ORIGINAL RESEARCH

Heart Transplantation Survival and the Use of Traumatically Brain-Injured Donors: UNOS Registry Propensity-Matched Analysis

Yaron D. Barac, MD, PhD; Oliver K. Jawitz, MD; Jacob Klapper, MD; Jacob Schroder, MD; Mani A. Daneshmand, MD; Chet Patel, MD; Matt G. Hartwig, MD; Nancy K. Sweitzer, MD; Carmelo A. Milano, MD

***Background*—**The transplantation of hearts from traumatically brain-injured (TBI) donors has been associated with inferior long-term survival in single-center analyses. However, in a more recent analysis, death caused by cerebrovascular accident was associated with worse posttransplant survival in recipients. The purpose of this study was to explore the outcomes of heart transplantation in recipients receiving donor hearts from TBI and non-TBI donors in a large national registry.

***Methods and Results*—**We performed a retrospective cohort analysis of the UNOS (United Network of Organ Sharing) Registry Organ Procurement and Transplantation Network between 2006 and 2018 for adult candidates wait-listed for isolated heart transplantation. Recipients were stratified into 2 groups, TBI and non-TBI donors. Propensity score matching was performed. Kaplan-Meier analysis was used to estimate survival posttransplant. A total of 24 894 candidates met inclusion criteria. TBI was the leading cause of death in the donor population. Recipients of TBI donor hearts (N=13 07) were younger (median age, 55 versus 57 years; $P<0.001$) and less likely women (21.6% versus 29.8%; $P<0.001$). At 10 years, the TBI group had better long-term survival compared with the non-TBI group (62.8% versus 59.9%; $P<0.001$). After propensity group matching, the 10-year survival was similar between groups.

***Conclusions*—**In the largest analysis of heart transplants and their survival, according to the type of donor injury (TBI versus non-TBI), we found similar survival in heart transplant recipients. Future studies should address specific subpopulations (eg, hemorrhagic stroke) in the non-TBI group to address concerns about reduced posttransplant survival. **(*J Am Heart Assoc*. 2019;8: e012894. DOI: 10.1161/JAHA.119.012894.)**

Key Word: heart transplant • trauma brain injury • UNOS

Heart transplantation is the gold standard therapy for end-stage heart disease. Heart transplantation continues to be provided to an increasing number of recipients as a total of 3273 heart transplants were performed in the United States in 2017, the highest volume year to date.[1] Because of an ongoing mismatch between donor organ supply and the demand for suitable organs, wait list mortality continues to represent a major concern in thoracic transplantation.[2]

Although donation after circulatory death has recently become available for lung transplantation in the United States, for cardiac transplantation candidates, brain dead donors are still the only source of donated allografts. Among the brain-dead donors, traumatic brain injury (TBI) is still the main source for cardiac donation, although an increase in drug intoxication brain dead donors has occurred during the past 20 years in the United States.[3]

The effect of TBI on the cardiac muscle has been studied extensively in both rats and humans. In rats, it was found to affect blood pressure, affect cardiac contractility, and cause accumulation of reactive oxygen species.[4] Furthermore, in humans, TBI has been shown to induce cardiac uncoupling, which is associated with alterations in the autonomic nervous system and reduced heart rate variability. Such uncoupling is a predictor of mortality after TBI.[5] Because of these findings, and the fact that clinical studies were performed more than a decade ago and were mainly done using single-center data, uncertainty about the significance of these findings exists.[6–8]

Others have pointed out the increased risk of reduced posttransplant survival when using hearts from donors who died because of cerebrovascular accidents, specifically donors who experienced hemorrhagic stroke. Hemorrhagic stroke may be considered as a surrogate marker for untreated

From the Division of Cardiovascular and Thoracic Surgery (Y.D.B., O.K.J., J.K., J.S., M.A.D., M.G.H., C.A.M.) and Department of Cardiology (C.P.), Duke University Medical Center, Durham, NC; Division of Cardiology, Sarver Heart Center, University of Arizona, Tucson, AZ (N.K.S.).

Correspondence to: Yaron D. Barac, MD, PhD, Duke University Medical Center, 10 Duke Medicine Cir, Durham, NC 27710. E-mail: yaron.barac@duke.edu

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Clinical Perspective

What Is New?

- The recipients of traumatically brain-injured and non–traumatically brain-injured donor hearts have similar posttransplant survival.

What Are the Clinical Implications?

- Concern about using traumatically brain-injured hearts may be mitigated by the current findings, which suggests one option for expanding the donor pool for heart transplantation.

hypertensive disease, a known cause for a covert myocardial disease, particularly left ventricular hypertrophy, which is known to be associated with worse posttransplant outcomes.[9–11]

The scarcity of organs remains the major issue of cardiac transplantation. Thus, in this study, we sought to ascertain the magnitude by which transplantation of hearts from TBI donors or non-TBI donors is associated with inferior long-term survival in a large national registry.

Methods

The data that support the findings of this study are available from the corresponding author on reasonable request.

Data Source

A retrospective cohort analysis was performed using the UNOS (United Network of Organ Sharing) Registry Standard Analysis and Research database. The UNOS Registry administers the Organ Procurement and Transplantation Network under contract with the US Department of Health and Human Services. This database contains data on all transplant candidates undergoing listing for solid organ transplantation in the United States since October 1987. The data set used for this investigation included all recipients who were transplanted with a heart between 2006 and 2018 and their respective donors. The institutional review board at Duke University approved this study before data collection, and a waiver for informed consent was given.

Study Design and Outcomes

All first-time adult recipients of an isolated heart transplantation during the study dates were included. Exclusion criteria included candidates <18 years old; those undergoing simultaneous lung, liver, or abdominal transplantation; and those with incomplete donor data or survival data. The study population was then stratified by donor cause of death (eg, TBI or non-TBI [anoxia, cerebrovascular accident, central nervous system tumor, and other]). The primary outcome was recipient long-term survival and its relation to both recipient and donor characteristics.

Propensity Matching

Propensity score matching was used to estimate causal effects by using observational data. To account for treatment effect, patients were propensity scored by using the FUZZY extension of SPSS for matching. Propensity scoring was performed with the following variables from the UNOS Registry SRTR data set: donor (age, race, and ischemic time) and recipient (age, sex, diabetes mellitus, recipient being treated with intravenous antibiotics or inotropes pretransplant, ventricular assist device, heart failure cause, hospitalization status pretransplant, and transplant year). Recipients of TBI donors were matched to recipients of non-TBI donors 1:1 without replacement by nearest neighbor matching. The donor matched groups were not matched for donor age and sex mismatch, as these factors reduced the ability to successfully match.

Statistical Analysis

Demographic data for both donors and recipients were compiled and described. Baseline characteristics and outcomes were compared between groups using the Kruskal-Wallis ANOVA test for continuous variables and Pearson's χ^2 test for categorical variables.

To adjust for factors that may influence the rate of each competing outcome, propensity score matching was performed to address differences in both recipient and donor demographics. Propensity score matching was performed across key baseline demographic variables (mentioned above), and a 1:1 match was done.

Finally, posttransplant survival was estimated for those candidates in each propensity-matched group that underwent heart transplantation using the Kaplan-Meier method. The log-rank test was used to determine statistical significance. Kaplan-Meier analysis was used to estimate survival posttransplant. Cox proportional hazards modeling was performed to identify independent predictors of survival.

Analyses were performed using SPSS, Version 25, for Mac (IBM, Armonk, NY), with $P<0.05$ indicating statistical significance.

Results

Demographic Characteristics

A total of 24 894 recipients met inclusion criteria for analysis. Of these, 13 207 (53%) were of the TBI group. At the time of

Table 1. Demographic Characteristics of Recipients of Heart Transplantation, Segregated by Presence of TBI in the Donor

Variable	Non-TBI (n=11 687)	TBI (n=13 207)	*P* Value
Male sex, % (n)	70.2 (8210)	78.4 (10 352)	<0.001
Age, y	57 (16)	55 (16)	<0.001
BMI, kg/m^2	27.0 (7.1)	27.1 (6.8)	0.434
Ethnicity, % (n)			0.248
White	66.4 (7766)	67.5 (8911)	
Black	21.1 (2469)	20.2 (2664)	
Hispanic	8.0 (930)	8.0 (1063)	
Other	4.5 (522)	4.3 (569)	
Recipient history			
Diabetes mellitus, % (n)	27.7 (3240)	27.3 (3604)	0.454
Malignancy, % (n)	8.3 (967)	7.1 (939)	0.001
Cerebrovascular disease, % (n)	5.7 (672)	5.2 (686)	0.058
Dialysis, n (%)	238 (2.0)	342 (2.6)	0.004
Heart failure cause, % (n)			0.011
Ischemic cardiomyopathy	32.8 (3828)	34.1 (4500)	
Nonischemic dilated cardiomyopathy	50.7 (4924)	50.6 (6682)	
Other	16.6 (1935)	15.3 (2025)	
Recipient creatinine (mg/dL), median (IQR)	1.2 (0.5)	1.2 (0.5)	0.025
Recipient bilirubin (mg/dl), median (IQR)	0.7 (0.6)	0.8 (0.7)	<0.001
Pretransplant status, % (n)			0.582
ICU	28.6 (3344)	28.2 (3727)	
Hospitalized (non-ICU)	15.9 (1857)	15.6 (2064)	
Not hospitalized	55.5 (6485)	56.1 (7415)	
Medical therapy, % (n)			
Intravenous antibiotics in 2 wk before transplant	9.4 (1098)	10.7 (1413)	0.001
Intravenous inotropes at transplant	39.2 (4576)	37.1 (4903)	0.001
IABP at transplant	6.7 (788)	5.4 (718)	<0.001
VAD at transplant	41.0 (4789)	43.1 (5694)	0.001
Ventilator at transplant	1.6 (191)	1.3 (166)	0.014
ECMO at transplant	0.7 (76)	0.6 (77)	0.551
ABO blood type, % (n)			0.003
A	40.6 (4741)	40.8 (5382)	
B	14.3 (1672)	15.0 (1978)	
AB	5.2 (608)	6.0 (795)	
O	39.9 (4666)	38.3 (5052)	
Time on wait list, median (IQR), d	87 (227)	97 (236)	<0.001

BMI indicates body mass index; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; ICU, intensive care unit; IQR, interquartile range; TBI, traumatic brain injury; VAD, ventricular assist device.

transplant, the TBI recipients tended to be younger (median age, 55 versus 57 years; $P<0.001$) and the percentage of men was higher (78.4% versus 70.2%; $P<0.001$) compared with the non-TBI group. The TBI group had less history of malignancy (7.1% versus 8.3%; $P<0.001$) but had a higher percentage of recipients in whom their heart failure cause was ischemic cardiomyopathy (34.1% versus 32.8%; $P=0.001$) compared with the non-TBI group. Although no difference was

Table 2. Demographic Characteristics of Heart Transplant Donors, Segregated by TBI as Cause of Brain Death

Variable	Non-TBI (n=11 687)	TBI (n=13 207)	*P* Value
Donor male sex, % (n)	58.0 (6783)	82.5 (10 890)	<0.001
Donor age, median (IQR), y	35 (19)	26 (15)	<0.001
Donor BMI, median (IQR), kg/m^2	27.2 (7.8)	25.6 (6.3)	<0.001
Donor ethnicity, % (n)			<0.001
White	67.2 (7857)	62.6 (8263)	
Black	14.9 (1738)	17.1 (2263)	
Hispanic	14.7 (1720)	17.5 (2307)	
Other	3.2 (372)	2.8 (374)	
Donor history, % (n)			
Cigarette use	16.6 (1941)	10.8 (1425)	<0.001
Cocaine use	20.5 (2395)	14.8 (1951)	<0.001
Alcohol abuse	16.3 (1900)	15.6 (2057)	0.146
Diabetes mellitus	5.3 (625)	1.7 (225)	<0.001
Hypertension	23.9 (2796)	6.9 (916)	<0.001
Cancer	2.4 (275)	0.7 (96)	<0.001
Donor creatinine (mg/dL), median (IQR)	1.0 (0.8)	1.0 (0.5)	<0.001
Donor bilirubin (mg/dl), median (IQR)	0.6 (0.6)	0.9 (0.8)	<0.001
Donor cause of death, % (n)			…
Anoxia	51.6 (6034)	…	
Cerebrovascular/stroke	42.4 (4956)	…	
Head trauma	…	100 (13 207)	
CNS tumor	1.3 (156)	…	
Other	4.6 (541)	…	
ABO blood type, % (n)			<0.001
A	35.6 (4161)	36.4 (4809)	
B	10.8 (1259)	11.2 (1473)	
AB	2.0 (231)	2.5 (329)	
O	51.6 (6036)	49.9 (6596)	
Graft ischemic time, median (IQR), h	3.2 (1.4)	3.2 (1.4)	0.151
Sex mismatch, % (n)	28.9 (3383)	20.9 (2758)	<0.001

BMI indicates body mass index; CNS, central nervous system; IQR, interquartile range; TBI, traumatic brain injury.

found between the groups in terms of their hospitalization status pretransplant, fewer TBI recipients were on intravenous inotropes when transplanted (37.1% versus 39.2%; *P*<0.001) but more were receiving intravenous antibiotics (10.7% versus 9.4%; *P*<0.001) compared with the non-TBI group. Furthermore, more TBI recipients were on a left ventricular assist device at time of transplant (13.5% versus 12.8%; *P*<0.001) but less were on intra-aortic balloon pump (5.4% versus 6.7%; *P*<0.001) compared with the non-TBI group, and their median wait list time was 97 versus 87 days (*P*<0.001) in the non-TBI group (Table 1).

TBI donors were mostly men (82.5% versus 58%; *P*<0.001), were younger (median, 26 versus 35 years *P*<0.001), had a lower body mass index (25.6 versus 27.2 kg/m^2; *P*<0.001), and experienced less diabetes mellitus, hypertension, and cancer compared with the non-TBI group. Furthermore, fewer used cocaine (14.8% versus 20.5%; *P*<0.001) and were cigarette smokers (10.8% versus 16.6%; *P*<0.001) compared with the non-TBI group (Table 2). There was a larger tendency to perform sex mismatch of organs allocation in the non-TBI group compared with the non-TBI group (28.9% versus 20.9%; *P*<0.001).

Table 3. Propensity-Matched Demographic Characteristics of Recipients and Donors of Heart Transplantation, Segregated by Presence of TBI in the Donor

Variable	Non-TBI (n=8989)	TBI (n=8989)	*P* Value
Donor characteristics			
Donor age, y	32 (16)	30 (16)	<0.001
Donor ethnicity, % (n)			0.645
White	66.0 (5936)	65.2 (5865)	
Black	15.5 (1389)	15.6 (1401)	
Hispanic	15.5 (1390)	16.1 (1448)	
Other	3.0 (274)	3.1 (275)	
Recipient characteristics			
Recipient male sex, % (n)	74.5 (6694)	74.6 (6704)	0.878
Sex mismatch, % (n)	29.0 (2611)	22.8 (2053)	<0.001
Recipient age, y	56 (17)	56 (17)	0.077
Recipient ethnicity, % (n)			0.885
White	66.8 (6007)	66.4 (5970)	
Black	21.0 (1887)	21.0 (1891)	
Hispanic	7.9 (707)	8.2 (733)	
Other	4.3 (388)	4.4 (395)	
Recipient diabetes mellitus, % (n)	27.9 (2510)	27.6 (2481)	0.641
Intravenous antibiotics in 2 wk before transplant, % (n)	10.1 (907)	10.2 (921)	0.748
Heart failure cause, % (n)			0.654
Ischemic cardiomyopathy	33.4 (2999)	32.8 (2951)	
Nonischemic dilated cardiomyopathy	50.7 (4561)	50.9 (4573)	
Other	15.9 (1429)	16.3 (1465)	
Pretransplant status, % (n)			0.906
ICU	28.6 (2567)	28.3 (2544)	
Hospitalized (non-ICU)	15.8 (1417)	15.9 (1433)	
Not hospitalized	55.7 (5005)	55.8 (5012)	
Inotropes at transplant, % (n)	38.3 (3443)	37.5 (3372)	0.282
VAD at transplant, % (n)	43.1 (3872)	43.2 (3885)	0.857
Ischemic time >3.5 h, % (n)	37.3 (3355)	37.6 (3384)	0.666
Year of transplant	2013 (6)	2013 (7)	0.283

ICU indicates intensive care unit; TBI, traumatic brain injury; VAD, ventricular assist device.

Propensity-Matched Analysis

Using propensity score matching, a 1:1 balanced cohort was developed, representing 8989 candidates in each cohort. The groups were matched according to the variables mentioned in the Methods section; in the TBI group, the donor age at the time of transplant was statistically significant compared with the non-TBI group (30 versus 32 years; $P<0.001$), and the TBI group had a lower percentage of sex mismatch of organ allocation compared with the non-TBI group (29% versus 22.8%; $P<0.001$) (Table 3).

Unadjusted Analysis and Propensity Score Kaplan-Meier Survival Curves

The cohort long-term posttransplant survival was estimated using the Kaplan-Meier method; there was a significant

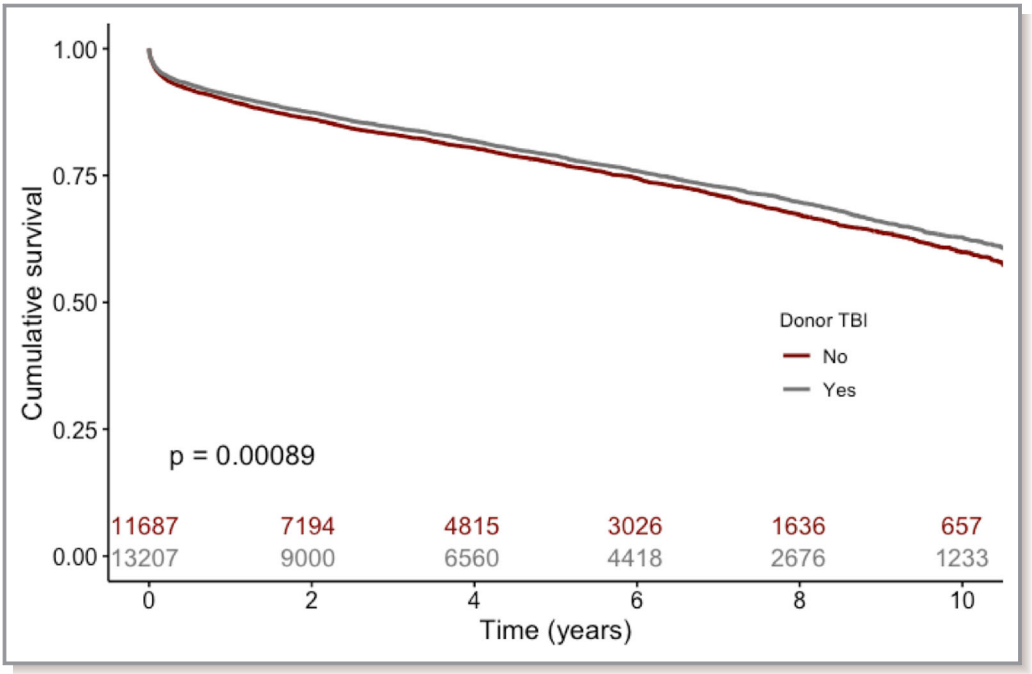

Figure 1. Ten-year Kaplan-Meier estimate of long-term survival of recipients after heart transplantation in the entire cohort, stratified by traumatic brain injury (TBI).

difference in the 10-year survival (the TBI group had better survival compared with the non-TBI group: 10-year survival of 62.8% versus 59.9%; *P*=0.00089; Figure 1). However, when analyzing the propensity-matched groups for outcomes, no difference was found between the groups in the Kaplan-Meier survival analysis up to 10 years posttransplant (Figure 2).

Cox Proportional Hazards

To account for potential confounders and identify independent predictors of recipient survival, a Cox proportional hazard model was created. Independent predictors of improved recipient survival in propensity score analysis included

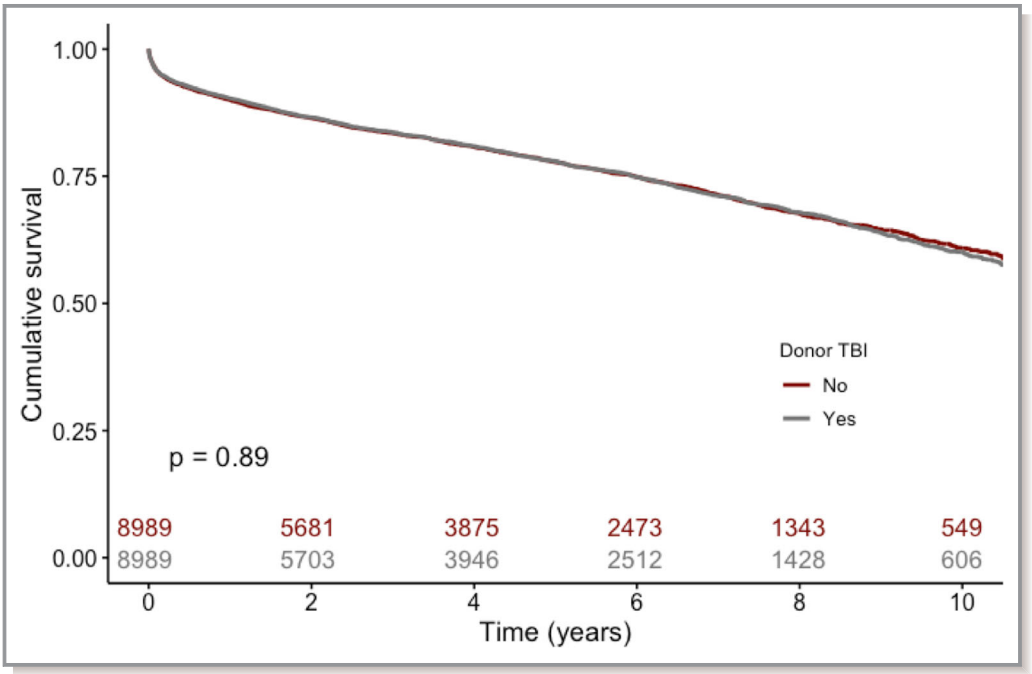

Figure 2. Ten-year Kaplan-Meier estimate of long-term survival of recipients after heart transplantation in the propensity-matched cohort, stratified by traumatic brain injury (TBI).

Table 4. Cox Proportional Hazard model for the Propensity-matched cohort

Predictor	Hazard Ratio	95% CI		*P* Value
		Lower	Upper	
Donor/graft characteristics				
Cause of death: TBI	1.04	0.98	1.11	0.238
Age (per 5 y)	1.05	1.04	1.07	<0.001
Ischemic time >3.5 h	1.23	1.15	1.3	<0.001
Ethnicity				
White	Reference	Reference	Reference	Reference
Black	1.08	0.99	1.18	0.077
Hispanic	1.06	0.97	1.15	0.206
Other	1.27	1.06	1.51	0.009
Recipient characteristics				
Aged <50 y (per 5 y)	0.98	0.98	0.99	<0.001
Aged ≥50 y (per 5 y)	1.03	1.02	1.03	<0.001
Male sex	1.03	0.95	1.11	0.442
Sex mismatch	1.09	1.01	1.17	0.021
Ethnicity				
White	Reference	Reference	Reference	Reference
Black	1.3	1.2	1.4	<0.001
Hispanic	1.01	0.89	1.14	0.891
Other	0.92	0.77	1.09	0.309
BMI >25 kg/m^2	1.14	1.06	1.22	<0.001
Diabetes mellitus	1.26	1.17	1.35	<0.001
Pretransplant status				
ICU	Reference	Reference	Reference	Reference
Hospitalized (non-ICU)	0.97	0.88	1.07	0.522
Not hospitalized	0.88	0.82	0.95	0.002
Intravenous antibiotics in 2 wk before transplant	1.31	1.19	1.44	<0.001

BMI indicates body mass index; ICU, intensive care unit; TBI, traumatic brain injury.

younger donor age and shorter ischemic time, as well as younger recipient age, no sex mismatch, not being black, body mass index <25 kg/m^2, not having diabetes mellitus, not being hospitalized pretransplant, and not receiving intravenous antibiotics in the 2 weeks before transplant (Table 4).

Discussion

TBI is the largest source of cardiac donation in the United States. Although historically, concern about cardiac dysfunction in TBI donors and the impact on posttransplant survival has been raised, recently it was shown that non-TBI hearts are actually associated with reduced posttransplant survival.[9] Our UNOS Registry–based propensity-matched retrospective study demonstrate similar posttransplant survival for TBI heart recipients versus non-TBI heart recipients.

Understanding the effect of brain death on the human myocardium has been the subject of many studies. As most of the 30-days posttransplant mortality is attributed to cardiac dysfunction, there is a continued attempt to ensure that the cause of brain death is not contributing to posttransplant myocardial dysfunction. The observed reduction in cardiac contractility of the donor heart is attributed to the insult caused by brain death known as "catecholamine storm," which occurs in response to rapidly increasing intracranial pressure. Microscopic specimens from both donor hearts and stress cardiomyopathy hearts exhibit similar endomyocardial injury; in both cases, prompt cardiac recovery is usually seen.[12] Others have attributed the depressed myocardial function to the fact that critically ill patients go through a rapid decline in thyroid hormone, causing a phenomenon called a "stunned myocardium," thus leading to administration

of triiodothyronine (T3)/tetraiodothyronine (T4) pretransplant and posttransplant.[13] Specifically, the effect of TBI on the cardiac muscle and the neurohormonal system was studied comprehensively in both rats and humans as it was found to affect blood pressure, affect cardiac contractility, and cause accumulation of reactive oxygen species in rats.[4] Furthermore, it was shown to induce cardiac uncoupling (reduced heart rate variability) in humans, which is a known predictor of mortality after TBI.[5]

Reports on the victims of TBI and their associated cardiac dysfunction have demonstrated an increase in hospital mortality[14] as well as hemodynamic instability.[8] These reports have raised the question whether the time elapsed from the brain injury until organ procurement assists in maximizing cardiac recovery. Wauters et al concluded that survival after lung transplant is not related to the cause of death but rather the time interval; when that time was >10 hours before organ recovery, recipients had improved survival.[15] No such data exist in heart transplantation.

Older single-center studies have shown reduced posttransplant survival when using TBI donor hearts; Cohen et al,[6] using a single US center database, showed that donor traumatic brain death is a risk factor for recipient mortality after heart transplantation. Similarly, Mehra et al[7] studied a subpopulation of donors who experienced explosive brain death, which is accompanied by a sudden increase in intracranial pressure, and demonstrated that recipients of these hearts had lower survival, higher cardiac events, and greater posttransplant intimal thickening. More important, in a recently published report by the International Society for Heart and Lung Transplantation, using its own registry, the opposite was demonstrated, showing that donor death caused by cerebrovascular accident and other reasons was associated with reduced recipient survival after transplantation compared with TBI as the donor cause of death.[9] Most recently, similar survival after lung transplant has been shown by Crawford et al[16] between those receiving organs from TBI donors and non-TBI donors in a retrospective study using the UNOS Registry database.

When comparing TBI with non-TBI recipients in a large registry, both our group and Crawford et al[16] found differences in pretransplant severity of illness between groups, thus necessitating propensity matching. Failure to propensity match might explain the results reported by Khush et al[9] in their International Society for Heart and Lung Transplantation registry analysis, showing reduced survival when not using TBI donor hearts. Despite propensity matching, some differences still existed between the matched groups in our analysis; in the donor group, an age difference existed compared with the non-TBI group (32 versus 30 years); in the recipient group compared with the non-TBI group, there was a lower percentage of organ sex mismatch (29% versus 22.8%). As in the entire cohort, the TBI group had better survival; we would have expected that in the propensity matching when the TBI group had younger donors and less sex mismatch, the long-term survival would be even better. Nevertheless, posttransplant survival rates were equal between the propensity-matched groups despite the differences mentioned above that still existed, thus emphasizing the importance and quality of the work transplant groups routinely perform in matching the recipients to donors, accounting for numerous variables.

Because of the nature of this retrospective analysis and the data available, we could not address the question about elapsed time from injury until procurement. Moreover, it should be emphasized that these data are relevant to the North American donor population only. This pool is known to differ from available donors in Europe, specifically on donor age.[17] It is important to acknowledge that our analysis is limited to donor hearts selected for transplant; there are TBI donors whose hearts are not used, typically because of severe left ventricular dysfunction that was unexplained and did not recover with aggressive donor management. These donors are not examined in this analysis. Finally, this analysis looked at TBI as a factor, in a dichotomized manner, comparing it with non-TBI hearts; future studies should address outcomes in recipients receiving hearts from donors who die of hemorrhagic stroke. Because of associations with hypertension, left ventricular hypertrophy, and myocardial abnormalities, posttransplant results may differ in this population.

In summary, in the largest UNOS Registry analysis of heart transplants and their survival, according to the type of donor injury, assisted by propensity matching, donor death from either TBI or non-TBI cause had no impact on posttransplant survival. Future studies should address the time of procurement in relation to the time of injury and the time of brain death as well as the impact of hemorrhagic stroke as a risk factor for posttransplant reduced survival.

Disclosures

None.

References

1. Colvin M, Smith JM, Hadley N, Skeans MA, Carrico R, Uccellini K, Lehman R, Robinson A, Israni AK, Snyder JJ, Kasiske BL. OPTN/SRTR 2016 annual data report: heart. *Am J Transplant*. 2018;18(suppl 1):291–362.
2. Singh TP, Milliren CE, Almond CS, Graham D. Survival benefit from transplantation in patients listed for heart transplantation in the United States. *J Am Coll Cardiol*. 2014;63:1169–1178.
3. Mehra MR, Jarcho JA, Cherikh W, Vaduganathan M, Lehman RR, Smits J, Stehlik J. The drug-intoxication epidemic and solid-organ transplantation. *N Engl J Med*. 2018;378:1943–1945.
4. Larson BE, Stockwell DW, Boas S, Andrews T, Wellman GC, Lockette W, Freeman K. Cardiac reactive oxygen species after traumatic brain injury. *J Surg Res*. 2012;173:e73–e81.
5. Norris PR, Ozdas A, Cao H, Williams AE, Harrell FE, Jenkins JM, Morris JA Jr. Cardiac uncoupling and heart rate variability stratify ICU patients by mortality:

a study of 2088 trauma patients. *Ann Surg*. 2006;243:804–812; discussion 812–814.

6. Cohen O, De La Zerda DJ, Beygui R, Hekmat D, Laks H. Donor brain death mechanisms and outcomes after heart transplantation. *Transplant Proc*. 2007;39:2964–2969.
7. Mehra MR, Uber PA, Ventura HO, Scott RL, Park MH. The impact of mode of donor brain death on cardiac allograft vasculopathy: an intravascular ultrasound study. *J Am Coll Cardiol*. 2004;43:806–810.
8. Godino M, Lander M, Cacciatore A, Perez-Protto S, Mizraji R. Ventricular dysfunction associated with brain trauma is cause for exclusion of young heart donors. *Transplant Proc*. 2010;42:1507–1509.
9. Khush KK, Cherikh WS, Chambers DC, Goldfarb S, Hayes D Jr, Kucheryavaya AY, Levvey BJ, Meiser B, Rossano JW, Stehlik J; International Society for Heart and Lung Transplantation. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: thirty-fifth adult heart transplantation report-2018; focus theme: multiorgan transplantation. *J Heart Lung Transplant*. 2018;37:1155–1168.
10. Tsai FC, Marelli D, Bresson J, Gjertson D, Kermani R, Patel J, Kobashigawa JA, Laks H. Use of hearts transplanted from donors with atraumatic intracranial bleeds. *J Heart Lung Transplant*. 2002;21:623–628.
11. Yamani MH, Erinc K, Starling RC, Young JB, Ratliff NB, Cook DJ, Crowe T, Hobbs R, Rincon G, Bott-Silverman C, Bennett R, Smedira N, Tuzcu EM. Donor intracranial bleeding is associated with advanced transplant coronary vasculopathy: evidence from intravascular ultrasound. *Transplant Proc*. 2004;36:2564–2566.
12. Berman M, Ali A, Ashley E, Freed D, Clarke K, Tsui S, Parameshwar J, Large S. Is stress cardiomyopathy the underlying cause of ventricular dysfunction associated with brain death? *J Heart Lung Transplant*. 2010;29:957–965.
13. Novitzky D, Cooper DK. Thyroid hormone and the stunned myocardium. *J Endocrinol*. 2014;223:R1–R8.
14. Prathep S, Sharma D, Hallman M, Joffe A, Krishnamoorthy V, Mackensen GB, Vavilala MS. Preliminary report on cardiac dysfunction after isolated traumatic brain injury. *Crit Care Med*. 2014;42:142–147.
15. Wauters S, Verleden GM, Belmans A, Coosemans W, De Leyn P, Nafteux P, Lerut T, Van Raemdonck D. Donor cause of brain death and related time intervals: does it affect outcome after lung transplantation? *Eur J Cardiothorac Surg*. 2011;39:e68–e76.
16. Crawford TC, Lui C, Magruder JT, Suarez-Pierre A, Ha JS, Higgins RS, Broderick SR, Merlo CA, Kim BS, Bush EL. Traumatically brain-injured donors and the impact on lung transplantation survival. *Ann Thorac Surg*. 2018;106:842–847.
17. Monteagudo Vela M, García Sáez D, Simon AR. Current approaches in retrieval and heart preservation. *Ann Cardiothorac Surg*. 2018;7:67–74.