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ORIGINAL RESEARCH

Impact of Obesity on Heart Transplantation Outcomes

Fouad Chouairi, MD; Aidan Milner, MD; Sounok Sen, MD; Avirup Guha, MD; James Stewart, MD; Ania M. Jastreboff, MD, PhD; Makoto Mori, MD; Katherine A. Clark, MD, MBA; P. Elliott Miller, MD; Michael A. Fuery, MD; Joseph G. Rogers, MD; Andrew Notarianni, MD; Daniel Jacoby, MD; Christopher Maulion, MD; Muhammad Anwer, MBBS; Arnar Geirsson, MD; Nihar R. Desai, MD, MPH; Tariq Ahmad, MD, MPH; Clancy W. Mullan, MD

BACKGROUND: Patients with obesity and advanced heart failure face unique challenges on the path to heart transplantation. There are limited data on waitlist and transplantation outcomes in this population. We aimed to evaluate the impact of obesity on heart transplantation outcomes, and to investigate the effects of the new organ procurement and transplantation network allocation system in this population.

METHODS AND RESULTS: This cohort study of adult patients listed for heart transplant used the United Network for Organ Sharing database from January 2006 to June 2020. Patients were stratified by body mass index (BMI) (18.5–24.9, 25–29.9, 30–34.9, 35–39.9, and 40–55 kg/m^2). Recipient characteristics and donor characteristics were analyzed. Outcomes analyzed included transplantation, waitlist death, and posttransplant death. BMI 18.5 to 24.9 kg/m^2 was used as the reference compared with progressive BMI categories. There were 46 645 patients listed for transplantation. Patients in higher BMI categories were less likely to be transplanted. The lowest likelihood of transplantation was in the highest BMI category, 40 to 55 kg/m^2 (hazard ratio [HR], 0.19 [0.05–0.76]; P=0.02). Patients within the 2 highest BMI categories had higher risk of posttransplantation death (HR, 1.29; P<0.001 and HR, 1.65; P<0.001, respectively). Left ventricular assist devices among patients in obese BMI categories decreased after the allocation system change (P<0.001, all). After the change, patients with obesity were more likely to undergo transplantation (BMI 30–35 kg/m^2: HR, 1.31 [1.18–1.46], P<0.001; BMI 35–55 kg/m^2: HR, 1.29 [1.06–1.58]; P=0.01).

CONCLUSIONS: There was an inverse relationship between BMI and likelihood of heart transplantation. Higher BMI was associated with increased risk of posttransplant mortality. Patients with obesity were more likely to undergo transplantation under the revised allocation system.

Key Words: body mass index ■ heart transplantation ■ obesity ■ outcomes research ■ United Network for Organ Sharing

Obesity is a well-recognized epidemic in the United States, with increasing prevalence of both obesity and severe obesity,[1] and notable projections that nearly half of adults in the United States will have obesity by 2030.[2] Heart transplantation for patients with end-stage heart failure with obesity could be perceived as riskier than for those without obesity, because patients with obesity have a higher prevalence of comorbidities including type 2 diabetes, dyslipidemia, systemic hypertension, and pulmonary hypertension.[3–5] Additionally, given the institutional nature of decisions on transplantation, patients with obesity could be negatively affected by substantial selection biases.[6] There are limited data on the waitlist and posttransplantation outcomes of this cohort.

Additionally, in 2018, the Organ Procurement and Transplantation Network allocation system changed from a 3-status to a 6-status system to better stratify

Correspondence to: Clancy W. Mullan, MD, Division of Cardiac Surgery, Yale School of Medicine, New Haven, CT 06517. E-mail: clancy.mullan@yale.edu

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CLINICAL PERSPECTIVE

What Is New?

- This study shows that even after controlling for recipient characteristics, higher recipient body mass index category is associated with a lower likelihood of transplantation and worse posttransplantation outcomes.
- Additionally, this study shows that the 2018 allocation system changes increased the likelihood of transplantation for patients across body mass index categories.

What Are the Clinical Implications?

- Although the likelihood of transplantation has increased for patients in higher body mass index categories, they still suffer from worse outcomes.
- Physicians should be cognizant of the worse outcomes patients with obesity face following heart transplantation, and this article will help contextualize the risks inherent to transplanting patients with higher body mass index, especially given the increasingly prevalent obesity epidemic in the United States.

Nonstandard Abbreviations and Acronyms

UNOS	United Network for Organ Sharing

the medical urgency of waitlisted patients and to expand access to organs across regions for the most medically urgent patients. Initial data have shown an increase in rates of transplantation, especially among patients who would previously have undergone left ventricular assist device (LVAD) implantation.[7] The effects of this systemic change on the access to transplantation by patients with obesity and end-stage heart failure is unknown.

The goal of this analysis was to understand the characteristics, waitlist outcomes, and posttransplantation outcomes of patient with and without obesity or severe obesity listed for cardiac transplantation. We also sought to investigate the effects of the new Organ Procurement and Transplantation Network allocation system on the characteristics or outcomes of patients with obesity. We hypothesized that, with increasing body mass index (BMI), there would be a decrease in transplantation and an increase in posttransplant mortality. Furthermore, the new allocation system would increase rates of transplantation in this patient population that preferentially underwent LVAD implantation during the previous system.[7]

METHODS

Data

This study used the UNOS (United Network for Organ Sharing) registry. This is a prospectively maintained database consisting of every organ transplant performed in the United States each year.[8] We are not able to make the data, methods, and materials available to other research groups because of the data-use agreement necessary to use UNOS data. However, data can be requested and obtained from the Organ Procurement and Transplantation Network website. This study was approved as exempt by the Yale Institutional Review Board.

Study Population

We reviewed the UNOS registry for all adult patients (aged >18 years) listed for heart transplantation between January 1, 2006 and June 12, 2020. Simultaneous heart–lung transplant recipients were excluded. Patients were stratified into cohorts based on BMI: 18.5 to 24.9, 25 to 29.9, 30 to 34.9, 35 to 39.9, and 40 to 55 kg/m^2. Patients with a BMI >55 kg/m^2 and a BMI <18.5 kg/m^2 were excluded from the analysis. Patients with <30 days of follow-up were excluded.

For analysis of allocation change effects, patients listed between April 12, 2017 and June 12, 2020 were included. June 12, 2020 was the last day of follow-up. Patients with an initial listing before the allocation change and an end listing after the allocation change were excluded to avoid potential confounding. Patients with obesity were stratified into the same groups as before. These 2 groups were further stratified into allocation system–based cohorts that took effect October 18, 2018, with those listed before October 18, 2018 compared with those listed after October 18, 2018.

The primary outcomes of interest across all analyses were transplantation, waitlist mortality, and posttransplantation survival. Secondary outcomes were ischemic time and travel distance.

Statistical Analysis

Patient demographics, comorbidities, socioeconomic status, and outcomes were compared between cohorts using χ^2 analysis for categorical variables and Mann-Whitney *U* and Kruskal-Wallis tests for continuous variables. Recipient and donor heart masses were calculated using the International Society for Heart and Lung Transplantation Heart Mass calculator.[9] Unadjusted and adjusted Cox regressions were used to predict outcomes of interest including transplantation, waitlist death, and posttransplant death, individually. Transplantation death was defined as patient death any time after transplantation. BMI 18.5 to 24.9 kg/m^2 was used as the reference for all Cox

regression analysis. Models were adjusted for sex, age, race, insurance payor, cardiomyopathy diagnosis, extracorporeal membrane oxygenation (at listing), intra-aortic balloon pump (at listing), inotropes, ventilator status, LVAD, right ventricular assist device, total artificial heart, diabetes, end-stage renal disease, prior cerebrovascular accidents, malignancy, implantable cardioverter defibrillator, tobacco use, and prior cardiac surgery. A second model used only for posttransplant death adjusted for all of the above covariates and waitlist time. A third model included all the above covariates, waitlist time, and percent heart-mass discrepancy. Analysis was performed using SPSS version 26 (IBM, Armonk, NY).

RESULTS

Population and Donor Characteristics

In total, 46 645 patients were listed for transplantation between January 1, 2006 and June 12, 2020, with 14 263 patients with a BMI 18.5 to 24.9 kg/m^2, 17 061 patients with a BMI 25 to 29.9 kg/m^2, 11 629 patients with a BMI 30 to 34.9 kg/m^2, 3305 patients with a BMI 35 to 39.9 kg/m^2, and 387 patients with a BMI 40 to 55 kg/m^2 during the time period. The median BMI of patients listed increased from 27.0 kg/m^2 in 2006 to 28.1 kg/m^2 in 2020, the BMI of patients transplanted increased from 26.4 kg/m^2 in 2006 to 28.0 kg/m^2 in 2020, and the BMI of donors increased from 25.9 kg/m^2 in 2006 to 26.9 kg/m^2 in 2020 (Figure). Patients with obesity were significantly more likely to be Black, younger, and have public insurance compared with people with a BMI 18.5 to 24.9 kg/m^2 (P<0.001, all). In addition, these patients were significantly more likely to have a diagnosis of dilated cardiomyopathy, an LVAD at time of listing, and to be on extracorporeal membrane oxygenation at time of listing (P<0.001) (Table 1). Patients with obesity had urgency statuses at listing and transplantation that were similar to those of patients without obesity (Figure S1), with a majority of patients in all groups ultimately transplanted either as Status 1 or Status 2. As BMI category increased, waitlist time increased (P<0.001). Patients with a BMI 40 to 55 kg/m^2 spent the longest time on the waitlist (225 days; interquartile range, 52–609 days), whereas patients with BMI 18.5 to 24.9 kg/m^2 spent the shortest time on the waitlist (81 days; interquartile range, 21–273 days).

Donor characteristics are included in Table 2. Patients from the highest BMI cohort received hearts from older patients with higher BMIs (P<0.001). In addition, patients with higher BMI cohorts had significantly larger discrepancies in transplanted heart mass (P<0.001), with the highest BMI cohort having the largest discrepancy (–23.2 g; interquartile range, –43.8 to –0.8 g; P<0.001).

Waitlist and Posttransplantation Outcomes

Results of waitlist and posttransplantation outcomes analysis are presented in Table 3. The reference BMI category was 18.5 to 24.9 kg/m^2. In all cohorts, increased BMI had a lower hazard of transplantation than the reference category. Although patients with BMI 25 to 29.9 kg/m^2 had a slightly decreased chance of undergoing transplantation (hazard ratio [HR], 0.83; 95% CI, 0.81–0.85; P<0.001), this decreased with each increase in BMI category, with the lowest chance of transplantation in the highest BMI category, 40 to 55 kg/m^2 (HR, 0.42; 95% CI, 0.36–0.75; P<0.001 versus reference) (Table S1). This same pattern was not detected for waitlist mortality, where only BMI 40 to 55 kg/m^2 was associated with increased hazard of death (HR, 1.40; 95% CI, 1.07–1.84; P=0.02) (Table S2).

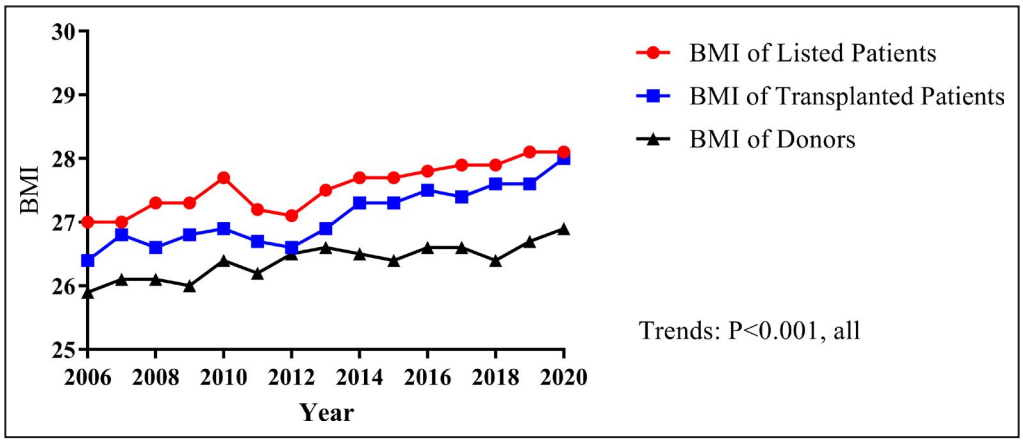

Figure. Body mass index (BMI) of listed patients, transplanted patients, and donors over time. Median BMI was plotted for these 3 groups between 2006 and 2020. These trends were analyzed by unadjusted linear regression. P<0.001 for all trends.

Table 1. Baseline Characteristics of Patients According to BMI Groups

Variables	BMI 18.5–24.9 kg/m², n=14 263	BMI 25–29.9 kg/m², n=17 061	BMI 30–34.9 kg/m², n=11 629	BMI 35–39.9 kg/m², n=3305	BMI 40–55 kg/m², n=387	*P* value
Age, y	56.0 [43.0–63.0]	57.0 [48.0–63.0]	55.0 [46.0–61.0]	51.0 [42.0–59.0]	44.0 [35.0–54.0]	<0.001*
Women, %	31.8	21.2	23.2	25.8	34.4	<0.001*
BMI, kg/m²	22.7 [21.2–23.9]	27.4 [26.2–28.7]	32.1 [31.0–33.5]	36.3 [35.6–37.6]	41.6 [40.6–43.3]	<0.001*
Estimated heart mass, g	165.0 [135.0–180.6]	190.1 [171.0–203.9]	209.0 [185.4–223.7]	224.0 [191.3–240.8]	236.7 [192.8–259.1]	<0.001*
Pulmonary vascular resistance, dynes	197.7 [121.0–278.3]	175.0 [114.3–253.6]	167.2 [110.3–241.1]	160.0 [109.8–231.9]	174.1 [106.7–248.7]	<0.001*
Race/ethnicity, %						<0.001*
White	63.8	66.9	66.1	61.5	52.2	
Black	20.7	21.4	23.9	29.5	38.0	
Hispanic	9.0	8.4	7.3	6.9	8.0	
Asian	5.4	2.3	1.3	0.7	0.5	
Primary payer, %						<0.001*
Private	53.9	51.2	49.6	48.3	47.3	
Public	44.5	47.6	49.4	50.9	52.5	
Cardiac diagnosis, %						
Dilated cardiomyopathy	50.3	47.4	51.5	56.8	66.1	<0.001*
Restrictive cardiomyopathy	3.3	2.7	2.1	1.5	0.5	<0.001*
Ischemic cardiomyopathy	30.3	38.2	36.4	31.4	22.5	<0.001*
Congenital cardiomyopathy	4.9	2.6	2.1	2.2	2.3	<0.001*
Hypertrophic cardiomyopathy	2.3	2.2	2.4	2.5	1.0	0.36
Valvular	2.0	1.6	0.9	0.7	1.3	<0.001*
Cardiac support at time of listing, %						
Ventilator	2.5	2.3	2.1	3.1	6.7	<0.001*
Inotropes	36.3	30.9	27.2	25.8	26.9	<0.001*
LVAD	17.7	23.6	27.8	32.6	36.4	<0.001*
RVAD±LVAD or MCS unspecified	2.2	1.7	1.6	1.9	2.8	0.001*
TAH	0.5	0.6	0.4	0.6	1.6	0.02*
ECMO	1.7	1.5	1.2	2.4	4.1	<0.001*
IABP	6.9	6.1	4.8	5.6	7.0	<0.001*
Comorbidities, %						
Diabetes	18.9	29.5	38.6	42.4	41.6	<0.001*
Tobacco user	41.6	48.5	49.8	47.1	39.0	<0.001*
Malignancy	8.9	7.8	7.0	5.7	5.9	<0.001*
Prior CVA	5.5	5.6	5.8	5.4	4.7	0.65
ESRD	3.2	3.1	3.1	3.0	3.6	0.94
AICD	70.3	74.8	78.2	78.9	70.8	<0.001*
Prior cardiac surgery	37.4	40.8	40.8	41.7	35.9	<0.001*
Outcomes						
Waitlist time	81 [21–273]	126 [32.5–374]	181 [51–476]	199 [53–532]	225 [52–609]	<0.001*
Median posttransplant follow-up time	1454 [389–2635]	1404 [384–2575]	1103 [366–2297]	1057 [353.5–2266]	1262.5 [329.8–2561.8]	<0.001*

AICD indicates automatic implantable cardioverter-defibrillator; BMI indicates body mass index; CVA, cerebrovascular accident; ECMO, extracorporeal membrane oxygenation; ESRD, end-stage renal disease; IABP, intra-aortic balloon pump; IQR, interquartile range; LVAD, left ventricular assist device; MCS, mechanical circulatory support; RVAD, right ventricular assist device; and TAH, total artificial heart.

Data presented as % or Median [IQR].

Table 2. Donor Characteristics

Variables	BMI 18.5–24.9 kg/m^2, n=10 294	BMI 25–29.9 kg/m^2, n=11 546	BMI 30–34.9 kg/m^2, n=7201	BMI 35–39.9 kg/m^2, n=1903	BMI 40–55 kg/m^2, n=162	*P* value
Age, y, median [IQR]	29.0 [22.0–40.0]	30.0 [22.0–40.0]	31.0 [23.0–41.0]	31.0 [24.0–41.0]	33.0 [25.0–42.3]	<0.001*
Women, %	36.2	26.4	23.5	23.3	22.2	<0.001*
BMI, median [IQR]	24.8 [22.1–28.3]	26.4 [23.5–30.1]	28.1 [24.8–32.2]	29.3 [25.8–33.6]	29.9 [27.3–35.8]	<0.001*
Estimated donor heart mass, g, median [IQR]	174.3 [151.4–194.2]	188.8 [168.6–206.9]	197.0 [175.3–217.0]	201.7 [178.4–222.4]	202.6 [173.4–224.1]	<0.001*
Heart-mass discrepancy, g, median [IQR]	12.4 [–0.8 to 27.5]	0.9 [–12.7 to 16.5]	–6.8 [–21.2 to 8.9]	–14.9 [–31.8 to 2.1]	–23.2 [–43.8 to –0.8]	<0.001*
Heart-mass discrepancy, %	+8.0	+0.5	–3.4	–7.1	–9.9	<0.001*
High risk donor, %	20.1	21.6	21.4	22.8	19.8	0.02*
Race/ethnicity, %						<0.001*
White	62.5	64.2	65.8	68.8	67.9	
Black	15.6	16.1	16.1	16.0	14.8	
Hispanic	18.1	16.6	15.7	12.9	14.2	
Asian	2.3	1.6	1.1	1.2	1.9	
Substance use, %						
Alcohol use	16.0	16.6	16.3	15.6	16.0	0.71
Tobacco user	11.8	11.6	11.8	11.4	11.1	0.98
Cocaine use	9.0	9.7	10.2	10.5	8.6	0.048*
Other drug user	33.7	35.0	36.0	36.2	28.4	0.004*
Comorbidities, %						
Hypertension	30.3	29.8	30.8	29.3	29.6	0.58
Malignancy	1.6	1.3	1.5	1.4	1.2	0.56
Diabetes	3.2	3.2	4.2	3.7	1.2	0.001*
Infections, %						
Pneumonia	60.8	60.6	61.2	59.8	58.0	0.72
UTI	12.1	10.1	8.9	8.8	7.4	<0.001*
HCV	1.5	1.8	1.9	2.8	0.6	0.002*
CMV	62.1	61.6	60.4	59.1	63.6	0.04
Transplant outcomes, median [IQR]						
Ischemic time, h	3.2 [2.4–3.8]	3.2 [2.4–3.8]	3.2 [2.5–3.9]	3.3 [2.5–3.9]	3.3 [2.6–3.9]	<0.001*
Distance traveled, nautical miles	104 [16–310]	99 [13–297]	99 [14–293]	113 [15–321]	91.5 [10.8–283.8]	<0.001*

BMI indicates body mass index; CMV, cytomegalovirus; HCV, hepatitis C virus; IQR, interquartile range; and UTI, urinary tract infection.

Table 3. Association of BMI Categories With Outcomes

BMI group	Unadjusted hazard ratio	*P* value	Adjusted hazard ratio*	*P* value	Adjusted hazard ratio†	*P* value	Adjusted hazard ratio‡	*P* value
Transplantation								
18–24.9, kg/m^2	Reference		Reference		…	…	…	…
25–29.9, kg/m^2	0.80 (0.78–0.82)	<0.001	0.83 (0.81–0.85)	<0.001	…	…	…	…
30–34.9, kg/m^2	0.64 (0.62–0.66)	<0.001	0.68 (0.66–0.70)	<0.001	…	…	…	…
35–39.9, kg/m^2	0.57 (0.54–0.60)	<0.001	0.61 (0.58–0.64)	<0.001	…	…	…	…
40–55, kg/m^2	0.40 (0.34–0.46)	<0.001	0.42 (0.36–0.49)	<0.001	…	…	…	…
Waitlist death								
18–24.9, kg/m^2	Reference		Reference		…	…	…	…
25–29.9, kg/m^2	0.90 (0.83–0.98)	0.01	0.92 (0.85–1.00)	0.06	…	…	…	…
30–34.9, kg/m^2	0.85 (0.78–0.93)	0.001	0.92 (0.84–1.01)	0.06	…	…	…	…
35–39.9, kg/m^2	0.89 (0.78–1.01)	0.07	0.96 (0.84–1.09)	0.51	…	…	…	…
40–55, kg/m^2	1.34 (1.02–1.75)	0.04	1.40 (1.07–1.84)	0.02	…	…	…	…
Posttransplant death								
18–24.9, kg/m^2	Reference		Reference		Reference		Reference	
25–29.9, kg/m^2	1.08 (1.02–1.14)	0.01	1.03 (0.97–1.09)	0.33	1.03 (0.97–1.09)	0.37	1.03 (0.97–1.09)	0.41
30–34.9, kg/m^2	1.23 (1.16–1.31)	<0.001	1.16 (1.09–1.24)	<0.001	1.16 (1.09–1.23)	<0.001	1.15 (1.08–1.23)	<0.001
35–39.9, kg/m^2	1.36 (1.24–1.50)	<0.001	1.29 (1.17–1.43)	<0.001	1.29 (1.16–1.42)	<0.001	1.28 (1.16–1.42)	<0.001
40–55, kg/m^2	1.76 (1.36–2.28)	0.001	1.65 (1.27–2.14)	<0.001	1.64 (1.26–2.12)	<0.001	1.62 (1.25–2.11)	<0.001

BMI indicates body mass index.

*Adjusts for sex, age, race, insurance payor, cardiomyopathy diagnosis, extracorporeal membrane oxygenation, intra-aortic balloon pump, inotropes, ventilator status, left ventricular assist device, right ventricular assist device, total artificial heart, diabetes, end-stage renal disease, cerebrovascular accident, malignancy, automatic implantable cardioverter-defibrillator, tobacco use, and prior cardiac surgery.

†Adjusts for all above covariates and waitlist time.

‡Adjusts for all above covariates, waitlist time, and percent heart-mass discrepancy.

Data presented as hazard ratio (95% CI).

Overall, patients with a BMI 40 to 55 kg/m^2 had the highest mortality posttransplant (BMI 18.5–24.9 kg/m^2: 22.7%, BMI 25–29.9 kg/m^2: 23.7%, BMI 30–34.9 kg/m^2: 25.0%, BMI 35–39.9 kg/m^2: 26.7%, BMI 40–55 kg/m^2: 36.4%; *P*<0.001). The most common causes of mortality by BMI category are demonstrated in Table S3. Patients with BMI 35 to 40 and 40 to 55 kg/m^2 had significantly higher hazard of posttransplantation death (HR, 1.29; 95% CI, 1.17–1.43; *P*<0.001; and HR, 1.65; 95% CI, 1.27–2.14; *P*<0.001, respectively). After adjusting for percent heart-mass discrepancy in addition to all covariates in the model, patients with BMI 35 to 40 and 40 to 55 kg/m^2 had increased risk of posttransplantation death (HR, 1.28; 95% CI, 1.16–1.42; *P*<0.001; and HR, 1.62; 95% CI, 1.25–2.11; *P*<0.001, respectively) (Table S4).

Allocation System Analysis

In all patients with a BMI ≥30 kg/m^2, there was a decrease in pretransplant LVAD support following the allocation system changes and a concomitant increase in the use of an intra-aortic balloon pump (*P*<0.001). Under the new allocation system, recipients were more likely to receive transplantation across all BMI categories except for the 40 to 55 kg/m^2 group (BMI 18.5–24.9 kg/m^2: HR, 1.32; 95% CI, 1.21–1.45; *P*<0.001; BMI 25–29.9 kg/m^2: HR, 1.37; 95% CI, 1.26–1.49; *P*<0.001; BMI 30–34.9 kg/m^2: HR, 1.31; 95% CI, 1.18–1.46; *P*<0.001; BMI: 35–39.9 kg/m^2: HR, 1.30; 95% CI, 1.06–1.60; *P*=0.01; BMI 40–55 kg/m^2: HR, 1.36; 95% CI, 0.44–4.26; *P*=0.59; BMI 35–55: HR, 1.29; 95% CI, 1.06–1.58; *P*=0.01). There was a significant decrease in waitlist time for all BMI groups except for BMI 40 to 55 kg/m^2 (*P*<0.001), although donor hearts in the new allocation system traveled a longer distance with longer ischemic times for these groups (*P*<0.001) (Table 4). The risk of posttransplant death was increased in the BMI 25 to 29.9 and BMI 30 to 34.9 kg/m^2 subgroups (BMI 18.5–24.9 kg/m^2: HR, 0.97; 95% CI, 0.68–1.36; *P*=0.84; BMI 25–29.9 kg/m^2: HR, 1.53; 95% CI, 1.12–2.08; *P*=0.01; BMI 30–34.9 kg/m^2: HR, 1.44; 95% CI, 1.02–2.04; *P*=0.04; BMI: 35–39.9 kg/m^2: HR, 1.49; 95% CI, 0.83–2.66; *P*=0.18; BMI 40–55 kg/m^2: HR, 1880.2; 95% CI, 0.00–1.26×10^{39}; *P*=0.86; BMI 35–55 kg/m^2: HR, 1.44; 95% CI, 0.82–2.54; *P*=0.20).

DISCUSSION

In this study of the UNOS registry, we found that patients with obesity were less likely to receive a heart

Table 4. Differences Based on Allocation Systems

Variables	BMI 18.5–24.9 kg/m²			BMI 25–29.9 kg/m²			BMI 30–34.9 kg/m²			BMI 35–39.9 kg/m²			BMI 40.0+ kg/m²		
	Preallocation system changes, n=1169	Postallocation system changes, n=1270	*P* value	Preallocation system changes, n=1407	Postallocation system changes, n=1411	*P* value	Preallocation system changes, n=871	Postallocation system changes, n=988	*P* value	Preallocation system changes, n=235	Postallocation system changes, n=305	*P* value	Preallocation system changes, n=27	Postallocation system changes, n=19	*P* value
Age, y	58.0 [46.0–65.0]	57.0 [43.0–64.0]	0.007	58.0 [48.0–64.0]	57.0 [48.0–64.0]	0.27	56.0 [48.0–62.0]	55.0 [46.0–63.0]	0.28	53.0 [44.0–61.0]	52.0 [43.5–59.0]	0.22	47.0 [30.0–56.0]	47.0 [35.0–56.0]	0.72
Women, %	34.6	32.0	0.18	23.1	23.8	0.66	25.8	29.0	0.12	69.8	67.2	0.52	63.0	73.7	0.45
BMI, kg/m^n	22.6 [21.1–23.9]	22.6 [21.1–23.9]	0.70	27.4 [26.1–28.7]	27.3 [26.2–28.6]	0.60	32.3 [31.2–33.6]	32.3 [31.1–33.6]	0.34	36.3 [35.4–37.2]	36.3 [35.6–37.4]	0.33	41.3 [40.4–42.9]	42.5 [40.5–43.9]	0.70
Race/ethnicity, %			0.15			0.12			0.79			0.17			0.96
White	64.2	59.0		64.4	60.5		64.5	64.2		64.3	56.4		63.0	63.2	
Black	19.2	22.0		21.7	24.2		25.5	24.1		25.5	35.7		29.6	31.6	
Hispanic	9.8	10.9		9.4	11.3		7.2	9.0		7.7	6.2		0.0	0.0	
Asian	5.9	6.9		3.2	3.3		1.5	1.8		0.4	0.7		7.4	5.3	
Primary payer, %			0.007			<0.001			0.04			0.14			0.10
Private	53.5	51.9		48.7	48.5		46.0	48.3		42.1	44.6		55.6	78.9	
Public	45.9	45.7		50.5	48.9		53.4	50.1		57.9	52.8		44.4	21.1	
Cardiac diagnosis, %															
Dilated cardiomyopathy	51.1	52.1	0.60	49.8	51.3	0.43	54.4	55.5	0.63	55.7	60.3	0.28	55.6	63.2	0.61
Restrictive cardiomyopathy	5.2	6.0	0.41	4.5	4.4	0.84	3.2	4.6	0.12	2.6	2.3	0.85	0.0	0.0	…
Ischemic cardiomyopathy	27.5	24.5	0.09	33.7	31.1	0.14	31.1	27.5	0.09	29.4	21.3	0.03	25.9	36.8	0.43
Congenital cardiomyopathy	5.3	6.1	0.42	2.5	3.6	0.08	1.6	3.0	0.046	3.4	3.3	0.94	7.4	0.0	0.23
Hypertrophic cardiomyopathy	3.1	2.4	0.34	2.8	2.6	0.63	3.4	3.2	0.78	3.0	5.6	0.15	0.0	0.0	…
Valvular	1.0	1.3	0.59	1.3	0.8	0.19	1.0	0.9	0.78	0.0	1.0	0.13	0.0	0.0	…
Cardiac support at time of listing, %															
Ventilator	1.6	2.5	0.12	1.6	2.8	0.04	2.4	2.6	0.78	3.4	3.0	0.77	3.7	5.3	0.80
Inotropes	45.9	41.8	0.045	34.3	36.9	0.15	30.7	31.2	0.79	29.4	28.2	0.77	37.0	36.8	0.99
LVAD	19.2	15.4	0.01	29.2	21.5	<0.001	43.9	27.3	<0.001	42.1	33.2	0.03	44.4	31.6	0.38
RVAD±LVAD or MCS unspecified	1.1	2.0	0.09	1.0	2.1	0.02	1.3	1.6	0.54	1.7	2.3	0.63	0.0	5.3	0.23
TAH	0.3	0.3	0.91	0.4	0.4	0.76	0.3	0.3	0.99	0.0	1.0	0.13	0.0	0.0	…
ECMO	1.8	4.2	0.001	2.2	4.3	0.002	2.0	3.6	0.03	4.7	6.2	0.44	11.1	10.5	0.95
IABP	7.4	20.5	<0.001	5.5	16.9	<0.001	4.1	13.8	<0.001	3.4	12.1	<0.001	14.8	15.8	0.93

(*Continued*)

Table 4. Continued

Variables	BMI 18.5–24.9 kg/m^2			BMI 25–29.9 kg/m^2			BMI 30–34.9 kg/m^2			BMI 35–39.9 kg/m^2			BMI 40.0+ kg/m^2		
	Preallocation system changes, n=1169	Postallocation system changes, n=1270	*P* value	Preallocation system changes, n=1407	Postallocation system changes, n=1411	*P* value	Preallocation system changes, n=871	Postallocation system changes, n=988	*P* value	Preallocation system changes, n=235	Postallocation system changes, n=305	*P* value	Preallocation system changes, n=27	Postallocation system changes, n=19	*P* value
Comorbidities, %															
Diabetes	22.6	19.3	0.046	26.6	29.5	0.09	41.4	34.4	0.002	42.6	42.3	0.95	40.7	31.6	0.53
Tobacco user	39.9	37.6	0.26	48.2	41.1	<0.001	45.5	44.2	0.59	48.5	43.7	0.26	29.6	36.8	0.61
Malignancy	9.6	9.8	0.88	8.8	9.0	0.90	6.8	8.7	0.12	8.1	9.0	0.71	7.4	10.5	0.71
Prior CVA	5.3	8.0	0.01	6.9	6.3	0.52	6.6	6.4	0.82	8.5	6.4	0.34	7.4	0.0	0.24
ESRD	2.7	3.5	0.21	3.6	4.5	0.26	5.3	4.2	0.28	3.4	3.3	0.94	11.1	5.3	0.49
AICD	69.1	62.7	0.001	74.9	70.9	0.02	78.8	72.6	0.002	77.2	72.0	0.18	70.4	68.4	0.89
Prior cardiac surgery	34.8	32.5	0.23	40.4	36.8	0.06	38.5	39.4	0.68	43.0	45.9	0.51	44.4	42.1	0.88
Outcomes															
Waitlist time, d	36 [13–90]	16 [6–54]	<0.001	53 [20–128]	21 [7–70]	<0.001	59 [22–143]	26 [10–90]	<0.001	65 [28.8–144.3]	30.5 [9–102]	<0.001	61 [13.3–82.8]	36.5 [10.3–97]	0.61
Transplant outcomes															
Ischemic time, h	3.0 [2.3–3.7]	3.4 [2.7–4.0]	<0.001	3.0 [2.3–3.7]	3.4 [2.8–4.0]	<0.001	3.1 [2.3–3.7]	3.5 [2.9–4.0]	<0.001	3.0 [2.2–4.0]	3.5 [2.9–4.0]	<0.001	2.9 [2.2–3.3]	3.5 [2.7–3.6]	0.06
Distance traveled, nautical miles	84 [15–270.8]	220 [78–396]	<0.001	86 [13–248.5]	222 [75–394]	<0.001	73.5 [12–216.8]	230 [88–406]	<0.001	80 [9.8–322.5]	280 [105–437]	<0.001	46 [8.3–146.3]	137 [61–349]	0.07

AICD indicates automatic implantable cardioverter-defibrillator; BMI, body mass index; CVA, cerebrovascular accident; ECMO, extracorporeal membrane oxygenation; ESRD, end-stage renal disease; IABP, intra-aortic balloon pump; LVAD, left ventricular assist device; MCS, mechanical circulatory support; RVAD, right ventricular assist device; and TAH, total artificial heart.

Data presented as % or median [IQR].

transplant and experienced an increased risk of death after transplantation. Increasing BMI category was associated with increasing waitlist time, and patients in the highest category experienced greater risk of waitlist mortality. The 2018 allocation system changes appeared to increase rates of transplantation among patients with obesity, who were most likely to be UNOS Status 2 at time of transplantation, with greater distances traveled to procure organs compared with those undergoing transplantation under the prior system.

Transplantation in patients with an elevated BMI can be challenging, which can be driven by both comorbidities and by recommendations to match donor and recipient size. With increasing BMI, the concomitant increase in multiple comorbidities (type 2 diabetes, hypertension, and cardiovascular disease) raises the risk of perioperative complications and mortality.[10,11] In addition, obesity is independently associated with pulmonary hypertension, which when irreversible is a contraindication to transplantation.[12,13] Size matching for patients with and without obesity also remains a concern. Recipients without obesity receiving a heart with a donor of <70% of the recipients weight has been associated with worse outcomes,[14] and current recommendations from the International Society of Heart and Lung Transplantation are to match donors to recipients with a <30% body weight discrepancy.[15] Additionally, donor predicted heart mass >15% below the recipient's has been associated with increased mortality; however, that study did not include patients with BMI >40 kg/m^2.[16] Overall, patients with obesity face increased barriers to receiving a transplant compared with patients without obesity.

In a previous evaluation of donors within the UNOS database, Krebs et al noted that the prevalence of obesity is increasing in recipients,[17] but that there has been a concomitant increase of donors with obesity and severe obesity. In their analysis, a lower proportion (19.5%) of hearts from donors with severe obesity were used, compared with 31.6% of donors without severe obesity. We corroborate their findings in the contemporary population. Our study also found that with increasing BMI strata, there was an increase in estimated heart-mass discrepancy between recipient and donor, which was not associated with posttransplantation mortality after adjustments. Efforts to promote size matching to patients who have obesity or severe obesity should be carefully measured against the urgency for transplantation.[18,19]

We found that patients with obesity had significantly longer waitlist times than lean-weight transplant recipients; notably, patients with BMI 30 to 34.9 or 35 to 39.9 kg/m^2 had waitlist times more than twice as long as patients who were lean/normal weight, and patients with BMI 40 to 55 kg/m^2 had waitlist times about 3 months longer than that lean/normal weight group. With increasing waitlist time, there is not only a decreased likelihood of transplantation but also an increased likelihood of posttransplant death and graft failure.[8] Here, a BMI >40 kg/m^2 was independently associated with increased waitlist death, and increasing BMI strata was associated with a higher risk of posttransplantation death. To address this potential confounding by adverse events accumulated while on the waitlist, we controlled for time from listing to transplantation, and we found that severe obesity remained associated with posttransplantation survival difference. This suggests that it is unlikely that only delays to transplantation may be driving the differential posttransplantation outcomes for these patients. Compared with patients with a lean/normal BMI, those with a BMI >30 kg/m^2 were at greater risk of death.

We then sought to evaluate whether the allocation system change in 2018 had impacted these observed outcome differences in patients with obesity. We found that in both BMI groups (30–34.9 and 35–55 kg/m^2), patients were less likely to have durable LVADs at listing and more likely to be supported with an intra-aortic balloon pump after the allocation system change, and the BMI group 30 to 34.9 kg/m^2 also saw an increase in extracorporeal membrane oxygenation use at time of listing, findings that reflected those from analyses other populations after the allocation system change.[7,20] Despite some evidence that obesity is not associated with long-term survival differences in LVAD recipients,[21] these changes may be beneficial given the posttransplantation survival advantage of primary transplantation compared with transplantation from an LVAD.[22]

Additionally, both the patients with obesity and severe obesity were significantly more likely to receive a transplant in the new allocation system, with an ≈50% reduction in median wait times and dramatic increases in the percentage of patients transplanted within their first month of wait time. However, both groups had increased ischemic time and distance traveled for their hearts, which has also been described in other populations[7] and may be reflective of an overall change in the heart transplantation landscape rather than a finding specific to patients with obesity.[23,24] Despite having an overall shorter period of follow-up, patients with obesity appear to have had greater access to donor hearts, and a greater percentage underwent heart transplantation under the new allocation system. This was, however, accompanied by an increase in posttransplant mortality among patients with BMI 30 to 34.9 kg/m^2.

Limitations

Despite being prospectively maintained data, there are limitations to this study, including those that are

pertinent to all analyses of retrospective analysis of clinical data. Importantly, patients in the UNOS registry were preselected by their institutions to be reasonable transplant recipients, so there does exist a selection bias in the patients available for analysis, which is reflected in the proportions of each BMI category in this study, which were not reflective of the actual proportions of each category in the United States as reported by the Centers for Disease Control and Prevention.[25] Additionally, a weakness of the study is the low sample size of the highest BMI category, which makes the statistics more prone to weakness from multiple comparisons. Finally, the new allocation system has been in effect for <2 years, so practices may still be evolving and continue to evolve in response to this policy change. In addition to the limited time since the allocation system change, the effects of the ongoing COVID-19 pandemic on transplantation of patients with obesity are not evaluated within this article but may have influenced transplantation rates and/or outcomes in a way that is difficult to capture. Analyses containing the early postchange period may not be entirely reflective of future outcomes for this reason.

CONCLUSIONS

Patients with increasing levels of obesity were less likely to receive a transplant than patients without obesity, and were more likely to die after transplant, even after controlling for patient characteristics, waitlist time, and predicted heart-mass discrepancies. Patients in the highest BMI category were on the waitlist for longer with greater waitlist mortality. With the 2018 allocation system changes, patients with obesity had a higher likelihood of undergoing transplantation; however, as the obesity and heart failure epidemics continue, further research is needed into appropriate candidate selection, the biases of transplant centers and clinicians, and the long-term outcomes of obese solid-organ recipients.

ARTICLE INFORMATION

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Affiliations

Division of Cardiac Surgery (J.S., M.M., M.A., A.G., C.W.M.); Section of Cardiovascular Medicine (A.M., S.S., K.A.C., P.E.M., M.A.F., D.J., C.M., N.R.D., T.A.); Section of Endocrinology & Metabolism, Department of Internal Medicine (A.M.J.); Section of Pediatric Endocrinology, Department of Pediatrics (A.M.J.); and Department of Anesthesiology (A.N.), Yale School of Medicine, New Haven, CT; Division of Cardiology, Duke University Medical Center, Durham, NC (J.G.R.); Case Western Reserve University School of Medicine, Columbus, OH (A.G.); and Duke University Department of Internal Medicine, Durham, NC (F.C.).

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Supplementary Material

Tables S1–S4
Figure S1

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SUPPLEMENTAL MATERIAL

Table S1. Effects of all Variables on Transplantation

Variables	**Adjusted Hazard Ratio**	**P-Value**
BMI Categories		
18-24.9	Reference	
25-29.9	0.83 (0.81-0.85)	<**0.001**
30-34.9	0.68 (0.66-0.70)	<**0.001**
35-39.9	0.61 (0.58-0.64)	<**0.001**
40-55	0.42 (0.36-0.49)	<**0.001**
Female	0.92 (0.90-0.95)	<**0.001**
Age	1.01 (1.00-1.01)	<**0.001**
Race/Ethnicity		
White	Reference	
Black	0.86 (0.84-0.89)	<**0.001**
Hispanic	1.03 (0.99-1.07)	0.21
Asian	1.26 (1.18-1.34)	<**0.001**
Insurance Payor		
Private	Reference	
Public	0.98 (0.95-0.99)	**0.04**
Self	1.28 (1.05-.155)	**0.01**
Dilated Cardiomyopathy	1.03 (0.98-1.09)	0.24
Restrictive Cardiomyopathy	1.29 (1.18-1.40)	<**0.001**
Ischemic Cardiomyopathy	0.97 (0.92-1.03)	0.32
Congenital Cardiomyopathy	0.74 (0.68-0.81)	<**0.001**
Hypertrophic Cardiomyopathy	1.14 (1.04-1.24)	**0.004**
Valvular Cardiomyopathy	0.97 (0.87-1.08)	0.53

ECMO	1.66 (1.49-1.86)	<**0.001**
IABP	1.59 (1.51-1.66)	<**0.001**
Inotropes	1.55 (1.51-1.59)	<**0.001**
Ventilator	0.62 (0.57-0.69)	<**0.001**
LVAD	1.76 (1.61-1.92)	<**0.001**
RVAD	1.76 (1.61-1.92)	<**0.001**
TAH	1.92 (1.65-2.23)	<**0.001**
Diabetes	0.98 (0.95-1.00)	0.10
ESRD	0.88 (0.82-0.95)	<**0.001**
CVA	1.08 (1.03-1.14)	**0.002**
Malignancy	1.01 (0.97-1.05)	0.61
AICD	0.99 (0.96-1.02)	0.52
Tobacco Use	0.94 (0.92-0.96)	<**0.001**
Prior Cardiac Surgery	1.02 (1.00-1.05)	0.10

Table S2. Effect of all Variables on Waitlist Mortality

Variables	**Adjusted Hazard Ratio**	**P-Value**
BMI Categories		
18-24.9	Reference	
25-29.9	0.92 (0.85-1.00)	0.06
30-34.9	0.92 (0.84-1.01)	0.06
35-39.9	0.96 (0.84-1.09)	0.51
40-55	1.40 (1.07-1.84)	**0.02**
Female	1.06 (0.98-1.15)	0.17
Age	1.01 (1.017-1.01)	**<0.001**
Race/Ethnicity		
White	Reference	
Black	0.94 (0.87-1.03)	0.18
Hispanic	1.01 (0.90-1.15)	0.83
Asian	0.84 (0.67-1.06)	0.14
Insurance Payor		
Private	Reference	
Public	1.05 (0.98-1.13)	0.14
Self	0.81 (0.41-1.63)	0.56
Dilated Cardiomyopathy	0.53 (0.47-0.60)	**<0.001**
Restrictive Cardiomyopathy	0.80 (0.63-1.01)	0.06
Ischemic Cardiomyopathy	0.55 (0.48-0.63)	**<0.001**
Congenital Cardiomyopathy	0.60 (0.49-0.74)	**<0.001**
Hypertrophic Cardiomyopathy	0.56 (0.42-0.73)	**<0.001**
Valvular Cardiomyopathy	0.71 (0.54-0.92)	**0.01**

ECMO	3.61 (2.98-4.36)	**<0.001**
IABP	1.72 (1.52-1.95)	**<0.001**
Inotropes	1.70 (1.57-1.83)	**<0.001**
Ventilator	1.74 (1.47-2.06)	**<0.001**
LVAD	0.77 (0.70-0.84)	**<0.001**
RVAD	2.07 (1.71-2.51)	**<0.001**
TAH	1.83 (1.28-2.62)	**0.001**
Diabetes	1.12 (1.04-1.21)	**0.003**
ESRD	2.24 (1.96-2.55)	**<0.001**
CVA	1.20 (1.05-1.38)	**0.010**
Malignancy	0.91 (0.80-1.04)	0.16
AICD	0.88 (0.81-0.96)	**0.002**
Tobacco Use	1.00 (0.93-1.07)	0.99
Prior Cardiac Surgery	1.20 (1.11-1.29)	**<0.001**

Table S3. Most Common Causes of Post-Transplant Mortality

Variables	BMI 18.5-24.9 (N=2258)	BMI 25-29.9 (N=2634)	BMI 30-34.9 (N=1737)	BMI 35-39.9 (N=488)	BMI 40-55 (N=59)	P-Value
Unknown	13.7	14.3	12.8	11.1	8.5	0.20
Other Specify	7.0	5.2	6.4	5.9	3.4	0.10
Graft Failure-Primary Failure	3.4	4.9	4.8	6.1	5.1	**0.03**
Graft Failure: Rejection-Acute	3.8	3.4	4.1	4.3	5.1	0.69
Graft Failure: Rejection-Chronic	2.6	2.3	2.9	3.7	1.7	0.37
Infection: Bacterial Septicemia	6.3	7.4	6.3	6.6	6.8	0.49
Cardiovascular: Cardiac Arrest	10.6	9.3	11.2	9.6	16.9	0.10
Pulmonary: Respiratory Failure	4.6	3.9	3.7	2.3	1.7	0.12
Malignancy: Metastatic, Other Specify	4.4	4.4	3.5	2.7	0.0	0.10
Multiple Organ Failure	8.1	8.8	9.6	8.4	10.2	0.62

IQR-interquartile range, BMI-body mass index

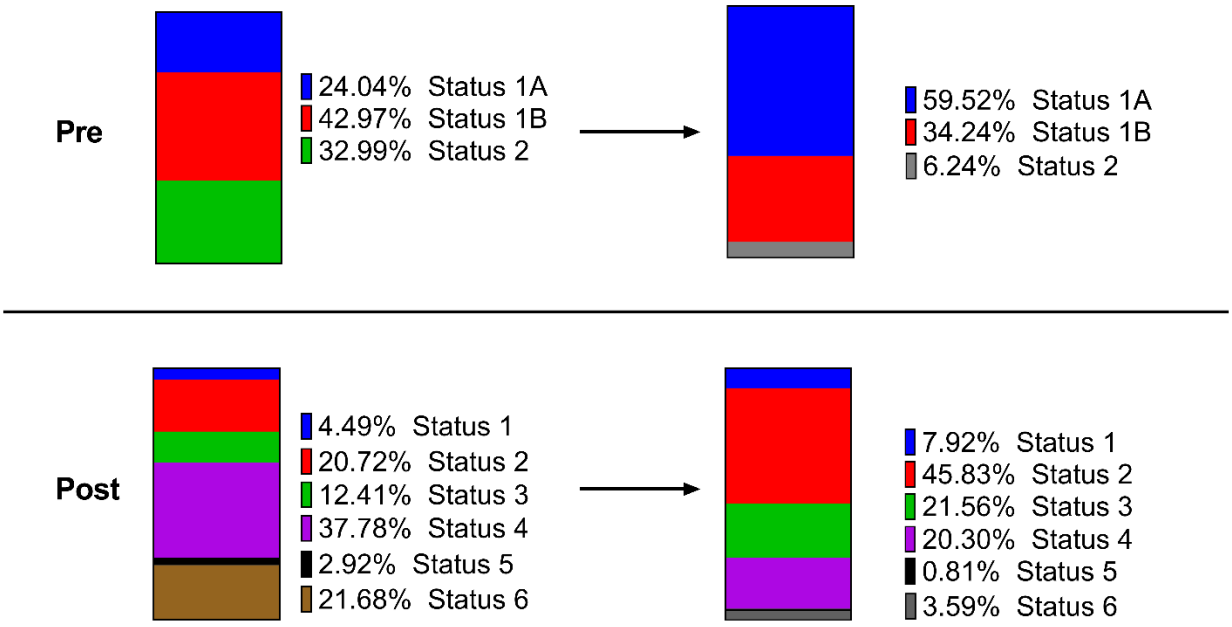
Table S4. Effects of all Variables on Post-Transplantation Mortality

Variables	**Adjusted Hazard Ratio**	**P-Value**
BMI Categories		
18-24.9	Reference	
25-29.9	1.03 (0.97-1.09)	0.41
30-34.9	1.15 (1.08-1.23)	<**0.001**
35-39.9	1.28 (1.16-1.42)	<**0.001**
40-55	1.62 (1.25-2.11)	<**0.001**
Female	0.97 (0.92-1.03)	0.33
Age	1.002 (1.000-1.004)	0.05
Race/Ethnicity		
White	Reference	
Black	1.27 (1.20-1.35)	<**0.001**
Hispanic	0.95 (0.87-1.04)	0.31
Asian	0.95 (0.82-1.10)	0.47
Insurance Payor		
Private	Reference	
Public	1.24 (1.18-1.30)	<**0.001**
Self	1.13 (0.74-1.68)	0.54
Dilated Cardiomyopathy	0.76 (0.68-0.85)	<**0.001**
Restrictive Cardiomyopathy	1.02 (0.85-1.22)	0.82
Ischemic Cardiomyopathy	0.92 (0.82-1.04)	0.18
Congenital Cardiomyopathy	1.05 (0.88-1.25)	0.61
Hypertrophic Cardiomyopathy	0.62 (0.50-0.77)	<**0.001**
Valvular Cardiomyopathy	0.66 (0.53-0.83)	<**0.001**

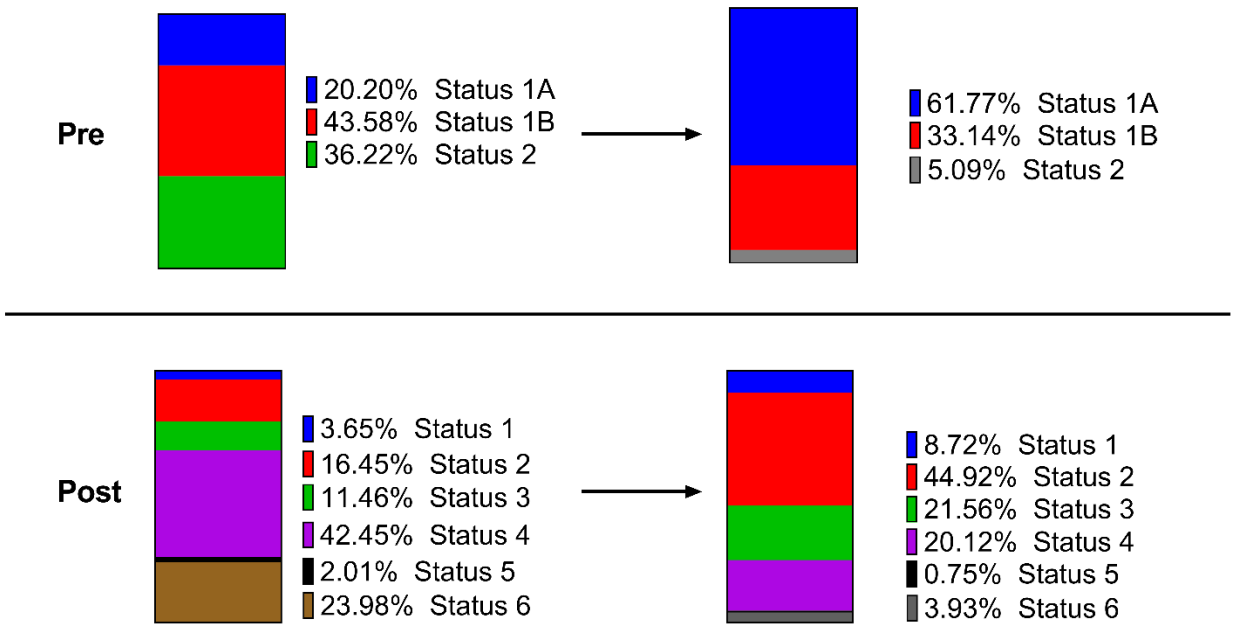
ECMO	1.42 (1.12-1.81)	**0.004**
IABP	0.94 (0.85-1.05)	0.28
Inotropes	1.03 (0.98-1.08)	0.32
Ventilator	1.22 (1.03-1.46)	**0.02**
LVAD	0.93 (0.87-0.99)	**0.02**
RVAD	1.28 (1.10-1.49)	**0.002**
TAH	1.50 (1.15-1.94)	**0.003**
Diabetes	1.23 (1.17-1.30)	**<0.001**
ESRD	1.33 (1.16-1.52)	**<0.001**
CVA	1.01 (0.92-1.12)	0.82
Malignancy	1.18 (1.13-1.24)	<**0.001**
AICD	0.93 (0.88-0.98)	**0.01**
Tobacco Use	1.18 (1.13-1.24)	**<0.001**
Prior Cardiac Surgery	1.17 (1.11-1.24)	**<0.001**
Waitlist Time (per day)	1.00 (1.000-1.000)	0.08
Heart Mass Discrepancy (per % difference)	1.000 (0.998-1.001)	0.65

Figure S1. a) Medical urgency status at listing and at transplant for patients with BMI 18.5-29.9 kg/m2 before and after (bottom) the 2018 donor heart allocation changes. b) Medical urgency status at listing (left) and at transplant (right) for patients with BMI 30-39.9 kg/m2 (Class 1 and 2 Obesity) before (top) and after (bottom) the 2018 donor heart allocation changes. c) Medical urgency status at listing (left) and at transplant (right) for patients with BMI 40-55 kg/m2 (Class 3 Obesity) before (top) and after (bottom) the 2018 donor heart allocation changes.

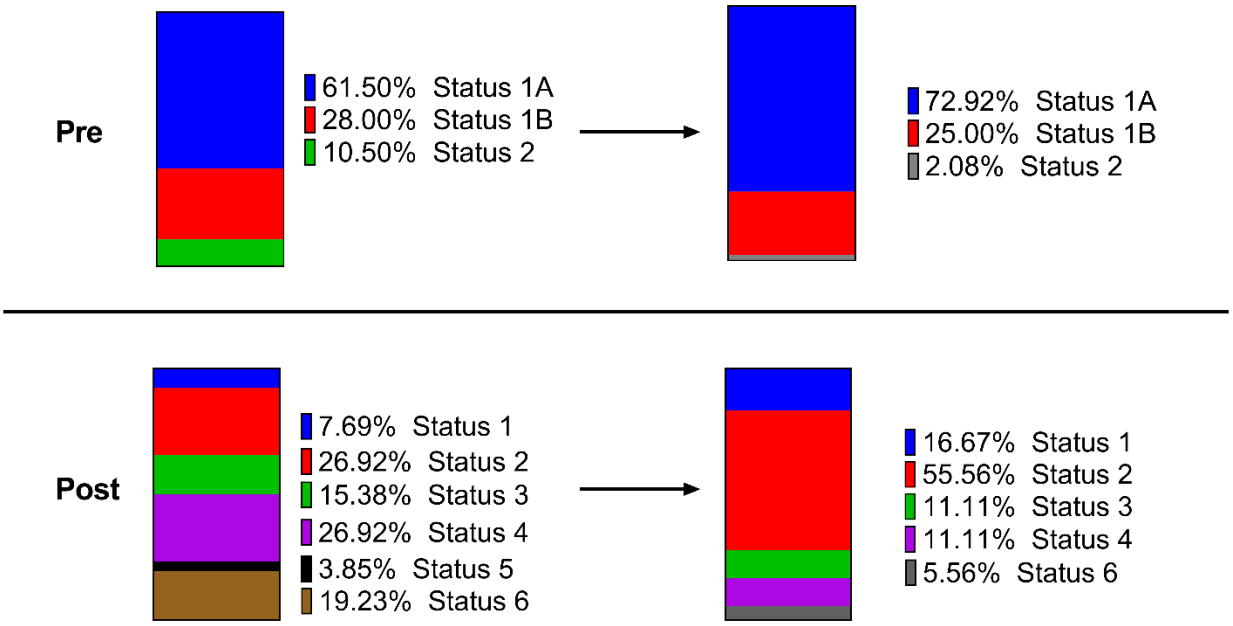
a.



b.


Pre
20.20% Status 1A
43.58% Status 1B
36.22% Status 2
61.77% Status 1A
33.14% Status 1B
5.09% Status 2
Post
3.65% Status 1
16.45% Status 2
11.46% Status 3
42.45% Status 4
2.01% Status 5
23.98% Status 6
8.72% Status 1
44.92% Status 2
21.56% Status 3
20.12% Status 4
0.75% Status 5
3.93% Status 6

c.


Pre
61.50% Status 1A
28.00% Status 1B
10.50% Status 2
72.92% Status 1A
25.00% Status 1B
2.08% Status 2
Post
7.69% Status 1
26.92% Status 2
15.38% Status 3
26.92% Status 4
3.85% Status 5
19.23% Status 6
16.67% Status 1
55.56% Status 2
11.11% Status 3
11.11% Status 4
5.56% Status 6