Long-term outcomes and clinical predictors for pacemaker-requiring bradyarrhythmias after cardiac transplantation: Analysis of the UNOS/OPTN cardiac transplant database

Daniel J. Cantillon, MD, Khaldoun G. Tarakji, MD, Tingfei Hu, MS, Amy Hsu, MS, Nicholas G. Smedira, MD, Randall C. Starling, MD, MPH, Bruce L. Wilkoff, MD, Walid I. Saliba, MD

From the Cleveland Clinic, Heart and Vascular Institute, Cleveland, Ohio.

BACKGROUND Pacemaker-requiring bradyarrhythmias after cardiac transplantation are common, and rarely can lead to sudden cardiac death. Prior outcomes studies have been limited to single-center data.

OBJECTIVE This study sought to define the long-term outcomes and clinical predictors for pacemaker-requiring bradyarrhythmias in the cardiac transplant population.

METHODS This study used multivariable analysis of the United Network for Organ Sharing/Organ Procurement and Transplantation Network (UNOS/OPTN) database of sequential U.S. cardiac transplant recipients from 1997 to 2007 stratified by postoperative bradyarrhythmias requiring a pacemaker. The primary end point was all-cause mortality.

RESULTS Among 35,987 cardiac transplant recipients (age 46.1 ± 18.3 years, 76% male, 22% bicaval technique) with a follow-up of 6.3 ± 4.7 years, pacemaker-requiring bradyarrhythmias occurred in 3,940 patients (10.9%). Pacemaker recipients demonstrated improved survival (median 8.0 years vs. 5.2 years, $P < .001$), decreased 5-year mortality (13.8% vs. 17.7%, $P < .001$), and overall crude mortality (42.9% vs. 45.9%, $P < .001$). Multivariable propensity-score-adjusted analysis demonstrated improved survival among pacemaker recipients (adjusted hazard ratio 0.84, 95% confidence interval [CI] 0.80 to 0.88, $P < .001$) after adjustment for donor/recipient age, UNOS listing status, donor heart ischemic time, surgical technique, graft rejection, and other common comorbidities. The bicaval surgical technique was strongly protective against a postoperative pacemaker requirement (odds ratio [OR] 0.33, 95% CI 0.29 to 0.36, $P < .001$) in multivariable analysis. Among the other variables studied, only increasing donor age (OR 1.04, 95% CI 1.00 to 1.09, $P < .001$) and recipient age (OR 1.09, 95% CI 1.0 to 1.12, $P < .001$) were associated with a permanent pacemaker requirement.

CONCLUSION Cardiac transplant recipients with pacemaker-requiring bradyarrhythmias have an excellent long-term prognosis. Increased mortality in the nonpacemaker group merits further investigation. Biatrial surgical technique and increasing donor/recipient age are associated with postoperative pacemaker requirement.

KEYWORDS Pacing; Transplantation; Bradyarrhythmias

ABBREVIATIONS CAD = coronary artery disease; **CI** = confidence interval; **HR** = hazard ratio; **OPTN** = Organ Procurement and Transplantation Network; **OR** = odds ratio; **PPM** = permanent pacemaker; **UNOS** = United Network for Organ Sharing

(Heart Rhythm 2010;7:1567–1571)

Bradyarrhythmias after cardiac transplantation are common and frequently limit postoperative recovery and rehabilitation.[1,2] They can also rarely lead to sudden cardiac death.[3,4] A permanent pacemaker (PPM) is required postoperatively in 7% to 10% of cardiac transplants recipients,[1,2] with specialized indications detailed in current practice guidelines.[5]

Long-term outcomes and clinical predictors for bradyarrhythmias in this population have been limited to single-center data. The present analysis evaluates the clinical outcomes for cardiac transplant patients with pacemaker-requiring bradyarrhythmias across U.S. transplant centers. In addition, this analysis examines previously associated variables with bradyarrhythmias, including donor and recipient age, donor heart ischemic time, graft rejection requiring treatment, the presence of obstructive allograft coronary atherosclerosis, and surgical technique.

This work was supported in part by Health Resources and Services Administration contract 234-2005-370011C. The content is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.

Daniel J. Cantillon MD, Khaldoun G. Tarakji MD, Tingfei Hu MS, Amy Hsu MS, Nicholas G. Smedira MD, have no conflict of interest. Randall C. Starling MD, MPH, Consultant/research support from Medtronic, and Thoratec; Bruce L. Wilkoff MD, Consultant/research support and lectures supported by Medtronic, Boston Scientific, St. Jude Medical, Biotronik, Spectranetics and LifeWatch; Walid I. Saliba MD, Consultant/research support from Medtronic, St. Jude Medical and Biotronik.

Address reprint requests and correspondence: Dr. Daniel J. Cantillon, Cardiovascular Medicine/Electrophysiology, Cleveland Clinic, 9500 Euclid Avenue, Desk J2-2, Cleveland, OH 44195. E-mail address: cantild@ccf.org. (Received April 21, 2010; accepted June 17, 2010.)

1547-5271/$ -see front matter doi:10.1016/j.hrthm.2010.06.026

Methods

Study design and protocol

The United Network for Organ Sharing (UNOS) database was queried for sequential, cardiac-only transplantation procedures performed between October 1997 and 2007. UNOS administers the Organ Procurement and Transplantation Network (OPTN) to collect and manage data regarding all U.S. transplant events. For each transplant recipient, all subsequent yearly follow-up forms were queried to record interval events including the last clinical follow-up date, death, allograft rejection requiring treatment, epicardial coronary artery disease, and whether a pacemaker had been implanted. The patients were divided into those with and without a pacemaker postoperatively, and index hospitalization deaths were excluded to avoid selection bias against patients too systemically ill to be considered for pacemaker implantation. The UNOS/OPTN data forms do not record a specific device implantation date, indication, programming, or follow-up interrogation data.

Statistical analysis

Categorical variables, expressed as numbers and percentages, were analyzed by the chi-square method. Continuous variables, expressed as mean with standard deviation, were compared by Student *t*-test or nonparametric tests. A multivariable propensity-score-adjusted survival analysis was performed to compare outcomes between those patients with and without a pacemaker. The primary end point was all-cause mortality. The primary independent variable of interest was PPM requirement after cardiac transplantation. Other variables studied included donor/recipient age, UNOS listing status, donor heart ischemic time, transplant coronary artery disease (CAD), surgical technique, and allograft rejection requiring treatment. Deaths during the index hospitalization were excluded to avoid selection bias against patients too systemically ill to be considered as pacemaker candidates. Logistic regression analysis was performed to evaluate donor/recipient age, surgical technique, donor heart ischemic time, transplant CAD, and allograft rejection requiring treatment for association with postoperative pacemaker requirement. At reviewer request, subgroup analyses of the pediatric population (<18 years) and congenital heart disease patients were performed in a propensity-score-adjusted analysis with Cox multivariable regression using all of the previous listed variables. Statistical analysis was performed using SAS 8.0.2 (SAS Institute Inc., Cary, North Carolina). All *P* values were 2-tailed, with statistical significance set at .05. All confidence intervals were calculated at the 95% interval.

Results

Clinical characteristics

We identified 35,987 sequential U.S. cardiac-only transplant procedures (mean age 46.1 ± 18.3 years, 76% male, 22% bicaval surgical technique) between October 1997 and 2007 with a mean follow-up of 6.3 ± 4.7 years. The mean donor heart ischemic time was 179.7 ± 69.0 minutes. Bradyarrhythmias requiring a pacemaker occurred in 3,940 patients (10.9%). The clinical characteristics of the patients with comparisons between the PPM and non-PPM groups

Table 1 Clinical characteristics of the cardiac transplant recipients (n = 35,987)

	All (n = 35,987)	PPM (n = 3,940)	None (n = 32,047)	*P*
Age, recipient (yrs)	46.5 ± 18.0	49.5 ± 14.7	46.1 ± 18.3	<.001
Age, donor (yrs)	28.0 ± 13.9	31.2 ± 13.6	27.6 ± 13.9	<.001
Male gender	27,169 (75.5%)	3,056 (77.6%)	24,113 (75.2%)	.001
UNOS status				
Ia	13,027 (36.2%)	1,474 (37.4%)	11,553 (36.1%)	.040
Ib	10,437 (29.0%)	1,076 (27.3%)	9,361 (29.2%)	
II	12,499 (34.8%)	1,386 (35.2%)	11,113 (34.7%)	
Donor heart ischemic time (min)	179.7 ± 69.0	175.0 ± 61.0	180.3 ± 65.4	<.001
Bicaval anastomosis	7,993 (22.2%)	365 (9.3%)	7,628 (23.8%)	.001
VAD bridge	4,247 (38.4%)	343 (45.6%)	3,904 (37.9%)	<.001
Pediatric patients <18 yrs	3,688 (10.2%)	210 (5.6%)	3,478 (94.3%)	<.001
Congenital heart disease	1,613 (4.5%)	83 (5.1%)	1,530 (94.9%)	
Diabetes, pretransplant	4,325 (17.0%)	389 (16.0%)	3,396 (17.1%)	.173
Hypertension, pretransplant	8,607 (24.3%)	888 (34.3%)	7,719 (37.1%)	.006
COPD, pretransplant	729 (2.1%)	60 (2.5%)	669 (2.9%)	.203
Cerebrovascular disease, pretransplant	867 (2.4%)	89 (3.7%)	778 (3.4%)	.498
Peripheral arterial disease, pretransplant	782 (2.2%)	82 (3.4%)	700 (3.1%)	.378
Transplant CAD >50% stenosis, during follow-up	11,483 (54.3%)	2,015 (74.7%)	9,468 (51.3)	<.001
Rejection requiring treatment, during follow-up	4,571 (12.7%)	367 (9.3%)	4,204 (13.1%)	<.001

CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; PPM = permanent pacemaker; UNOS = United Network for Organ Sharing; VAD = ventricular assist device.