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Trends and outcomes of cardiac transplantation from donors dying of drug intoxication

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ABSTRACT

Background: Deaths from drug intoxication have increased in the United States but outcomes of recipients of orthotopic heart transplantation (OHT) from these donors are not well characterized.
Methods: We performed a retrospective analysis of the United Network for Organ Sharing's STAR database between January 2000 and March 2014 and assessed mortality and retransplantation using adjusted Cox models by mechanism of donor death.
Results: Of the 31,660 OHTs from 2000 to 2014, 1233 (3.9%) were from drug intoxication. These donors were more likely to be female, white, with greater tobacco use and higher BMI compared to donors who died of other mechanisms. Drug intoxication accounted for 1.1% of OHT donors in 2000 and 6.2% in March 2014. No significant difference was observed in 10-year mortality (adjusted hazard ratio [HR], 95% confidence interval [CI]: 0.99, 0.87-1.13), 10-year retransplantation (adjusted HR 0.84, 0.49-1.41) or 1-year and 3-year rehospitalization with other mechanisms of death compared to drug intoxication.
Conclusion: There has been a large increase in OHT donors who die of drug intoxication in the United States. OHT outcomes from these donors are similar to those dying from other mechanisms. These data have important implications for donor selection in context of the ongoing opioid epidemic.

Orthotopic heart transplantation (OHT) is a life-saving therapy for eligible patients with advanced heart failure. However, the demand for OHT continues to exceed the supply.[1,2] This supply–demand mismatch is further complicated with an increase in organ turndown rates, suggesting there could be an opportunity for reexamining commonly held criteria for suitability of potential cardiac allografts.[3]

One of the reasons for the lack of increase in OHT rates in the United States has been the temporal reduction in deaths from vehicular accidents and gunshot injuries, which historically represented major contributors to donor availability.[4,5] However, there has been a rise in premature deaths in the US in recent years, largely driven by illicit opioid use, which has reached epidemic proportions.[6] Deaths from drug intoxication now exceed both vehicular- and gun-related deaths in the United States and are seen as a driver behind the overall increase in OHT in 2016.[7] OHT donors dying of drug intoxication drove an increase in overall OHT rates in 2016.[8]

There remains reluctance to procure organs from donors with increased-risk behaviors such as substance abuse,[9] since it is unclear if the outcomes of recipients who receive OHT from donors who die of drug intoxication are different from donors who die of other mechanisms. In this study, we used national data collected by the Organ Procurement and Transplantation Network (OPTN)/United Network for Organ Sharing (UNOS) from January 2000 to March 2014, to assess trends in the prevalence of OHT donors dying of drug intoxication and differences in characteristics of donors who died of different mechanisms. Furthermore, we assessed if there was any significant difference in clinical outcomes of recipients who received OHT from donors who died of drug intoxication compared to those dying of other mechanisms.

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; OHT, orthotopic heart transplantation; OPTN, Organ Procurement and Transplantation Network; UNOS, United Network for Organ Sharing.

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Table I
Comparison of baseline characteristics between donors dying of drug intoxication (DI) vs. those dying of other mechanisms.

Donor characteristic		DI death donors (n = 1233)	Non DI death donors (n = 30,427)	*P*
Age, years		28.5 (9.3)	28.3 (14.4)	.047
Sex	*Male*	754 (61.2%)	21,135 (69.5%)	<.001
	Female	479 (38.9%)	9292 (30.5%)	
Ethnicity	*White*	1059 (85.9%)	19,697 (64.7%)	<.001
	AA	56 (4.5%)	4739 (15.6%)	
	Hispanic	100 (8.1%)	5104 (16.8%)	
	Other	18 (1.5%)	882 (2.9%)	
Diabetes		30 (2.4%)	732 (2.4%)	.41
Hypertension		143 (11.6%)	3435 (11.3%)	.58
Previous MI		11 (0.9%)	246 (0.4%)	.59
Ejection Fraction, %		60.7 (7.3)	61.9 (8.0)	<.001
Cancer		13 (1.1%)	466 (1.5%)	.25
BMI >30		319 (25.9%)	5740 (18.9%)	<.001
Inotropic support		469 (43.0%)	12,066 (53.1%)	<.001
Clinical infection		728 (59.0%)	13,099 (43.1%)	<.001
Creatinine, mg/dl		1.9 (1.9)	1.2 (1.1)	<.001
HBsAg Serology	*Positive*	76 (8.2%)	1525 (9.3%)	.10
	Negative	129 (14.0%)	2392 (14.6%)	
	Not Done	716 (77.6%)	12,399 (75.6%)	
HCV Serology	*Positive*	1 (0.1%)	19 (0.1%)	.82
	Negative	1025 (99.9%)	20,460 (99.8%)	
	Not Done	0 (0.0%)	23 (0.1%)	
High-risk for BBD transmission		367 (36.1%)	1585 (7.9%)	<.001
Cocaine use		445 (36.7%)	3157 (10.8%)	<.001
Heavy alcohol use		200 (19.7%)	2558 (12.8%)	<.001
Non-IV drug use		917 (74.4%)	9235 (30.4%)	<.001
Cigarette use		260 (21.1%)	5678 (18.7%)	.10

The numbers represent mean (standard deviation) for continuous variables, and frequency (percentage) for categorical variables. Abbreviations: *AA*, African-American; *BBD*, blood borne disorders; *BMI*, body mass index; *MI*, myocardial infarction.

Methods

Design

We performed a retrospective analysis of the Standard Transplant Analysis and Research (STAR) database provided by UNOS. The STAR database contains de-identified, patient-level data with information from donors, waiting list patients, and transplant recipients inputted from UNOS registration forms filled for any organ transplant in the United States.[2] Given the de-identified nature of the data, the study was granted exemption from full review by the Institutional Review Board at Duke University Medical Center.

Study population

All deceased donor and recipients who received OHT between January 1, 2000, and March 31, 2014, with a donor mechanism of death listed in the STAR database were included in the analysis.

Primary and secondary outcomes

The primary outcome assessed in this study was OHT recipient long-term mortality at 10 years. Follow-up for recipients started at the time of transplantation. Secondary outcomes included long-term retransplantation through 10 years. We selected 10 years as our time frame to provide long-term outcomes and given that median survival after OHT ranges between 6.8 and 12.6 years depending on the year of OHT, and age of the donor and recipient.[2] To assess additional relevant short-term recipient outcomes, we analyzed all-cause rehospitalization at 1 and 3 years. All outcome data was assessed from entries in the STAR recipient follow-up worksheets. Additionally, we assessed baseline characteristics of deceased donors dying of different mechanisms of death. These included demographic characteristics such as age, gender, ethnicity and clinical characteristics such as comorbidities, infectious data, ejection fraction, laboratory data such as baseline creatinine and hepatitis C virus (HCV) and hepatitis B virus (HBV) serologies, and history of other substance use such as cocaine, non-intravenous drugs, tobacco and alcohol.

Statistical analysis

Categorical variables are presented as frequencies (percentages) and differences by death mechanism were assessed using the chi-square test. Continuous variables were compared using the Wilcoxon Rank-Sum test. Continuous variables are presented as mean (standard deviation) unless otherwise stated.

We described unadjusted cumulative incidence for long-term mortality among patients who received OHT from donors dying of different mechanisms of actions. Similar time to event analysis was performed for long-term retransplantation. For cumulative incidence of re-transplantation, we considered mortality as a competing risk. We also estimated the median follow-up time using the reverse Kaplan-Meier method. In addition, we examined the frequency of 1-year and 3-year rehospitalization among recipients that were alive and had hospitalization records.

We created two models for multivariable adjustment. In Model 1, we included the donor and recipient's age, ethnicity/race, mismatch, body mass index for recipient, BMI >30 for donor, creatinine and the donor's left ventricular ejection fraction, intensive care unit status and life support status. In Model 2, we included additional donor variables that had not been collected between 2000 and 2004, which included prior cardiac surgery, employment status, human immunodeficiency status, inotrope use, presence of clinical infection and alcohol, cocaine and non-intravenous drug use history. These variables were used based on prior research on outcomes amongst OHT recipients from donors with increased-risk social behaviors and clinical relevance.[10]

Cox proportional hazards regression were performed to adjust for confounding factors to assess if donor death by drug intoxication resulted in significant differences in the long-term mortality and retransplantation at 10 years. Both unadjusted and adjusted hazard ratios with 95% confidence intervals were calculated. We assessed the