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Outcomes in Patients With Symptomatic Cerebrovascular Disease Undergoing Heart Transplantation

Vishnu Patlolla, MD, MPH,* Vanajakshi Mogulla, MD,† David DeNofrio, MD,† Marvin A. Konstam, MD,† Rajan Krishnamani, MD‡

Worcester and Boston, Massachusetts; and Dayton, Ohio

Objectives We sought to determine outcomes in patients with and without symptomatic cerebrovascular disease (sCVD) undergoing heart transplantation. Second, we sought to determine factors associated with stroke in the perioperative period after heart transplantation.

Background sCVD is considered a relative contraindication to heart transplantation. Despite this concern, outcomes in patients with sCVD undergoing heart transplantation have not been well defined.

Methods Data on all single-organ heart transplants performed in the United States between April 1994 and December 2006 in patients age 40 years or older were analyzed. Survival analysis was performed to examine the effect of sCVD on the combined outcome of stroke or death, stroke, death, and functional decline, adjusting for potential confounding variables over long-term follow-up. In a separate analysis, predictors of perioperative stroke during the transplant-related hospitalization were examined using multiple logistic regression.

Results There were 1,078 patients with and 16,765 patients without sCVD. The annualized rates of stroke or death (11.5% vs. 7.8%; $p < 0.001$), stroke (4% vs. 1.4%; $p < 0.001$), death (8.9% vs. 7.4%; $p < 0.001$), and functional decline (3.7% vs. 3.0%; $p = 0.002$) were higher in patients with sCVD than in patients without sCVD. In multivariable analysis, patients with sCVD were at increased risk of stroke or death (hazard ratio [HR]: 1.29; 95% confidence interval [CI]: 1.17 to 1.42), stroke (HR: 2.24; 95% CI: 2.02 to 2.87), and functional decline (HR: 1.21; 95% CI: 1.03 to 1.42) compared with those without sCVD. We did not identify a higher risk of death in patients with sCVD (HR: 1.08; 95% CI: 0.98 to 1.20), compared with those without sCVD. sCVD, ventilator use, and ventricular assist device use were the most important predictors of perioperative stroke.

Conclusions Patients with sCVD are at an increased risk of stroke and functional decline after transplantation independent of other variables, but not death, during long-term follow-up. These results should assist programs in making informed decisions in patients with sCVD who are undergoing evaluation for heart transplantation. (J Am Coll Cardiol 2011;58:1036–41) © 2011 by the American College of Cardiology Foundation

Heart transplantation is increasingly being performed in patients older than 60 years of age and in those with comorbidities (1). Cerebrovascular disease is considered a relative contraindication to heart transplantation (2,3). Data on outcomes associated with a number of pre-transplant recipient comorbidities exist, but outcomes in patients with cerebrovascular disease undergoing heart transplantation have not been evaluated (4).

Patients with symptomatic cerebrovascular disease (sCVD), defined as previous transient ischemic attack (TIA) or stroke, are at increased risk of further cerebrovascular events (5,6). Patients with a history of TIA or stroke are also at increased risk of death in the long term, with

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60% of them dying at 10 years in 1 study (7). Heart transplantation involves allocation of a scarce resource among waitlisted candidates, and the benefits of improved survival and quality of life depend on the degree of recipient comorbidities. It is therefore important to define outcomes in patients with cerebrovascular disease undergoing heart transplantation.

From the *Department of Medicine, Division of Cardiovascular Medicine, University of Massachusetts Medical School, Worcester, Massachusetts; †The Cardiovascular Center and Division of Cardiology, Department of Medicine, Tufts Medical Center and Tufts University School of Medicine, Boston, Massachusetts; and the ‡Department of Medicine, Wright State University, Dayton, Ohio. The data reported here have been supplied by the United Network for Organ Sharing as the contractor for the Organ Procurement and Transplantation Network. The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the Organ Procurement and Transplant Network or the U.S. Government. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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We conducted a retrospective analysis of heart transplant recipients to examine the long-term risk of stroke and death, stroke, death, and functional decline, in patients with and without sCVD. In separate analysis, we examined factors associated with the risk of perioperative stroke during transplantation-related hospitalization.

Methods

This analysis was based on data on all heart transplantations performed in the United States between April 1, 1994, and December 31, 2006, obtained from the Organ Procurement and Transplant Network (OPTN), as of February 6, 2008. We restricted the analysis to all first-time, single-organ heart transplant recipients age 40 years or older. sCVD was a yes/no variable on the transplantation candidate registration form and was intended to capture patients with a previous cerebrovascular event or a TIA at registration. Additional data were available on cerebrovascular events between candidate registration and transplantation. We defined sCVD as the presence of sCVD at candidate registration or the occurrence of a cerebrovascular event between candidate registration and transplantation. Of the 20,227 eligible patients, 2,384 were excluded due to missing data on sCVD at candidate registration or missing data on cerebrovascular event between candidate registration and transplantation. Data on stroke during the transplant-related hospitalization and during follow-up were collected at discharge and at follow-up visits at 6 months, 1 year, and yearly thereafter. Data on patients' functional capacity were collected at transplant recipient registration and at follow-up visits as described previously. For patients who died during follow-up, the date of death as recorded by the OPTN was used. For patients who did not have a date of death recorded by the OPTN but a date of death was available from the social security death masterfile, included in the dataset from the OPTN, this date was used. In the analysis examining factors associated with perioperative stroke, patients without data on sCVD were included, but those without information on perioperative stroke were excluded. Of 20,227 patients, 1,092 were excluded due to missing data on perioperative stroke. Perioperative stroke was defined as stroke occurring anytime during the transplantation-related hospitalization.

One of 2 different scales for functional status was used for a given patient during the period under study in the OPTN database. These scales are shown in Online Table S1. We dichotomized functional status as either good or reduced for the purpose of this study. A functional status of "performs activities of daily living with no assistance" or higher or "80%, normal activity with effort: some symptoms of disease" or higher on these scales was arbitrarily defined as good functional status. A functional status of "performs activities of daily living with some assistance" or lower or "70%, cares for self: unable to carry on normal activity or active work" or lower was defined as reduced functional status. A transition from good functional status to reduced functional status as defined was considered functional decline for time-to-event analysis. Because patients could have a temporary decline in functional status, the definition of functional decline required that patients continue to have reduced functional status as defined for the rest of follow-up, excluding those with return to good functional status from this definition of functional decline. Patients who had reduced or missing functional status at transplantation and continued to have reduced or missing functional status throughout follow-up were excluded.

Abbreviations and Acronyms

AFT = accelerated failure time
CI = confidence interval
CM = cardiomyopathy
COPD = chronic obstructive pulmonary disease
HR = hazard ratio
HTN = hypertension
OPTN = Organ Procurement and Transplant Network
PH = proportional hazard
sCVD = symptomatic cerebrovascular disease
TIA = transient ischemic attack
VAD = ventricular assist device

Unadjusted annualized event rates (expressed as percent per year) of combined outcome of stroke or death, stroke, death, and functional decline in both groups were calculated by dividing the number of events by person-years of follow-up multiplied by 100. Unadjusted cumulative incidence of outcomes at various time points were obtained by the Kaplan-Meier product-limit method. For stroke or functional decline that occurred between 2 follow-up visits, this was assumed to have occurred at the midpoint of the interval. Equality of survival curves was tested using log-rank test.

Effect of sCVD on the risk of combined outcome of stroke or death, stroke, death, and functional decline during follow-up was examined using Weibull's accelerated failure time (AFT) model. Weibull's AFT model was chosen for its ability to handle interval censored data. Stroke and functional status were interval censored in our data, being collected only at follow-up visits. The models were adjusted for donor and recipient age, sex combination, race, etiology of cardiomyopathy (ischemic vs. nonischemic), drug-treated hypertension (HTN), diabetes, drug-treated chronic obstructive pulmonary disease (COPD), dialysis status, waitlist status, ventilator use, ventricular assist device (VAD) use, creatinine, bilirubin, ischemia time, and year of transplantation. Missing values of covariates were replaced by their median or most common value for continuous and categorical variables, respectively. Additionally, a Cox proportional hazards (PHs) model was created for the outcome of death and results compared with those of the Weibull AFT model.

A multiple logistic regression model was used to examine factors associated with perioperative stroke. The model was

adjusted for potential confounding variables as for other outcomes previously described.

Statistical analysis was performed using SAS version 9.1.3 (SAS Institute Inc., Cary, North Carolina).

Results

There were 1,078 patients with and 16,765 patients without sCVD as defined previously. Baseline characteristics of patients with and without sCVD are shown in Table 1. Patients with sCVD were more likely to be black; have ischemic cardiomyopathy (CM), HTN, or diabetes; and be on dialysis, ventilator, or VAD support compared with patients without sCVD. They were more likely to be in United Network for Organ Sharing 1A status at transplantation, have longer ischemia time, and have been transplanted in later years, compared with patients without sCVD.

Table 1 Baseline Characteristics in Patients With and Without sCVD

Variable	No sCVD (n = 16,765)	sCVD (n = 1,078)	p Value*
Recipient age, yrs	55.8	55.7	0.9
Donor age, yrs	31.5	31.7	0.5
Donor/recipient sex			
Male/male	59.9	62.7	0.3
Female/male	18.8	18.0	
Male/female	10.6	9.5	
Female/female	10.7	9.8	
Recipient race			
White	80.5	78.9	<0.001
Black	11.5	14.8	
Other	8.1	6.2	
Donor race			
White	74.3	75.0	0.5
Black	11.4	10.2	
Other	14.3	14.8	
Ischemic CM	55.7	60.6	0.002
Drug-treated HTN	39.5	48.1	<0.001
Diabetes	21.3	26.1	<0.001
Drug-treated COPD	3.7	4.6	0.1
Dialysis	0.6	1.9	<0.001
Waiting list status			
Old status 1	25.9	25.5	<0.001
Status 1A	19.8	31.1	
Status 1B	24.5	24.8	
Status 2	29.9	18.7	
Ventilator use	2.6	4.7	<0.001
VAD use	15.9	37.7	<0.001
Creatinine, mg/dl	1.37	1.34	0.5
Total bilirubin, mg/dl	1.3	1.3	0.8
Ischemia time, h	3.1	3.2	<0.001
Year of transplantation			
1994–1997	29.0	23.6	0.001
1998–2000	25.3	27.3	
2001–2003	23.4	26.2	
2004–2006	22.3	23.0	

Values are mean or %. *p value based on *t* test or chi-square test as appropriate.
CM = cardiomyopathy; COPD = chronic obstructive pulmonary disease; HTN = hypertension; sCVD = symptomatic cerebrovascular disease; VAD = ventricular assist device.

The follow-up in person-years for each of the outcomes, the total number of events, the annualized event rates, and percent cumulative incidence of events at various time points are shown in Table 2. The number of events at each time point and the number of patients remaining in the analyses at each time point are provided in Online Table S2.

Stroke or death. The annual rate of stroke or death was 11.5% in patients with sCVD and 7.8% in patients without sCVD ($p < 0.001$) (Table 2). After multivariable adjustment, risk of stroke or death was 29% higher in patients with sCVD (hazard ratio [HR]: 1.29; 95% confidence interval [CI]: 1.17 to 1.42) compared with those without sCVD (Table 3). Other factors that were associated with increased risk of stroke or death were recipient age, donor age, male donor/female recipient combination, black recipient race, ischemic CM, HTN, diabetes, COPD, dialysis, creatinine, bilirubin, ischemia time, and ventilator or VAD use at transplantation. Transplantations performed in later years were associated with a decreased risk of stroke or death.

Stroke. The annual rate of stroke was 4% in patients with sCVD and 1.4% in patients without sCVD ($p < 0.001$). After multivariable adjustment, risk of stroke was 2.41-fold higher in patients with sCVD (HR: 2.41; 95% CI: 2.02 to 2.87) compared with patients without sCVD. Other factors that were associated with increased risk of stroke were recipient age, male donor/female recipient combination, ischemic CM, diabetes, and ventilator or VAD use at transplantation. Later year of transplantation was associated with a decreased risk of stroke.

Death. The annual rate of death was 8.9% in patients with sCVD and 7.4% in patients without sCVD ($p < 0.001$). After multivariable adjustment, we did not identify a higher risk of death in patients with compared with those without sCVD (HR: 1.08; 95% CI: 0.98 to 1.20). Factors that were associated with increased risk of death during follow-up were recipient and donor age, male donor/female recipient combination, black recipient race, ischemic CM, HTN, diabetes, COPD, dialysis, creatinine, bilirubin, ischemia time, and ventilator or VAD use at transplantation.

Multivariable analysis for death was repeated using the Cox PHs model and gave results consistent with those of the Weibull AFT model except that HRs for transplantation years 1998 to 2000, 2001 to 2003, and 2004 to 2006 (compared with 1995 to 1997) were 0.95 (95% CI: 0.88 to 1.02), 0.89 (95% CI: 0.81 to 0.98), and 0.82 (95% CI: 0.73 to 0.92). Complete results of the Cox PH model are provided in Online Table S3. Cox PHs model could not be fitted to data on stroke, stroke and death, and functional decline due to the interval-censored nature of these outcomes.

Functional decline. The annual rate of functional decline was 3.7% in patients with sCVD and 3.0% in patients without sCVD ($p = 0.002$). After multivariable adjustment,

Table 2 Outcomes in Patients With and Without sCVD

	Before Discharge, %	1 yr, %	2 yrs, %	5 yrs, %	10 yrs, %	Total Events	Follow-Up (in Person-yrs)	Annualized Event Rate (per 100)	p Value†
Stroke or death									
No sCVD (n = 16,765)	8.6*	15.4	19.5	29.8	50.6	5,999	76,765	7.8	<0.001
sCVD (n = 1,078)	15.1*	23.7	28.1	40.5	60.5	480	4,169	11.5	
Stroke									
No sCVD (n = 16,765)	2.3	3.4	4.1	6.3	10.6	1,050	76,765	1.4	<0.001
sCVD (n = 1,078)	7.6	11.0	12.5	17.2	23.3	166	4,168	4.0	
Death									
No sCVD (n = 16,765)	7.7*	13.5	17.5	27.2	50.6	5,962	80,764	7.4	<0.001
sCVD (n = 1,078)	11.0*	16.9	20.7	32.6	55.7	423	4,774	8.9	
Functional decline									
No sCVD (n = 13,778)	—	0.5	2.5	10.7	32.5	2,212	73,417	3.0	0.002
sCVD (n = 826)	—	0.5	3.6	12.9	39.9	158	4,216	3.7	

*After excluding 99 without a discharge date. †Based on Kaplan-Meier analysis.
sCVD = symptomatic cerebrovascular disease.

risk of functional decline was 21% higher in patients with sCVD (HR: 1.21; 95% CI: 1.03 to 1.42) compared with patients without sCVD.

Perioperative stroke. Of 19,135 transplant recipients, 505 (2.6%) had a perioperative stroke. The odds ratios for perioperative stroke associated with various variables are

Table 3 Multivariable Adjusted Risk of Stroke or Death, Stroke, and Death in the Study Population

Variable	Stroke or Death			Stroke			Death		
	HR*	95% CI	p Value	HR*	95% CI	p Value	HR*	95% CI	p Value
sCVD (vs. none)	1.29	1.17–1.42	<0.001	2.41	2.02–2.87	<0.001	1.08	0.98–1.20	0.126
Recipient age (per yr)	1.01	1.01–1.02	<0.001	1.02	1.01–1.03	<0.001	1.01	1.01–1.02	<0.001
Donor age (per yr)	1.01	1.01–1.01	<0.001	1.00	1.00–1.01	0.417	1.01	1.01–1.01	<0.001
Donor/recipient sex (referent: male/male)									
Female/male	1.06	0.99–1.13	0.077	1.01	0.87–1.17	0.919	1.07	1.01–1.15	0.028
Male/female	1.23	1.13–1.34	<0.001	1.40	1.16–1.68	<0.001	1.19	1.09–1.29	<0.001
Female/female	1.06	0.98–1.16	0.146	1.12	0.92–1.36	0.274	1.08	0.99–1.18	0.074
Recipient race (referent: white)									
Black	1.22	1.13–1.32	<0.001	1.00	0.83–1.21	0.97	1.27	1.18–1.38	<0.001
Other	1.02	0.93–1.13	0.642	0.89	0.70–1.12	0.33	1.04	0.94–1.14	0.453
Donor race (referent: white)									
Black	1.03	0.95–1.11	0.533	0.98	0.81–1.18	0.842	1.04	0.96–1.12	0.394
Other	1.05	0.98–1.14	0.160	1.13	0.96–1.33	0.143	1.06	0.98–1.14	0.151
Ischemic CM (vs. nonischemic CM)	1.16	1.10–1.22	<0.001	1.28	1.13–1.45	<0.001	1.15	1.09–1.22	<0.001
Drug-treated HTN	1.09	1.04–1.15	<0.001	1.06	0.94–1.19	0.327	1.08	1.03–1.14	0.003
Diabetes	1.23	1.16–1.30	<0.001	1.49	1.31–1.70	<0.001	1.22	1.15–1.30	<0.001
Drug-treated COPD	1.27	1.13–1.43	<0.001	1.00	0.74–1.34	0.993	1.32	1.17–1.48	<0.001
Dialysis	1.98	1.56–2.53	<0.001	1.41	0.80–2.51	0.239	1.97	1.53–2.53	<0.001
Waiting list status (referent: old status 1)									
Status 1A	1.09	0.99–1.20	0.081	1.22	0.99–1.51	0.066	1.06	0.96–1.16	0.269
Status 1B	0.93	0.85–1.03	0.155	0.90	0.73–1.12	0.357	0.95	0.86–1.04	0.27
Status 2	0.95	0.89–1.02	0.155	1.05	0.90–1.24	0.525	0.94	0.88–1.01	0.083
Ventilator	1.63	1.44–1.86	<0.001	1.65	1.25–2.18	<0.001	1.65	1.45–1.88	<0.001
VAD	1.27	1.19–1.37	<0.001	1.53	1.31–1.78	<0.001	1.19	1.11–1.28	<0.001
Creatinine (per 1-mg/dl increase)	1.03	1.01–1.04	<0.001	1.02	0.99–1.06	0.163	1.03	1.02–1.04	<0.001
Total bilirubin (per 1-mg/dl increase)	1.01	1.01–1.02	<0.001	1.00	0.98–1.02	0.847	1.02	1.01–1.02	<0.001
Ischemia time (per 1-h increase)	1.06	1.04–1.09	<0.001	1.05	0.99–1.11	0.088	1.06	1.03–1.09	<0.001
Year of transplantation (referent: 1994–1997)									
1998–2000	0.78	0.73–0.84	<0.001	0.78	0.66–0.92	0.003	0.77	0.72–0.83	<0.001
2001–2003	0.62	0.56–0.68	<0.001	0.59	0.48–0.73	<0.001	0.62	0.57–0.68	<0.001
2004–2006	0.55	0.49–0.61	<0.001	0.46	0.36–0.59	<0.001	0.58	0.52–0.65	<0.001

*From Weibull accelerated failure time models.
CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 1.

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Table 4 Multivariable Adjusted Risk of Perioperative Stroke During Heart Transplant Hospitalization

Variable	Odds Ratio*	95% CI	p Value
sCVD	2.84	2.21–3.65	<0.001
Recipient age (per yr)	1.02	1.00–1.03	0.025
Donor age (per yr)	1.00	1.00–1.01	0.55
Donor/recipient sex (referent: male/male)			
Female/male	1.04	0.81–1.33	0.764
Male/female	1.59	1.20–2.11	0.001
Female/female	1.35	1.00–1.83	0.05
Recipient race (referent: white)			
Black	0.72	0.52–1.00	0.048
Other	0.84	0.58–1.22	0.365
Donor race (referent: white)			
Black	0.99	0.74–1.32	0.933
Other	1.07	0.82–1.39	0.631
Ischemic CM	1.19	0.98–1.46	0.077
Drug-treated HTN	1.07	0.89–1.29	0.469
Diabetes	1.29	1.04–1.59	0.02
Drug-treated COPD	0.82	0.49–1.36	0.432
Dialysis	1.04	0.45–2.43	0.926
Waiting list status (referent: old status 1)			
Status 1A	1.29	0.91–1.81	0.15
Status 1B	0.89	0.63–1.28	0.542
Status 2	1.03	0.78–1.36	0.828
Ventilator	2.37	1.67–3.35	<0.001
VAD	1.96	1.56–2.45	<0.001
Creatinine (per 1 mg/dl)	1.05	1.00–1.10	0.032
Bilirubin (per 1 mg/dl)	1.00	0.98–1.03	0.765
Ischemia time (per 1 h)	1.13	1.03–1.23	0.007
Year of transplantation (referent: 1994–1997)			
1998–2000	0.75	0.56–0.99	0.04
2001–2003	0.70	0.50–0.98	0.036
2004–2006	0.59	0.41–0.84	0.004

*Adjusted for all variables in the table.
Abbreviations as in Tables 1 and 3.

shown in Table 4. sCVD, recipient age, male donor/female recipient and female donor/female recipient combinations, black recipient race, diabetes, creatinine, ischemia time, and ventilator and VAD use were associated with increased risk of perioperative stroke. Recent year of transplantation was associated with a lower risk of perioperative stroke compared with 1994 to 1997. A total of 31.9% of patients with perioperative stroke died before discharge compared with 6.9% of patients without perioperative stroke.

Discussion

The 2009 annual report of the International Society of Heart and Lung Transplantation mentions the risk of death after heart transplantation is not increased in patients with cerebrovascular disease but no further details were available (8). To the best of our knowledge, the current study is the first to comprehensively examine outcomes in patients with sCVD undergoing heart transplantation, with a large enough sample size to be able to provide reasonably precise estimates of the effect of sCVD on stroke, death, and functional decline after heart transplantation.

In our study, patients with sCVD had a higher unadjusted annual rate of stroke, death, and functional decline than patients without sCVD. However, patients with sCVD had more comorbidities such as HTN, diabetes, COPD, and renal failure requiring dialysis, which likely contributed to worse outcomes. After adjustment for these and other potential confounding factors, sCVD was associated with an 2.4-fold increase in risk of stroke and a 1.2-fold increase in risk of functional decline. We did not identify a higher risk of death in patients with sCVD.

A number of other factors previously known to be associated with increased mortality after heart transplantation including recipient age, donor age, ischemic CM, diabetes, creatinine, bilirubin, ischemia time, dialysis status, and ventilator or VAD use at the time of transplantation were also significant predictors of mortality in our study (8). Our analyses also found the following factors to be associated with increased mortality: black recipient race, male donor/female recipient combination, HTN, and COPD. The following factors were associated with decreased mortality: United Network for Organ Sharing status 2 and later year of transplantation. Although the magnitude of effect differed between the 2 models (Weibull AFT and Cox PHs), both showed decreased mortality in recent years compared with 1994 to 1997. The reason for the difference in estimates of HRs obtained by the Weibull AFT and Cox PHs models is not clear, but a conservative approach would be to believe the estimates obtained by the Cox PHs model.

We did not find any large-scale study looking at risk factors for stroke in the long-term after heart transplantation. In addition to sCVD, our study identified the following factors to be associated with stroke in the long term after heart transplantation: recipient age, male donor/female recipient combination, ischemic CM, diabetes, and ventilator or VAD use. Risk of stroke in the long term was lower in recent transplant years compared with 1994 to 1997. Given the discrepancy in HRs for death obtained by the Weibull AFT and Cox PHs models, caution is advised in interpreting the HRs for stroke with year of transplantation, which were derived using the Weibull AFT model. Cox PHs model could not be fitted to stroke due to the interval-censored nature of this outcome.

Perioperative stroke after heart transplantation is a devastating complication, with a 32% in-hospital mortality in this study. There is considerable literature on the incidence, risk factors, and prognosis of perioperative stroke after nontransplantation cardiac surgery (i.e., coronary artery bypass graft surgery and valve surgery), but none after heart transplantation (9–21). The overall incidence of perioperative stroke after heart transplantation was 2.6% in this study, similar in magnitude to a stroke rate of 1.6% to 2.6% after nontransplantation cardiac surgery (11,13–15). Similar to the findings in nontransplantation cardiac surgery, sCVD, recipient age, recipient female sex, diabetes, and creatinine were significant predictors of perioperative stroke (9–16,19–22). In addition, our study identified ischemia time and ventilator or VAD use to be associated with

increased risk of perioperative stroke. Risk of perioperative stroke decreased significantly in recent years compared with 1994 to 1997.

Study limitations. sCVD was not explicitly defined and was left to the discretion of the transplantation coordinator. It is expected to include patients with a previous TIA or stroke, but the lack of an explicit definition during data collection leaves scope for misclassification. Data on the type of previous cerebrovascular event, whether a TIA or ischemic or hemorrhagic stroke, that led to a patient being classified as having sCVD and on imaging documentation of the presence of extracranial vascular stenosis was not available. Therefore, a proportion of patients classified as having sCVD could have had a cardioembolic source of a TIA or stroke and not true cerebrovascular disease. A proportion of patients with sCVD could have had revascularization procedures such as carotid endarterectomy or carotid stenting that could have decreased the subsequent risk of stroke, but these data were not available. Old status 1 was only reported through January 1999 and status 1A and 1B were only reported from January 1999 onward. Therefore, the effect of status and year of transplantation on outcomes should be interpreted with caution. Patients with sCVD who underwent transplantation are likely to have been a select group who met the criteria of the transplantation centers for a transplantation, and the outcomes noted in this study may not be representative of all patients with cerebrovascular disease screened for transplantation eligibility. It is not known whether any of the worse outcomes noted in the study are due to alternate donor hearts being given to patients with sCVD. There has been considerable improvement in VAD technology over the years, and the summary estimate of the risk of stroke associated with VADs may not be representative of the latest generation of VADs.

Conclusions

Patients with sCVD undergoing heart transplantation have an increased risk of stroke and functional decline but not death compared with those without sCVD. Although sCVD by itself should not be an absolute contraindication to heart transplantation, the worse outcomes should be considered in the context of other comorbidities in determining transplantation candidacy.

Reprint requests and correspondence: Dr. Rajan Krishnamani, Wright State University, 9000 North Main Street, Suite 202, Dayton, Ohio 45431. E-mail: krishnamanirajan@gmail.com.

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Key Words: cerebrovascular disorders ■ heart transplantation ■ mortality ■ outcomes ■ perioperative stroke ■ stroke.

APPENDIX

For supplemental tables, please see the online version of this article.