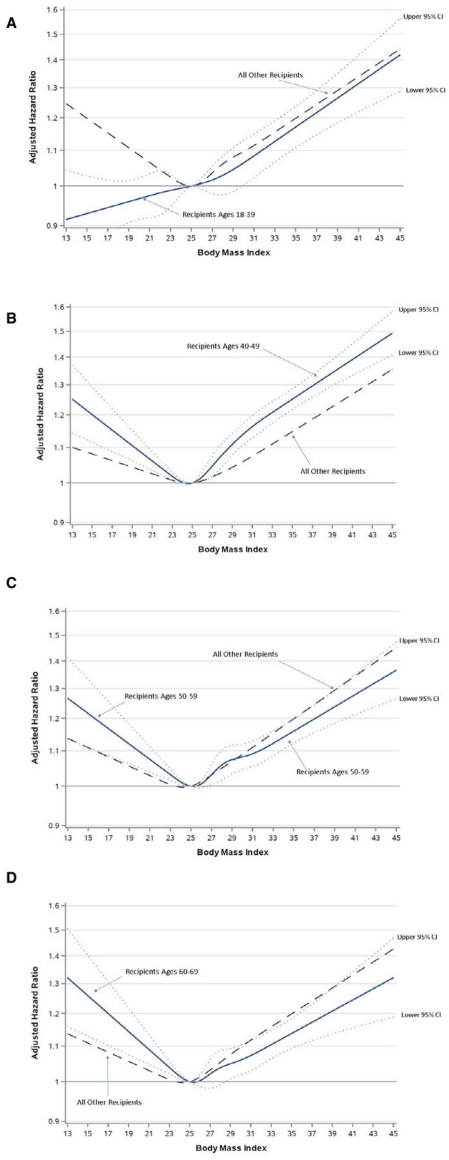

FIGURE 3.

Adjusted Hazard of BMI for overall graft loss by recipient age*. A, *models adjusted for age, race/ethnicity, gender, primary diagnosis, donor type, donor age, panel reactive antibody %, dialysis time prior to transplant, primary versus re-transplantation, HLA-mismatching, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, history of malignancy, drug-treated chronic obstructive pulmonary disease, year of transplant and primary insurance; *P*-value for interaction of BMI with age < 0.01. B, *models adjusted for age, race/ethnicity, gender, primary diagnosis, donor type, donor age, panel reactive antibody %, dialysis time prior to transplant, primary versus re-transplantation, HLA-mismatching, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, history of malignancy, drug-treated chronic obstructive pulmonary disease, year of transplant and primary insurance; P-value for interaction of BMI with age < 0.01. C, *models adjusted for age, race/ethnicity, gender, primary

diagnosis, donor type, donor age, panel reactive antibody %, dialysis time prior to transplant, primary versus re-transplantation, HLA-mismatching, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, history of malignancy, drug-treated chronic obstructive pulmonary disease, year of transplant and primary insurance; *P*-value for interaction of BMI with age < 0.01. D, *models adjusted for age,race/ethnicity, gender, primary diagnosis, donor type, donor age, panel reactive antibody %, dialysis time prior to transplant, primary versus re-transplantation, HLA-mismatching, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, history of malignancy, drug-treated chronic obstructive pulmonary disease, year of transplant and primary insurance; *P*-value for interaction of BMI wth age < 0.01. [Color figure can be viewed at wileyonlinelibrary.com]

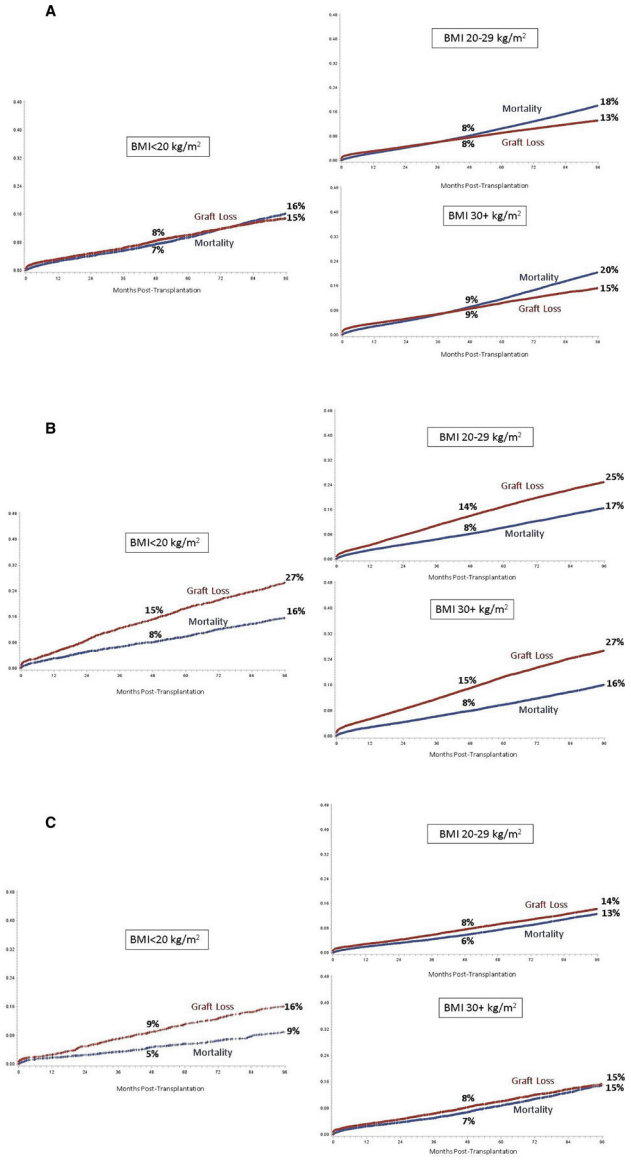

FIGURE 4.

Cumulative incidence of graft loss and mortality by race/ethnicity from competing risks models. A, Non-hispanic Caucasian recipients. Sample sizes for each BMI group: n = 9410, BMI < 20 kg/m^2, n = 94 858, BMI 20–29 kg/m^2, n = 49 523, BMI 30+ kg/m^2. B, African American recipients. Sample sizes for each BMI group: n = 3683, BMI < 20 kg/m^2, n = 43 837, BMI 20–29 kg/m^2, n = 28 763, BMI 30+ kg/m^2. C, Hispanic recipients. Sample sizes for each BMI group: n = 2552, BMI < 20 kg/m^2, n = 28 960, BMI 20–29 kg/m^2, n = 13 002, BMI 30+ kg/m^2 [Color figure can be viewed at wileyonlinelibrary.com]

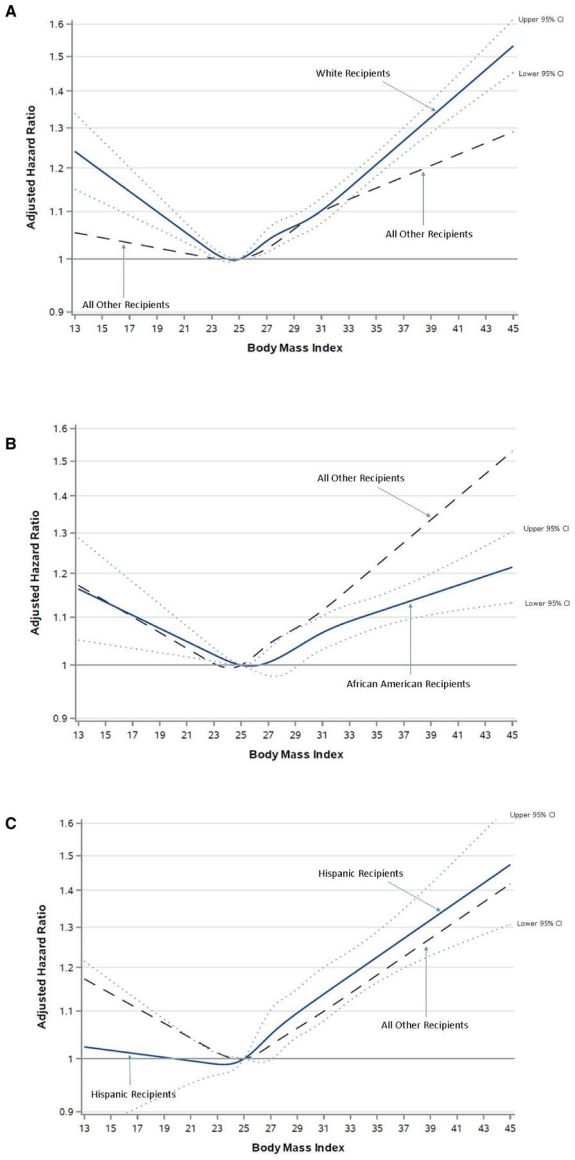

FIGURE 5.

Adjusted hazard of BMI for overall graft loss by race/ethnicity*. A, *models adjusted for age, race/ethnicity, gender, primary diagnosis, donor type, donor age, panel reactive antibody %, dialysis time prior to transplant, primary versus re-transplantation, HLA-mismatching, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, history of malignancy, drug-treated chronic obstructive pulmonary disease, year of transplant and primary insurance; *P* value for interaction of BMI with race/ethnicity < 0.01. B, *models adjusted for age, race/ethnicity, gender, primary diagnosis, donor type, donor age, panel reactive antibody %, dialysis time prior to transplant, primary versus re-transplantation, HLA-mismatching, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, history of malignancy, drug-treated chronic obstructive pulmonary disease, year of transplant and primary insurance; *P* value for interaction of BMI with race/ethnicity < 0.01. C, *models adjusted for age, race/ethnicity, gender,

primary diagnosis, donor type, donor age, panel reactive antibody %, dialysis time prior to transplant, primary versus re-transplantation, HLA-mismatching, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, history of malignancy, drug-treated chronic obstructive pulmonary disease, year of transplant and primary insurance; *P* value for interaction of BMI with race/ethnicity < 0.01 [Color figure can be viewed at wileyonlinelibrary.com]

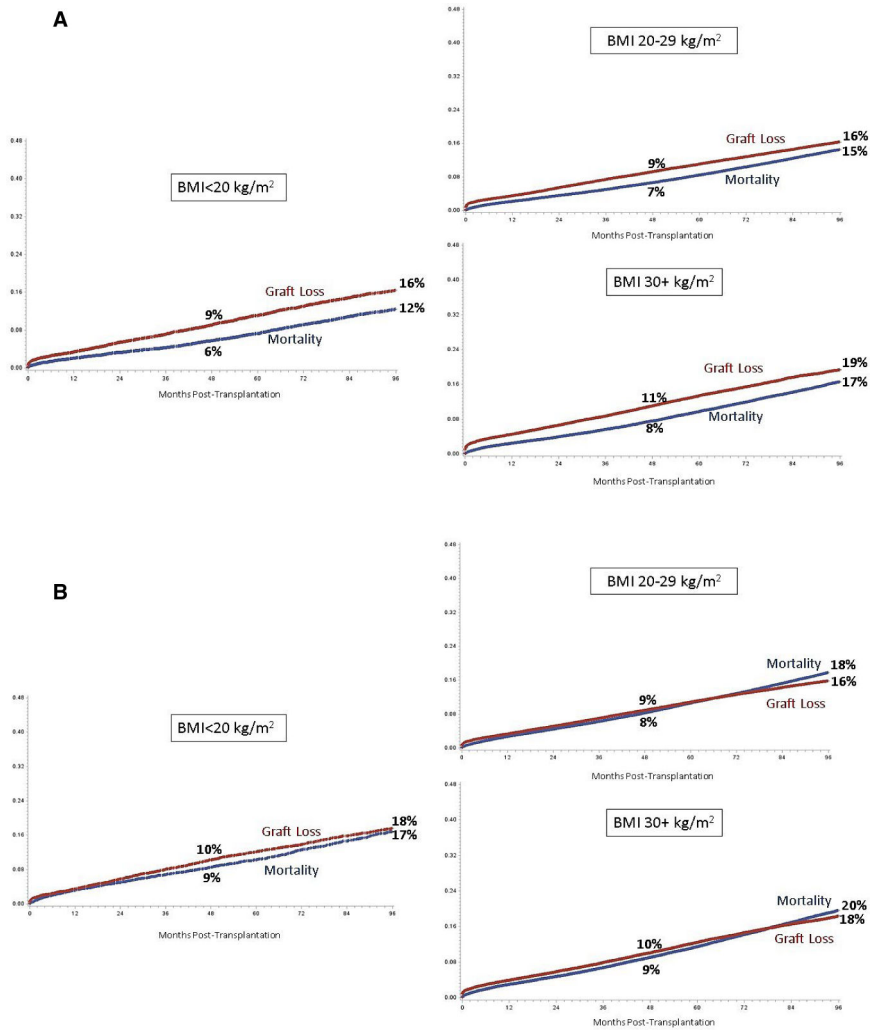

FIGURE 6.

Cumulative incidence of graft loss and mortality by gender from competing risks models. A, Female recipeints. Sample sizes for each BMI group: n = 10 912, BMI < 20 kg/m^2, n = 68 186, BMI 20–29 kg/m^2, n = 38 223, BMI 30+ kg/m^2. B, Male recipients. Sample sizes for each BMI group: n = 7310, BMI < 20 kg/m^2, n=114 881, BMI 20–29 kg/m^2, n = 57 295, BMI 30+ kg/m^2 [Color figure can be viewed at wileyonlinelibrary.com]

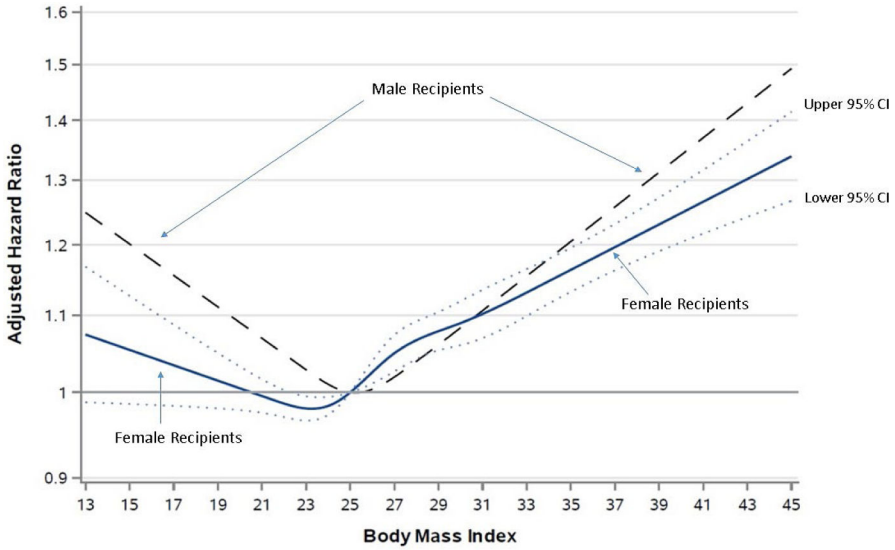

FIGURE 7.

Adjusted Hazard of BMI for overall graft loss by gender*. * models adjusted for age, race/ethnicity, gender, primary diagnosis, donor type, donor age, panel reactive antibody %, dialysis time prior to transplant, primary versus re-transplantation, HLA-mismatching, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, history of malignancy, drug-treated chronic obstructive pulmonary disease, year of transplant and primary insurance; *P* value for interaction of BMI with gender < 0.01 [Color figure can be viewed at wileyonlinelibrary.com]

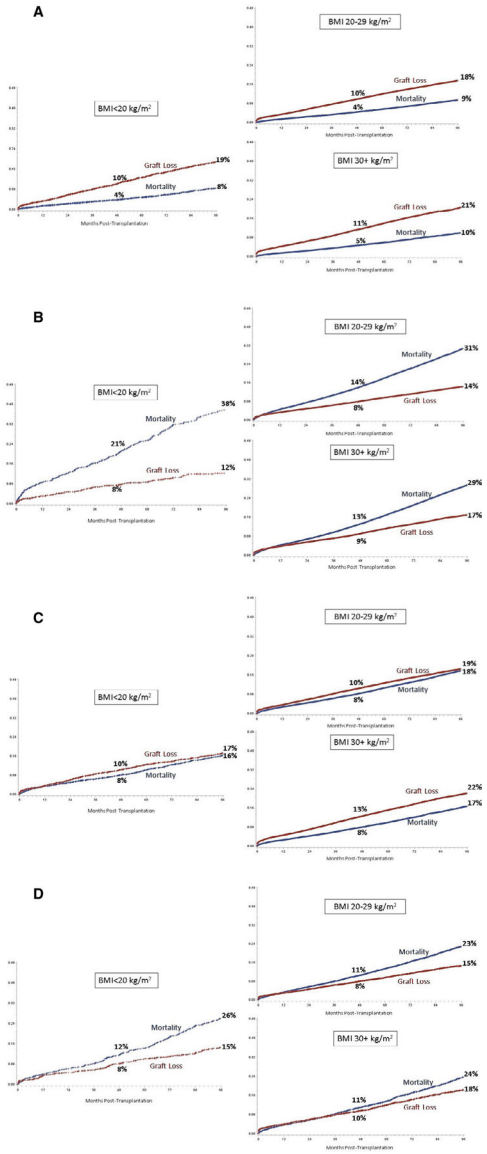

FIGURE 8.

Cumulative incidence of graft loss and mortality by primary diagnosis from competing risks models. A, Recipients with Primary Diagnosis of Glomerulonephritis. Sample sizes for each BMI group: n = 6430, BMI < 20 kg/m^2, n = 49 310, BMI 20–29 kg/m2, n = 20 983, BMI 30+ kg/m^2. B, Recipients with Primary Diagnosis of Type-II Diabetes. Sample sizes for each BMI group: n = 941, BMI<20 kg/m2, n = 30,515, BMI 20–29 kg/m2, n = 28,605, BMI 30+ kg/m2. C, Recipients with Primary Diagnosis of Hypertension. Sample sizes for each BMI group: n = 3125, BMI < 20 kg/m^2, n = 38 573, BMI 20–29 kg/m^2, n = 20 508, BMI 30+ kg/m^2. D, Recipients with Primary Diagnosis of Type-I Diabetes. Sample sizes for each BMI group: n = 977, BMI < 20 kg/m^2, n = 10 892, BMI 20–29 kg/m^2, n = 4268, BMI 30+ kg/m^2 [Color figure can be viewed at wileyonlinelibrary.com]

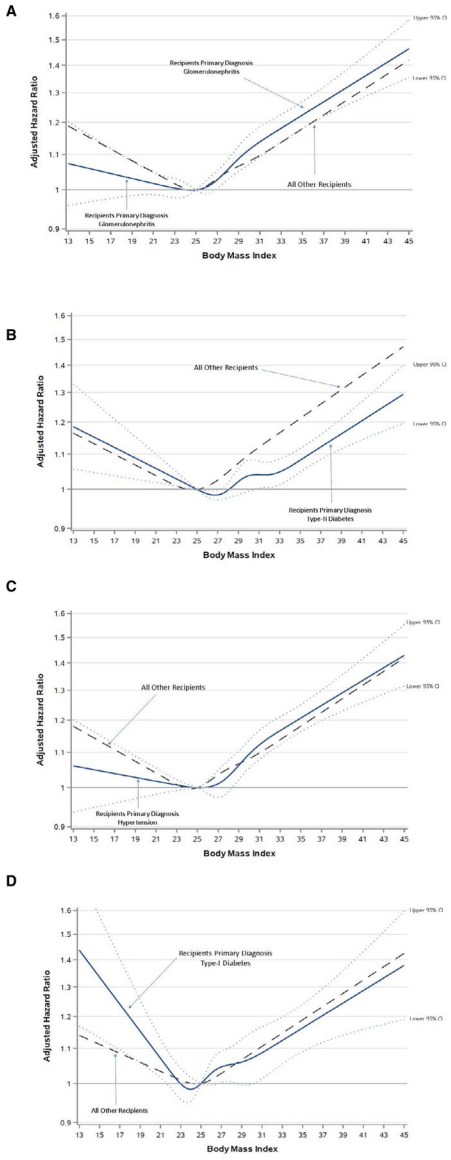

FIGURE 9.

Association of body mass index (BMI) with overall graft loss by primary diagnosis. A, *models adjusted for age, race/ethnicity, gender, primary diagnosis, donor type, donor age, panel reactive antibody %, dialysis time prior to transplant, primary versus re-transplantation, HLA-mismatching, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, history of malignancy, drug-treated chronic obstructive pulmonary disease, year of transplant and primary insurance; *P* value for interaction of BMI with diagnosis < 0.01. B, *models adjusted for age, race/ethnicity, gender, primary diagnosis, donor type, donor age, panel reactive antibody %, dialysis time prior to transplant, primary versus re-transplantation, HLA-mismatching, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, history of malignancy, drug-treated chronic obstructive pulmonary disease, year of transplant and primary insurance; *P* value for interaction of BMI with diagnosis < 0.01. C, *models adjusted for age, race/

ethnicity, gender, primary diagnosis, donor type, donor age, panel reactive antibody %, dialysis time prior to transplant, primary versus re-transplantation, HLA-mismatching, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, history of malignancy, drug-treated chronic obstructive pulmonary disease, year of transplant and primary insurance; *P* value for interaction of BMI with diagnosis < 0.01. D, *models adjusted for age, race/ethnicity, gender, primary diagnosis, donor type, donor age, panel reactive antibody %, dialysis time prior to transplant, primary versus re-transplantation, HLA-mismatching, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, history of malignancy, drug-treated chronic obstructive pulmonary disease, year of transplant and primary insurance; *P* value for interaction of BMI with diagnosis < 0.01. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1

Demographic characteristics of transplant recipients by body mass index level

		Body mass index at transplantation				
Recipient characteristics	**Level (n)**	**13–20 kg/m^2 (%)**	**21–24 kg/m^2 (%)**	**25–29 kg/m^2 (%)**	**30–34 kg/m^2 (%)**	**35+ kg/m^2 (%)**
Recipient age	18–39 (n = 44 194)	14.2	38.7	25.5	13.9	7.7
	40–49 (n = 124 972)	5.6	28.0	32.6	21.9	11.9
	50–59 (n = 78 386)	4.0	24.3	35.8	24.7	11.3
	60+ (n = 49 255)	3.6	25.7	39.2	23.4	8.1
Race/ethnicity	Non-Hispanic Caucasian (n = 153 791)	6.1	28.3	33.4	21.8	10.5
	African American (n = 78 283)	4.8	24.6	32.9	24.2	13.5
	Hispanic/Latino (n = 44 514)	5.7	29.1	35.9	21.1	8.1
	Other race/ethnicity (n = 22 219)	11.6	38.6	30.8	13.9	5.1
Gender	Male (n = 179 486)	4.1	27.4	36.6	22.4	9.5
	Female (n = 117 321)	9.3	29.5	28.7	20.6	12.0
Primary diagnosis	Glomerulonephritis (n = 76 723)	8.4	32.6	31.6	18.4	9.0
	Type II diabetes (n = 60 061)	1.6	16.1	34.7	31.4	16.2
	Hypertension (n = 62 206)	5.0	27.0	35.0	22.1	10.9
	Type I diabetes (n = 16 137)	6.1	34.8	32.7	18.3	8.1
	Other diagnosis (n = 81 680)	8.3	32.6	33.2	18.0	7.9
Transplant number	Primary (n = 260 514)	5.6	27.0	33.9	22.5	11.0
	Re-transplant (n = 36 293)	10.1	36.8	30.7	15.6	6.9
Donor type	Deceased donor (n = 189 000)	5.6	27.2	33.8	22.4	11.0
	Living donor (n = 107 807)	7.1	30.0	33.0	20.4	9.6
Primary insurance	Private (n = 109 168)	6.3	29.1	33.6	21.3	9.7
	Medicare (n = 141 347)	5.3	26.0	33.6	23.2	11.8
	Other (n = 46 292)	8.4	32.8	32.6	18.0	8.3
Pretransplant dialysis time (mo)	Preemptive (n = 51 944)	6.4	29.1	34.8	21.3	8.6
	1–12 mo (n = 46 726)	7.3	30.2	33.5	20.0	9.1
	13–24 mo (n = 43 655)	6.2	28.3	33.6	21.7	10.3
	25–48 mo (n = 66 363)	5.5	26.2	34.0	22.8	11.6
	49–72 mo (n = 43 123)	5.3	26.7	33.0	23.2	11.9

		Body mass index at transplantation				
Recipient characteristics	**Level (n)**	**13–20 kg/m^2 (%)**	**21–24 kg/m^2 (%)**	**25–29 kg/m^2 (%)**	**30–34 kg/m^2 (%)**	**35+ kg/m^2 (%)**
	>72 mo (n = 44 996)	6.5	29.6	31.6	20.9	11.4
Panel reactive antibody (%)	0% (n = 104 983)	5.8	28.5	34.3	21.4	10.0
	1%-10% (n = 38 265)	6.2	29.0	33.9	20.8	10.1
	11%-80% (n = 48 466)	7.0	29.1	32.5	21.0	10.4
	>80% (n = 20 998)	8.8	32.4	31.0	18.6	9.3
	Missing (n = 84 095)	5.3	26.0	33.3	23.6	11.7
Year of transplantation	2000–2004 (n = 62 985)	7.8	33.3	33.2	17.8	7.9
	2005–2009 (n = 73 673)	6.4	28.8	33.8	21.0	10.0
	2010–2014 (n = 76 825)	5.4	25.8	33.5	23.5	11.8
	2015–2019 (n = 83 324)	5.4	26.1	33.3	23.6	11.7
	Total study population	6.1	28.2	33.5	21.7	10.5

TABLE 2

Adjusted estimated 10-year overall graft survival of recipient characteristics by body mass index[a]

	Body mass index at transplantation				
Recipient characteristic	**18 kg/m^2 (%)**	**25 kg/m^2 (%)**	**30 kg/m^2 (%)**	**35 kg/m^2 (%)**	**40 kg/m^2 (%)**
Age 18–39	69.5	68.2	66.6	63.9	61.1
Age 40–49	70.7	73.6	70.5	68.1	65.7
Age 50–59	60.2	64.1	61.8	59.7	57.2
Age 60+	46.2	51.7	49.7	47.3	44.6
Non-Hispanic Caucasian	63.4	66.6	64.4	61.2	57.5
African American	58.4	61.1	59.5	57.8	56.4
Hispanic/Latino	72.9	73.1	70.5	68.1	65.6
Male	62.6	66.2	64.0	60.9	57.6
Female	67.9	68.5	66.2	64.4	62.4
Primary diagnosis: glomerulonephritis	69.8	70.8	68.0	65.5	63.0
Primary diagnosis: type II diabetes	50.1	53.5	52.2	50.8	47.7
Primary diagnosis: hypertension	66.5	67.4	64.9	62.1	59.5
Primary diagnosis: type I diabetes	50.8	56.7	54.5	51.7	48.8
Total study population	64.8	67.0	64.6	62.2	59.6

[a]Models adjusted for race/ethnicity, gender, primary diagnosis, donor type, donor age, panel reactive antibody %, dialysis time prior to transplant, primary vs re-transplantation, HLA-mismatching, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, history of malignancy, drug-treated chronic obstructive pulmonary disease, year of transplant and primary insurance.