ORIGINAL RESEARCH

Impact of Donor Obesity on Outcomes After Orthotopic Heart Transplantation

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Background—The impact of donor obesity on the outcome of orthotopic heart transplantation has not been studied. The aim of this study was to investigate the impact of donor obesity on the outcomes of adult orthotopic heart transplantation recipients.

Methods and Results—Data were obtained from the United Network for Organ Sharing database. All adult (age ≥18 years) patients undergoing orthotopic heart transplantation from 2000 through 2016 were included (n=31 920). We stratified the cohort by donor body mass index (BMI); 13 015 patients (40.8%) received a heart from a normal-weight donor (BMI 18.5–24.9), 11 271 patients (35.3%) received a heart from an overweight donor (BMI 25.0–29.9), 4910 patients (15.4%) received a heart from an obese donor (BMI 30.0–34.9), and 2724 patients (8.5%) received a heart from an extremely obese donor (BMI ≥35). The cohort of obese donors was older, included a higher incidence of diabetes mellitus, and had a higher creatinine. Our data also showed that the recipients of obese donor grafts were older, had a higher BMI, creatinine, percentage of diabetes mellitus, and longer total waiting period. There was no significant difference detected in the survival likelihood (P=0.08) of patients based on a donor's BMI-based categorized cohort. There were no significant differences found in the overall survival probability among 4 groups in the adjusted survival analyses (P=0.25).

Conclusions—This study demonstrated that patients receiving higher BMI donor hearts might not be subjected to an increased risk of death, at least during the short term after transplant, compared with those using the normal-weight donors. **(*J Am Heart Assoc*. 2018;7:e010253. DOI: 10.1161/JAHA.118.010253)**

Key Words: surgery • survival analysis • transplantation

Heart disease is the leading cause of death in the United States. Advanced or medically refractory heart failure represents the end-stage form of heart disease.[1] We are currently facing a pandemic of patients with end-stage heart failure. Many treatments have been developed for patients with end-stage heart failure, among which orthotopic heart transplantation (OHT) remains the criterion standard[2]; however, the persistent shortage of available donor organs has resulted in an ever-increasing waitlist for transplantation, as well as longer waiting periods before surgery. Although >20 000 patients may benefit from OHT per year, only 3000 will receive a new heart, with a waitlist mortality of 10.7 deaths per 100 000 waitlist-years.[3] Because of such persistent and worsening shortage of available donor hearts, we have previously proposed alternative approaches to maximize organ allocation including repairing donor valvular heart disease,[4] harvesting donor hearts from more distant locations, and accepting longer cold ischemic time,[5] and applying a unique domino heart transplantation strategy.[6] Despite growing evidence supporting the safety of using marginal organs, >60% of available hearts are still being discarded.[7]

Concurrently, obesity has reached staggering proportions, representing a significant public health concern. The prevalence of obesity in the general population has increased over the years.[8] We are faced with ever-increasing numbers of obese donors. Approximately one third of Americans have a body mass index (BMI) ≥30. Although obesity is not an absolute contraindication, most centers' concern about a high BMI of donors was one of the main medical reasons why donors were not allowed to proceed to donation.[9] However, there is limited evidence in the literature that these donors experience more adverse reactions. Unfortunately, we lack guidelines on the evaluation and acceptance of marginal organs, such as a high BMI donor graft. These deficiencies have resulted in variable practice patterns between transplant centers, leading to underutilization of a valuable resource.

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Clinical Perspective

What Is New?

- The demonstration of equivalent graft outcomes from obese donors in adults should encourage the utilization of obese donor grafts in carefully selected donors and recipients.

What Are the Clinical Implications?

- In the era of an ever-increasing obese population, the increased utilization of obese donor grafts can potentially improve the persistent and worsening shortage of available donor organs, shorten the waitlist times for heart transplantation, and reduce mortality rates for patients on the waiting list.

Therefore, one possible solution will be to maximize the use of obese donors, since the number of obese donors is anticipated to increase substantially in the future.

Thus, attention has focused on donor BMI in OHT. The impact of donor obesity on the quality of heart grafts has not been studied in detail. To our knowledge, no large multicenter study focusing on donor obesity has been performed. Lacking this, we felt the next best option would be to investigate this issue using data from the United Network for Organ Sharing (UNOS) database, which is a multi-institutional physician-overseen registry collecting data on all patients listed for OHT in the United States. Therefore, we seek to evaluate the impact of donor BMI status on the outcome of adult OHT recipients.

Methods

The data, analytical methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Patient Selection

The UNOS registry was analyzed for all patients ≥18 years old who underwent OHT between January 1, 2000 and December 31, 2016 (n=39 743). The exposure of interest was donor BMI, calculated utilizing height and weight measurements obtained at registration, and defined as weight (in kilograms) divided by height (in meters squared). Patients were excluded if they were 18 years or younger, did not undergo isolated heart transplantation, underwent re-heart transplantation, or underwent heart–lung transplantation (n=32 654). Patients with incomplete donor BMI data were excluded from the analysis (n=32 585). We stratified the cohort by disjoint categories of donor BMI established by the US Department of Health and Human Services and the US Department of Agriculture: BMI 18.5 to 24.9 (normal weight); BMI 25.0 to 29.9 (overweight); BMI 30.0 to 34.9 (obese); and BMI ≥35.0 (extreme obese). Donors with BMI <18.5 were excluded (n=31 920) (Figure 1).

Information obtained from the database included donor characteristics (age, sex, blood type), donor past medical history (diabetes mellitus, hypertension, cocaine use, coronary artery disease, renal function, and liver function), donor's left ventricular ejection fraction, recipient baseline characteristics (age, sex, blood type), recipient past medical history (diabetes mellitus, renal function, and liver function), cause of heart failure, total waiting time, and preoperative life support (hospitalization in intensive care unit, intra-aortic balloon pump, extracorporeal membrane oxygenation, durable ventricular assist device), and allograft ischemic time.

The primary outcome was the overall survival, which was defined as the patient death from transplantation. The hospitalization outcomes such as graft failure and acute rejection episodes were also assessed across the groups. Studies involving this data set have been determined to be

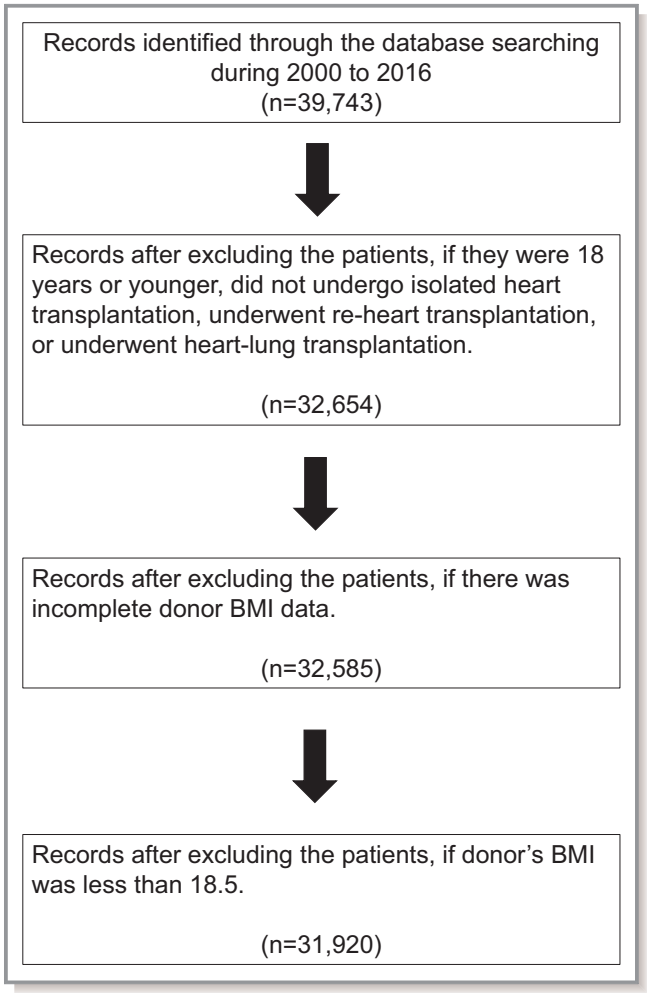

Figure 1. PRISMA flow diagram. BMI indicates body mass index; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

exempt from review by the Institutional Review Board of Stanford University School of Medicine. Survival curves were constructed using the Kaplan-Meier method, stratified over each donor BMI group.

Statistical Analysis

In the descriptive analyses of the study, continuous variables were presented as mean±SD and compared with the mean differences between groups by ANOVA, and χ^2 test was used to assess the association between categorical variables. The impact of donor BMI status on the post-transplant outcomes, such as overall mortalities, was investigated. Kaplan-Meier curves were created to visually represent graft survival and were compared by the Wilcoxon test and log-rank test. Cox proportional hazards regression analyses were conducted to estimate the effect of donor's BMI on the overall survival of the cohort. As a sensitivity analysis, the Cox proportional hazards model was fitted on the subcohort starting from 2005 as well, which had less incomplete data, included more important factors, and had higher data quality. For all analyses, $P<0.05$ was considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute Inc, NC).

Results

A total of 31 920 adult primary heart transplant patients who were identified from the UNOS database from 2000 to 2016 met the study entry criteria. The cohorts differed in demographic and preoperative clinical characteristics among the normal-weight, overweight, obese, and extreme obese groups, as defined by donor BMI. Among them, 13 015 patients (40.8%) received a heart from a normal-weight donor, 11 271 patients (35.3%) received a heart from an overweight donor, 4910 patients (15.4%) received a heart from an obese donor, and 2724 patients (8.5%) received a heart from an extremely obese donor.

Donor Characteristics

Donors' characteristics stratified by donor BMI are shown in Table 1. The extreme obese donors (35.3±11.1 years old), overweight donors (33.0±11.8 years old), and obese donors (34.9±11.6 years old) were significantly older than normal-weight donors (29.0±11.7 years old) ($P<0.0001$). The percentage of male donors was highest in the normal-weight group (73.1%), and lowest in the extreme obese group (50.8%). The percentage of diabetes mellitus was significantly

Table 1. Donor Characteristics Stratified by Donor BMI

	Normal Weight (BMI 18.5–24.9) n=13 015	Overweight (BMI 25.0–29.9) n=11 271	Obese (BMI 30.0–34.9) n=4910	Extreme obese (BMI ≥35) n=2724	*P* Value
Donors' baseline characteristics					
Age, y	29.0±11.7	33.0±11.8	34.9±11.6	35.3±11.1	<0.0001
Sex, male, n (%)	9511 (73.1)	8497 (75.4)	3329 (67.8)	1385 (50.8)	<0.0001
Body mass index, kg/m^2	22.4±1.7	27.2±1.4	32.0±1.4	39.7±4.6	<0.0001
Left ventricular ejection fraction, %	61.2±7.6	61.7±7.2	62.1±7.3	62.6±7.1	<0.0001
Allograft ischemic time, h	3.2±1.1	3.2±1.0	3.2±1.0	3.3±1.0	<0.0001
Past medical history					
Diabetes mellitus, n (%)	210 (1.6)	284 (2.5)	214 (4.4)	214 (7.9)	<0.0001
Hypertension, n (%)	131 (1%)	192 (1.7%)	120 (2.5%)	79 (2.9%)	<0.0001
Cocaine use, n (%)	1912 (15%)	1766 (15.9%)	726 (15%)	336 (12.5%)	0.0001
Coronary artery disease, n (%)	150 (1.2%)	251 (2.2%)	136 (2.8%)	88 (3.3%)	<0.0001
Preoperative data					
Creatinine, mg/dL	1.20±1.10	1.32±1.20	1.43±1.37	1.55±1.62	<0.0001
Total bilirubin, mg/dL	1.11±1.54	1.11±1.33	1.05±1.28	0.98±1.30	<0.0001
Blood type					
A, n (%)	4683 (36.0)	4031 (35.8)	1862 (37.9)	963 (35.4)	0.0063
B, n (%)	1447 (11.1)	1189 (10.5)	528 (10.8)	302 (11.1)	
AB, n (%)	265 (2.0)	283 (2.5)	105 (2.1)	42 (1.5)	
O, n (%)	6620 (50.9)	5768 (51.2)	2415 (49.2)	1417 (52.0)	

BMI indicates body mass index.

different among the extreme obese donors (7.9%), obese donors (4.4%), overweight donors (2.5%), and normal-weight donors (1.6%) ($P<0.0001$). Creatinine was also observed to be significantly different among the extreme obese donors (1.55±1.62 mg/dL), overweight donors (1.43±1.37 mg/dL), obese donors (1.32±1.20 mg/dL), and normal-weight donors (1.20±1.10 mg/dL) ($P<0.0001$). The abovementioned results, higher incidence of diabetes mellitus, and elevated creatinine, suggest that the cohort of higher BMI donors reflected typical characteristics of the obese population, even though the cohort included only accepted donor grafts for heart transplantation. Interestingly, the left ventricular ejection fraction was similarly excellent in all 4 groups. The incidences of coronary artery disease and hypertension were similarly low in all 4 groups.

Recipient Characteristics

Recipients' characteristics stratified by donor BMI are shown in Table 2. The mean BMI of the 4 recipient groups were 29.3±5.0 kg/m^2 in the extreme obese donor group, 28.5±4.9 kg/m^2 in the obese donor group, 27.5±4.7 kg/m^2 in the overweight donor group, and 25.7±4.5 kg/m^2 in the normal-weight donor group, respectively ($P<0.0001$). The

Table 2. Recipient Characteristics Stratified by Donor BMI

	Normal Weight (BMI 18.5–24.9) n=13 015	Overweight (BMI 25.0–29.9) n=11 271	Obese (BMI 30.0–34.9) n=4910	Extreme Obese (BMI ≥35) n=2724	*P* Value
Recipients' baseline characteristics					
Age, y	52.0±12.9	53.3±11.9	53.4±11.7	53.5±12.0	<0.0001
Sex, male, n (%)	9130 (70.1)	9002 (79.9)	4000 (81.5)	2116 (77.7)	<0.0001
BMI, kg/m^2	25.7±4.5	27.5±4.7	28.5±4.9	29.3±5.0	<0.0001
Past medical history					
Diabetes mellitus, n (%)	2891 (22.4)	2999 (26.8)	1451 (29.7)	833 (30.7)	<0.0001
On hemodialysis, n (%)	518 (4.0)	412 (3.7)	210 (4.3)	117 (4.3)	0.1757
Cause of heart failure					
Nonischemic cardiomyopathy, n (%)	6036 (46.4)	5177 (45.9)	2356 (48.0)	1339 (49.2)	<0.001
Ischemic cardiomyopathy, n (%)	4681 (36.0)	4310 (38.2)	1836 (37.4)	995 (36.5)	
Restrictive heart disease, n (%)	366 (2.8)	283 (2.5)	122 (2.5)	75 (2.8)	
Congenital heart disease, n (%)	465 (3.6)	264 (2.3)	85 (1.7)	56 (2.1)	
Hypertrophic cardiomyopathy, n (%)	331 (2.5)	206 (1.8)	85 (1.7)	47 (1.7)	
Valvular heart disease, n (%)	289 (2.2)	210 (1.9)	75 (1.5)	33 (1.2)	
Others, n (%)	847 (6.5)	821 (7.3)	350 (7.1)	179 (6.6)	
Total waitlist time, y	0.55±0.95	0.64±1.04	0.66±1.08	0.64±0.97	<0.0001
Previous cardiac surgery, n (%)	4670 (48.6)	4461 (50.8)	2078 (52.1)	1135 (49.8)	0.0008
Preoperative life support, n (%)					
Hospitalization in ICU, n (%)	3825 (29.5)	3336 (29.7)	1418 (29.0)	773 (28.5)	0.3797
IABP, n (%)	752 (5.8)	619 (5.5)	263 (5.4)	166 (6.1)	0.4357
ECMO, n (%)	65 (0.5)	50 (0.4)	19 (0.4)	17 (0.6)	0.4767
Blood type					
A, n (%)	5403 (41.5)	4547 (40.3)	2086 (42.5)	1129 (41.4)	0.0971
B, n (%)	1925 (14.8)	1612 (14.3)	676 (13.8)	399 (14.6)	
AB, n (%)	703 (5.4)	649 (5.8)	242 (4.9)	140 (5.1)	
O, n (%)	4984 (38.3)	4463 (39.6)	1906 (38.8)	1056 (38.8)	
Preoperative data					
Creatinine, mg/dL	1.32±0.85	1.35±0.85	1.36±0.76	1.36±0.81	0.0028
Total bilirubin, mg/dL	1.12±1.83	1.16±2.27	1.19±2.22	1.04±1.26	0.0126

BMI indicates body mass index; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; ICU, intensive care unit.

recipients' mean ages in the extreme obese group (53.5±12.0 years old), obese group (53.3±11.9 years old), and overweight group (53.3±11.9 years old) were significantly older than those of normal-weight donor grafts (52.0±12.9 years old) (P<0.0001). The prevalence of male recipients was lowest in the normal-weight group (70.1%), but higher in all other groups with BMI ≥25.0.

The percentage of diabetes mellitus in recipients was significantly greater in the extreme obese donor (30.7%), obese donor (29.7%), and overweight donor (26.8%) groups compared with normal-weight donors (22.4%) (P<0.0001).

Short-term mechanical circulatory system use before transplant was not significantly different between groups (intra-aortic balloon pump and extracorporeal membrane oxygenation; P=0.4357 and 0.4767). Similarly, the rate of hospital admissions in the intensive care unit before transplant was not significantly different between groups (P=0.3797). The abovementioned results suggest that the accepted obese donor heart grafts were utilized independently of recipient clinical status.

Mortality Outcomes

The P value of the Wilcoxon test on the Kaplan-Meier survival estimation of the 4 groups was 0.08 for mortality, suggesting that there was no significant difference detected by this test in the survival likelihood of patients in a donor's BMI-based categorized cohort. However, the log-rank test with a P value of 0.03 might imply there might be some variability in mortality between groups, given the long follow-up time (Figure 2).

Considering the effects of other important factors and controlling for possible confounding, the Cox Proportional Hazards regression models were used to assess the adjusted donor BMI effect on the overall survival probability. Compared with the normal-weight donor group, most groups except the

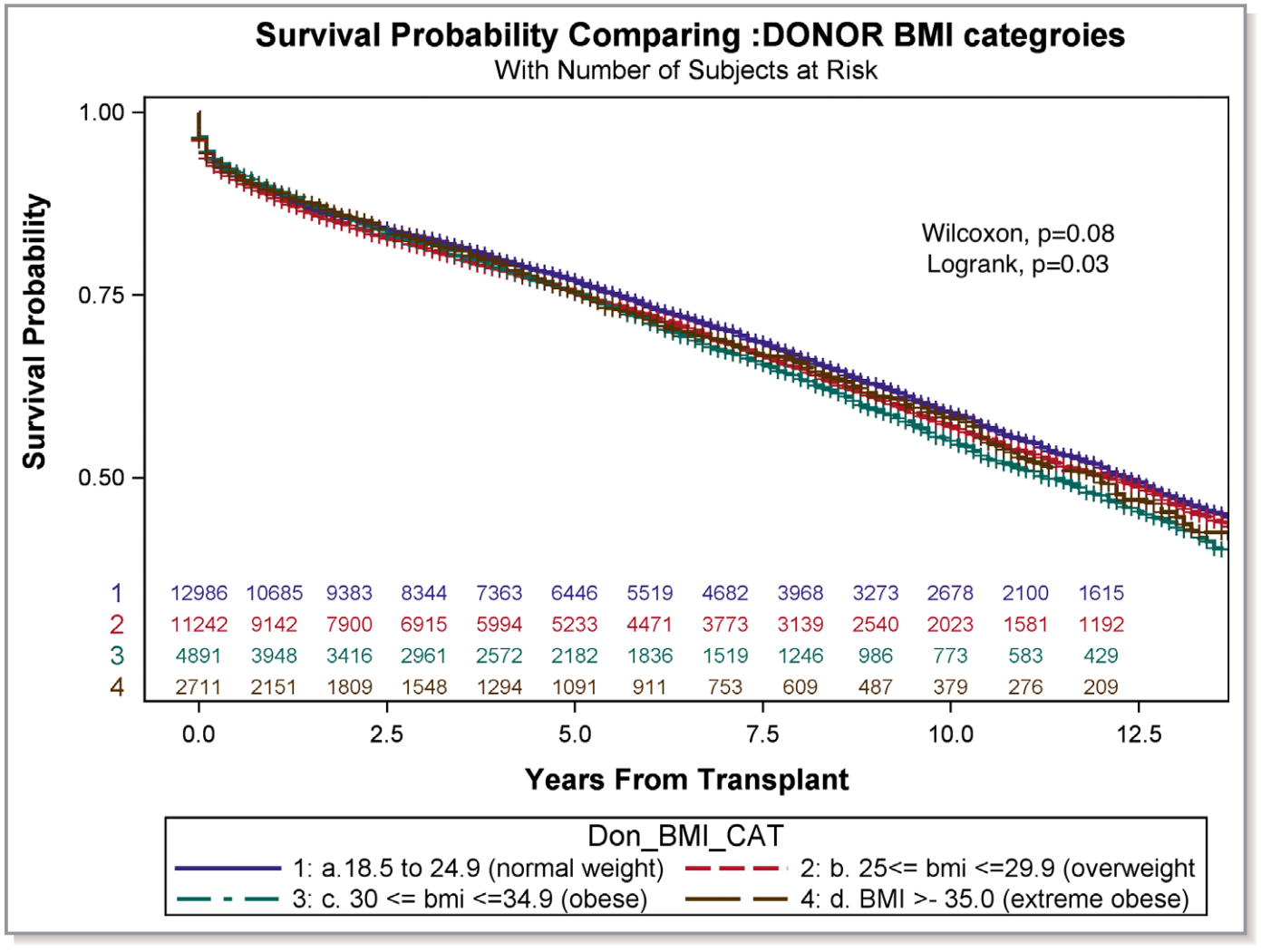

Figure 2. Overall survival Kaplan-Meier estimates stratified according to donor body mass index (BMI). Patients who received a graft from normal-weight donor (BMI, 18.5–24.9; blue line) vs overweight donor (BMI, 25.0–29.9; red line) vs obese donor (BMI, 30.0–34.9; green line) vs extreme obese donor (BMI ≥35; brown line) (P=0.08, Wilcoxon test; P=0.03, log-rank test).

extreme obese group showed no significant difference in the overall survival in the model (overall test P=0.2545, individual hazard ratios versus the normal-weight donor group and their corresponding 95% confidence intervals in Table 3). Of note, the recipients' history of previous cardiac surgery was available only from 2005, and ventricular assist device use was not collected from 2000 through 2003. To take these important mortality risk factors into account and obtain the more reliable assessment of donor BMI on survival by the higher quality and more complete data, 1 additional Cox Proportional Hazards model was fitted using the subcohort from 2005.

Table 3. Survival Effects of Obese Donor Hearts in Cox Models.

Parameters	Hazard Ratio	95% CI Lower Limit	95% CI Upper Limit	$P>\chi^2$	Type-3 Limits
Using all the data from 2000					
Overweight (BMI 25.0–29.9)*	0.987	0.94	1.037	0.6119	0.2545
Obese (BMI 30.0–34.9)*	0.972	0.91	1.037	0.3876	
Extreme obese (BMI ≥35)*	0.918	0.843	0.999	0.0486	
Calculated recipient BMI*	1.013	1.008	1.018	<0.0001	<0.0001
Year of transplant*	0.981	0.976	0.987	<0.0001	<0.0001
Recipients' age, y*	1.003	1.001	1.005	0.0043	0.0043
Donors' age, y*	1.01	1.008	1.012	<0.0001	<0.0001
Gender Match, female donor to male recipient*	1.1	1.026	1.179	0.007	0.0002
Gender Match, male donor to female recipient*	1.107	1.044	1.173	0.0006	
Recipients' creatinine, mg/dL*	1.035	1.011	1.059	0.0043	0.0043
Recipients' total bilirubin, mg/dL*	1.029	1.023	1.036	<0.0001	<0.0001
Recipients' history of diabetes mellitus*	0.785	0.748	0.824	<0.0001	<0.0001
Recipients' history of dialysis*	0.683	0.615	0.759	<0.0001	<0.0001
Donors' history of hypertension ≥10 y*	0.923	0.787	1.083	0.3267	0.3267
Allograft ischemic time, h*	1.061	1.04	1.083	<0.0001	<0.0001
Parameters	Hazard Ratio	95% CI Lower Limit	95% CI Upper Limit	$P>\chi^2$	Type-3 Limits
Overweight (BMI 25.0–29.9)†	0.997	0.934	1.065	0.9356	0.7473
Obese (BMI 30.0–34.9)†	0.991	0.911	1.077	0.8254	
Extreme obese (BMI ≥35)†	0.944	0.85	1.05	0.2888	
Calculated Recipient BMI†	1.014	1.008	1.02	<0.0001	<0.0001
Year of transplant†	0.987	0.977	0.997	0.012	0.012
Donors' age, y†	1.01	1.008	1.013	<0.0001	<0.0001
Gender Match, female donor to male recipient†	1.091	0.996	1.195	0.0621	0.0344
Gender Match, male donor to female recipient†	1.084	1.002	1.173	0.0432	
Recipients' creatinine, mg/dL†	1.047	1.017	1.078	0.0018	0.0018
Recipients' total bilirubin, mg/dL†	1.033	1.024	1.041	<0.0001	<0.0001
Recipients' history of diabetes mellitus†	0.825	0.776	0.876	<0.0001	<0.0001
Recipients' history of dialysis†	0.674	0.589	0.771	<0.0001	<0.0001
Recipients on VAD†	0.929	0.873	0.988	0.0191	0.0191
Recipients' history of previous cardiac surgery†	0.857	0.808	0.908	<0.0001	<0.0001
Donors' history of hypertension ≥10 y†	0.917	0.749	1.124	0.4049	0.4049
Allograft ischemic time, h†	1.085	1.057	1.113	<0.0001	<0.0001

BMI indicates body mass index; VAD, ventricular assist device.

*Results adjusted in Cox proportional hazards model by baseline characteristics—age, Gender Match, BMI, past medical history (diabetes mellitus, renal failure, liver function, hypertension), allograft from the year 2005 (With prior cardiac surgery and VAD).

†Results adjusted in Cox proportional hazards model by baseline characteristics—age, Gender Match, BMI, past medical history (diabetes mellitus, renal failure, liver function, hypertension), allograft ischemic time, prior VAD, previous cardiac surgery.

All mortality assessments from this sensitivity analysis indicated that patients receiving a higher BMI donor heart might not be subjected to an increased risk of death after transplant compared with those receiving normal-weight donors (overall test P=0.7473; individual hazard ratios versus the normal-weight donor group and their corresponding 95% confidence intervals in Table 3).

Discussion

This is a comprehensive study to investigate the impact of donor BMI status on the outcome of adult primary OHT recipients using the UNOS database. We stratified the cohort by disjoint categories of donor BMI established by the US Department of Health and Human Services and the US Department of Agriculture: BMI 18.5 to 24.9 (normal weight); BMI 25.0 to 29.9 (overweight); BMI 30.0 to 34.9 (obese); and BMI ≥35 (extreme obese).

Our data showed that the cohort of obese donors was older, had a higher incidence of diabetes mellitus, and had a higher creatinine in a stepwise manner from normal weight to the extreme obese group. This is consistent with the typical characteristics of the general obese population.[10] Our data also showed that the recipients of obese (eg, overweight, obese, and extreme obese) donor grafts were older, had a higher BMI, had a higher creatinine, had a higher incidence of diabetes mellitus, and had a longer total waiting period than those of normal-weight donor grafts, indicating that the obese donor grafts were utilized in similar obese recipients. Interestingly, the mean value of each donor group's BMI was higher than that of each recipient group's BMI in obese and extreme obese groups. This is likely the result of strategically avoiding a significant donor-to-recipient size mismatch, especially an undersized mismatch.[11] In addition to the abovementioned patient demographics, equally as important in this study were the factors that did not show significant difference in the baseline recipients' characteristics: blood type, incidence of mechanical circulatory support use, and incidence of pretransplant hospitalization in the intensive care unit. This suggests that the obese donor grafts were equally utilized, independent of recipient clinical status. Importantly, our data also showed that the left ventricular ejection fraction was similarly excellent between these 4 donor groups and the incidence of coronary artery disease was very low in all 4 donor groups, which did not reflect typical characteristics of the general obese population. This can likely be explained by the conservativeness for organ acceptance, because of the potential concern in obese donor graft populations.

Historically, many treatments have been developed for patients with end-stage heart failure, among which OHT remains the criterion standard; however, the persistent and worsening shortage of available donor organs resulted in an ever-increasing waitlist of patients and longer waiting periods for heart transplant. Approximately 10% of all candidates on the waiting list for solid organ transplantation die each year without receiving an organ.[6] Moreover, a significant number of marginal organs are not transplanted. In order to surmount this challenge, we have previously proposed alternative approaches to maximize organ allocation by utilizing marginally acceptable organs,[4] harvesting donor hearts from distant locations, and accepting longer cold ischemic time,[5] and applying a domino heart transplantation as a uniquely efficacious surgical strategy.[6]

Considering this, obesity has represented a significant public health concern, and the prevalence of obesity in the general population has increased over the years.[8] We are faced with ever-increasing numbers of obese donors. It should be noted that the mean donor BMI for our study population was 27.0, with 76% of patients between 18.5 and 29.9 (normal weight and overweight). This is in stark contrast to national estimates of obesity, in which >32% of Americans have a BMI ≥30.[12] These data, taken in the context of obesity as a known risk factor for cardiovascular disease and heart failure, may indicate a reluctance to accept obese donor grafts. Generally, the perception is that heart grafts from obese donors are of inferior quality, as compared with a normal-weight donor; however, there is very little actual evidence in the literature to support that perception. Moreover, obesity was considered one of the main medical reasons why donors were not allowed to proceed to donation, although there are many other reasons for donor heart nonacceptance. Any possible consequences of using organs from these potential donors will be important to determine. Therefore, 1 possible solution will be to maximize the use of obese donors, since a significant number of obese donors are anticipated to increase in the future.

Although issues relating to provider bias and allocation have not been explored in OHT, there has been extensive work in the area of abdominal organ transplantation. It has been reported that donor obesity negatively affects the outcomes of post–abdominal organ transplantation. In liver and pancreas transplants, donor obesity was associated with a higher incidence of primary graft dysfunction and surgical complications.[13,14] Nevertheless, our study focusing on thoracic organ transplantation identified that the overall posttransplant graft survival of severe donor obesity (BMI ≥35) was equivalent to survival of normal-weight donors, although obese donors were older and included a higher incidence of diabetes mellitus. This is an interesting phenomenon since it has been reported that donor age and sex were important risk factors of short-term heart graft survival.[15] Therefore, it is noteworthy that equivalent graft survival was demonstrated in short-term mortality in our

study, despite an expected reduced graft survival based on the donor age discrepancy between groups.

Since obesity increases mortality in the general population and can contribute both directly and indirectly to the posttransplant graft survival, one would expect that obesity might negatively impact survival for patients with heart failure. Additionally, the development of left ventricular hypertrophy correlates not only with obesity, but also with the duration of obesity. Moreover, obesity is an independent risk factor for the development of coronary artery disease. Furthermore, increased BMI also alters lipid metabolism, leading to increased serum cholesterol and low-density lipoprotein levels, which further accelerates the development of atherosclerosis. Beyond its effect on altered metabolism, obesity can also contribute to the development of heart failure. There is a strong association between obesity and heart failure: up to 35% to 45% of patients with heart failure are overweight or obese.[16] Moreover, there is also a strong relationship between obesity and heart failure with the preserved ejection fraction phenotype. This presents with left ventricular concentric remodeling and right ventricular dilatation and dysfunction.[17] Looking forward, the impact of heart failure with the preserved ejection fraction and associated left ventricular diastolic dysfunction may be of interest for further study.

Interestingly, our study identified that recipients who received a more significant degree of obese (ie, extreme obese) grafts showed a slightly better mortality, compared with obese and overweight donor grafts, even though all-cause mortality was reduced. This can be supported by the studies showing that obesity, defined through either increased BMI or other indices, in fact appears to be protective for patients with heart failure.[18] The phenomenon has been termed "the obesity paradox." The mechanism through which obese donor grafts appears to be protective is not well established; however, a number of plausible hypotheses have been proposed. Because heart failure is a catabolic condition, increased adipose and lean tissue in patients with higher BMI may serve as a buffer that confers a protective effect as a metabolic reserve. In addition, a higher BMI can be translated into clinical benefit through positive impact on cardiorespiratory fitness as well as indirectly through the hormonal modulation associated with adipose tissue–derived stem cell or adiponectin, which can potentially induce the adverse biological effects in acute and chronic heart failure.[19] Although it is possible that this is related to a confounding variable that we have not analyzed, it is also possible that this finding reflects altered metabolic needs for myocardium in the presence of brain death.

Limitations of the Database

This study has limitations consistent with retrospective analyses and the use of a national multicenter database. Specifically, the UNOS database has some considerable uncollected data for the important factors during some specific time periods. For example, recipients' history of previous cardiac surgery was only available from 2005 and ventricular assist device use was not collected from 2000 until 2003. Therefore, the overall adjusted analyses based on the entire cohort cannot incorporate these important mortality risk factors into the account. The additional sensitivity analysis based on the subcohort is necessary. Nevertheless, the UNOS/Organ Procurement and Transplantation Network registry has provided a large sample size to assess the impact of the obese donor on outcomes after heart transplantation in the current era.

The main focus of our current study is the influence of the obese donor on the outcome of recipients; however, specific recipient characteristics may certainly contribute to the recipient mortality as well, and several of those have not been included in our analysis.

The potential selection bias may be related to beliefs among physicians that obesity is a prohibitive risk factor for OHT. Additionally, only donors whose hearts were accepted for transplantation were included. Selecting a suitable donor is a complicated process. Clinicians need to consider multiple factors, weighing recipient urgency against donor characteristics, ischemic time, recipient sensitization, and donor/recipient size mismatch. Thus, there may be additional characteristics that are responsible for high rates of donor organ rejection, and those factors would not be accounted for in this analysis.

In addition, more information is needed to identify the impact of such practice. As this study addressed only mortality, further data are needed on the impact of the obese donor on the morbidity of OHT.

Conclusion

The demonstration of equivalent graft outcomes from obese donors in adults should encourage the utilization of obese donor grafts in carefully selected donors and recipients. This will expand the donor pool and aid in decision-making regarding organ allocation in times of critical donor shortage. In the era of an ever-increasing obese population, the increased utilization of obese donor grafts can potentially improve the persistent and worsening shortage of available donor organs, shorten the waitlist times for heart transplantation, and reduce mortality rates for patients on the waiting list. We contend that this is pertinent and important knowledge for transplant cardiologists at the time of donor graft evaluation.

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under contract with the federal government. This system serves as the model for transplant systems around the world.

Disclosures

None.

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