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Understanding the role of temporary epicardial pacemakers after heart transplantation in the cardiac intensive care unit

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The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients recommend the placement of temporary epicardial pacing wires at the time of surgery. However, there is little data regarding optimal postoperative pacing modality and its implications on intensive care unit (ICU) length of stay (LOS).

We conducted a single-center retrospective cohort study of 187 patients who underwent heart transplantation from January 1, 2019 to February 28, 2023 and had postoperative epicardial pacemaker wires placed. The study's primary outcome was to observe the association between pacing modalities and prolonged ICU LOS (greater than 5 days). The secondary outcome was to observe the association between pacing modalities and prolonged hospital LOS (greater than 15 days), readmission within 30 days of discharge, days on inotropic and pressor support, death, high-grade rejection on biopsy, coronary artery vasculopathy at 1 year, primary graft dysfunction, mediastinitis, and development of a malignancy.

Twenty-two patients (12%) had their pacing mode turned off at the time of arrival to the ICU, 36 patients (19%) had their pacing mode set to atrially paced, atrially sensed, inhibit, 101 patients (54%) had theirs set to dual chamber paced, dual chamber sensed, triger/inhibit sensed events, and 28 (15%) had theirs set to ventricularly paced, ventricularly sensed, inhibit. No mode of epicardial pacing was associated with an increased ICU LOS, hospital LOS, increased readmission rates, increased short-term adverse effects, increased long-term adverse effects, or increased duration of support with vasoactive medications.

Our study demonstrated no significant association between the mode of temporary pacing and LOS or adverse effects after heart transplantation.

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Background

The International Society of Heart and Lung Transplantation (ISHLT) guidelines for the care of heart transplant recipients recommend the placement of temporary epicardial pacing wires at the time of surgery.[1] This is done to prevent relative

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bradycardia and adverse hemodynamic effects after prolonged cold ischemic time during transplant. Heart transplant recipients are particularly prone to the development of diastolic dysfunction postoperatively in the setting of myocardial edema, immunotherapy induction, and large volume shifts. Similarly, their cardiac output is augmented by pacing to optimize atrioventricular synchrony.[2] Although the use of temporary epicardial pacemakers is strongly recommended, not all patients receive them. Furthermore, the optimal pacing modality has yet to be elucidated and there is significant heterogeneity in the pacing modes utilized postoperatively in the intensive care unit (ICU). Our study aims to determine if there is a significant association between the type of temporary epicardial pacing and ICU length of stay (LOS).

Materials and methods

This study was approved by the institutional review board and complies with the ISHLT ethics statement. This was a single-center, retrospective cohort study of patients who underwent heart transplantation from January 1, 2019 to February 28, 2023. Patients were included in the study if they underwent heart transplantation, received a comprehensive preoperative medical evaluation, and had epicardial pacemaker wires placed postoperatively.

The primary outcome of the study was prolonged ICU LOS defined as an ICU stay longer than 5 days after heart transplantation (the median LOS in the ICU after heart transplant at our institution). Secondary outcomes were also investigated during this study, including prolonged hospital LOS defined as greater than 15 days after transplant (the median LOS after heart transplant at our institution), readmission within 30 days of hospital discharge, total days on inotropic and pressor support after transplantation, death from any cause, grade 2 or greater rejection on heart biopsy, diagnosis of coronary artery vasculopathy at 1 year, primary graft dysfunction, mediastinitis, and development of a malignancy. Temporary epicardial pacemaker settings were collected from chart reviews of patients on postoperative day 1 and utilized to subset patients into different groups. Patients with their pacing mode turned off at the time of arrival to the ICU were used as the reference category throughout the study.

Baseline characteristics of individual patients before transplant were also collected. Informed consent was obtained. Categorical variables were characterized as total numbers and frequencies. They were analyzed via the chi-square test or Fisher's exact test. Median values for continuous variables were reported and analyzed via the Mann-Whitney U test. The distribution of data was checked using the Shapiro-Wilk test. Baseline characteristics of collected patients included demographic factors before transplant such as age, sex, race, family history of heart disease, and if they were ever a smoker. Data were also collected on comorbid medical conditions, such as obesity, hypertension, diabetes, hyperlipidemia, atrial fibrillation/flutter, ventricular tachycardia, prior stroke, chronic kidney disease, and if they were on dialysis. Factors related to transplant incorporated into the study included the diagnosis of non-ischemic, need for dual-organ transplant, type of induction agent used, doses of induction agent administered, and if a mechanical circulatory support (MCS) device was used as a bridge to transplant. Information regarding medications and advanced therapies utilized before admission for a heart transplant was also collected and is available in Supplementary Material 1. For example, if the patient was on aspirin, a P2Y12 inhibitor, a statin, a beta blocker, an angiotensin converting enzyme inhibitor/aldosterone receptor blocker/angiotensin receptor/neprilysin inhibitor, if they were on a mineralocorticoid receptor antagonist before admission to the hospital, or if they had an implantable cardiac defibrillator or a cardiac resynchronization therapy and defibrillator device.

Utilizing the baseline characteristics and temporary epicardial pacemaker settings, univariate logistic regression models were built for prolonged ICU LOS, prolonged hospital stay, and readmission within 30 days. These 3 outcomes were subsequently compiled into a category called "short-term outcomes." The outcomes of all-cause mortality, grade 2 or greater rejection on heart biopsy, diagnosis of coronary artery vasculopathy, and development of malignancy were compiled into a category called "long-term outcomes."

A univariate logistic regression model of patient characteristics and temporary pacing modalities was also generated to determine if there was an association between these factors and long-term outcomes. Kaplan-Meier survival curves were created to demonstrate the relationship between pacing modality and both short- and long-term outcomes. Patients in the short-term outcome group were censored at the time of the events or at 100 days after transplantation. Patients in the long-term outcome group were censored at the time of the events or the end of the study. The Kruskal-Wallis test was used to determine the presence of a statistical difference between the ICU LOS, hospital LOS, and duration of vasopressor and inotropic support for the various pacing groups as continuous variables. All statistical analysis was done using R studio v. 4.1.0 (Posit PBC, Boston, MA).

Results

Over the study period, 192 patients underwent cardiac transplantation and 187 met the inclusion criteria. Baseline characteristics are shown in Table 1. The average age at the time of transplantation was 56 years (standard deviation ± 12). A total of 120 patients were White (64%), 61 were Black (33%), and 6 (3%) were of other racial backgrounds. One hundred and twenty-seven were men (68%), and 60 were women (32%). Twenty-two patients (12%) had their pacing mode turned off at the time of arrival to the ICU, 36 patients (19%) had their pacing mode set to atrially paced, atrially sensed, inhibit (AAI), 101 patients (54%) had theirs set to dual chamber paced, dual chamber sensed, triger/inhibit sensed events (DDD), and 28 (15%) had theirs set to ventricularly paced, ventricularly sensed, inhibit (VVI). The average follow-up time of patients was 23 months (standard deviation ± 13). Of the 187 patients included in the study, 183 had temporary pacemakers implanted

Table 1 Baseline Characteristics

Characteristic	Off, N = 22	AAI, N = 36	DDD, N = 101	VVI, N = 28	*p*-value[a]
Age at transplant	59 (49, 65)	61 (55, 65)	57 (48, 64)	60 (54, 69)	0.13
Sex					0.6
Female	8 (36%)	8 (22%)	35 (35%)	9 (32%)	
Male	14 (64%)	28 (78%)	66 (65%)	19 (68%)	
Race					> 0.9
White	16 (73%)	23 (64%)	63 (62%)	18 (64%)	
Black	6 (27%)	12 (33%)	33 (33%)	10 (36%)	
Other	0 (0%)	1 (2.8%)	5 (5.0%)	0 (0%)	
Family Hx of heart disease	14 (64%)	18 (50%)	55 (54%)	13 (46%)	0.6
Current or former smoker	10 (45%)	16 (44%)	42 (42%)	12 (43%)	> 0.9
Obesity					0.2
Not obese	15 (68%)	19 (53%)	54 (53%)	20 (71%)	
Obese	7 (32%)	17 (47%)	47 (47%)	8 (29%)	
Hypertension	20 (91%)	34 (94%)	98 (97%)	26 (93%)	0.4
Diabetes	15 (68%)	28 (78%)	83 (82%)	23 (82%)	0.5
Hyperlipidemia	21 (95%)	35 (97%)	95 (94%)	26 (93%)	0.9
Atrial fibrillation/flutter	14 (64%)	27 (75%)	66 (65%)	21 (75%)	0.6
Ventricular tachycardia	12 (55%)	26 (72%)	73 (72%)	19 (68%)	0.4
Stroke/TIA	2 (9.1%)	1 (2.8%)	6 (5.9%)	2 (7.1%)	0.7
CKD stages 1-3	1 (4.5%)	3 (8.3%)	4 (4.0%)	1 (3.6%)	0.7
CKD stages 4 and 5	7 (32%)	7 (19%)	22 (22%)	14 (50%)	0.016
ESRD on dialysis	6 (27%)	7 (19%)	16 (16%)	8 (29%)	0.3
Reason for transplant					0.6
Ischemic cardiomyopathy	10 (45%)	13 (36%)	31 (31%)	9 (32%)	
Nonischemic cardiomyopathy	12 (55%)	23 (64%)	70 (69%)	19 (68%)	
Dual-organ transplant					0.4
Dual-organ transplant	5 (23%)	3 (8.3%)	13 (13%)	5 (18%)	
Single-organ transplant	17 (77%)	33 (92%)	88 (87%)	23 (82%)	
Type of induction agent used					0.017
Basiliximab	16 (73%)	25 (69%)	45 (45%)	15 (54%)	
Thymoglobulin	6 (27%)	11 (31%)	56 (55%)	13 (46%)	
Total doses of induction agent					
1	0 (0%)	1 (2.8%)	1 (1.0%)	1 (3.6%)	
2	16 (73%)	27 (75%)	52 (51%)	18 (64%)	
3	3 (14%)	3 (8.3%)	22 (22%)	7 (25%)	
4	2 (9.1%)	5 (14%)	24 (24%)	2 (7.1%)	
5	1 (4.5%)	0 (0%)	2 (2.0%)	0 (0%)	
MCS before transplant	12 (55%)	22 (61%)	53 (52%)	14 (50%)	0.8
DCD or DBD					< 0.001
DBD	18 (82%)	34 (94%)	97 (96%)	20 (71%)	
DCD	4 (18%)	2 (5.6%)	4 (4.0%)	8 (29%)	
Total ischemic time (minutes)	232 (181, 257)	259 (228, 285)	249 (214, 286)	259 (224, 339)	0.11
Cardiac bypass pump time (minutes)	162 (147, 192)	174 (156, 195)	175 (157, 200)	153 (134, 181)	0.037

Abbreviations: AAI, atrially paced, atrially sensed, inhibit; CKD, chronic kidney disease; DBD, donation after brain death; DCD, donation after circulatory death; DDD, dual chamber paced, dual chamber sensed, triger/inhibit sensed events; ESRD, end-stage renal disease; Hx, history; IQR, interquartile range; MCS, mechanical circulatory support; TIA, transient ischemic attack; VVI, ventricularly paced, ventricularly sensed, inhibit.

Median (IQR); *n* (%).

[a]Kruskal-Wallis rank sum test; Pearson's chi-square test; Fisher's exact test.

at the time of transplant. The 4 patients without temporary pacemakers are classified within the "off" category of our study. The decision to implant or not implant a temporary pacemaker was left at the discretion of the operating surgeon. Of the remaining patients who had their temporary pacemakers turned off, 3 had V wires, and 15 had AV wires placed after transplant. The median length of ICU stay was 5 days (interquartile range [IQR] 4-9 days), and the median hospital LOS was 15 days (IQR 11-20 days).

Of the included patients, 178 (95%) had hypertension, 177 (95%) had hyperlipidemia, 149 (80%) had diabetes, 80 (43%) were former or current smokers, and 79 (42%) patients were obese (body mass index > 30). Sixty-three (34%) patients were transplanted for ischemic cardiomyopathy and 124 (66%) for nonischemic cardiomyopathies. One hundred and sixty-nine (90%) patients received a heart from a donation after brain death donor, and 18 (10%) from a donation after circulatory death donor. Data regarding the induction agent used for heart transplantation were also collected. One hundred and one (54%) patients had induction with Basiliximab and 86 (46%) with Thymoglobulin. MCS devices were used in 101 (54%) patients as a bridge to transplantation. Forty-seven (25%) patients had

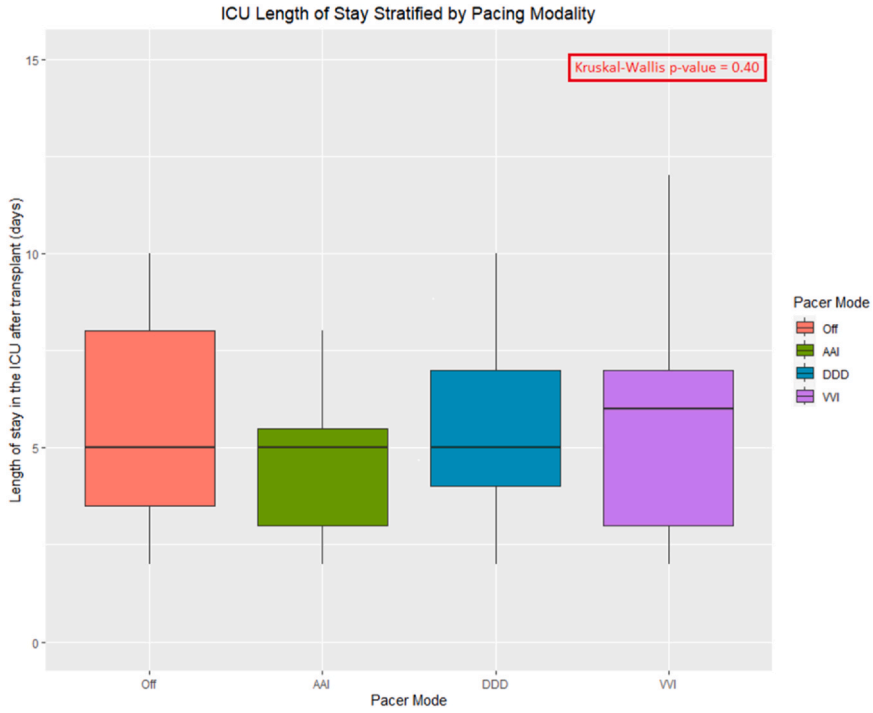

Figure 1 ICU length of stay stratified by pacing modality. ICU, intensive care unit.

an implantable cardiac defibrillator and 52 (28%) had a cardiac resynchronization therapy and defibrillator device implanted before undergoing heart transplantation. In our study, 21 (11%) patients had combined heart-kidney transplants, 4 (2%) had heart-liver transplants, and 1 (1%) had a heart-lung transplant.

ICU length of stay

The median ICU LOS was 5 days (IQR 4-9 days). The median length of ICU stay stratified by pacing modality was 5 days (IQR 4-10 days) for those with baseline AAI pacing, 7 days (IQR 4-14 days) for those with VVI pacing, 5 days (IQR 4-8 days) for those with DDD pacing, and 5.5 days (IQR 4-10 days) who did not require pacing within 24 hours post-operatively. The Kruskal-Wallis test resulted in a *p*-value of 0.40 (Figure 1). No mode of epicardial pacing was associated with an increased ICU LOS in the univariate logistic regression model (Table 2). Those with AAI pacing had an ICU LOS odds ratio (OR) of 0.57 [95% confidence interval (CI): 0.19-1.66], those with VVI pacing had an OR of 2.11 [95% CI: 0.67-6.86], and those with DDD pacing had an OR of 0.94 [95% CI: 0.37-2.39]. Baseline characteristics associated with an increased length of ICU stay were those who had MCS devices placed before transplant (OR: 2.06 [CI: 1.15-3.73]), those on dialysis (OR: 2.23 [95% CI: 1.07-4.82]), and those with a prolonged intraoperative cardiac bypass time (OR: 1.01 [95% CI: 1.00-1.02]).

Hospital length of stay

The median hospital LOS after transplant in this study was 15 days (IQR 11-19 days). The median LOS was also stratified by pacing modality. For patients receiving AAI pacing, the median LOS was 15 days (IQR 10-20 days); for VVI pacing, it was 18 days (IQR 14-27 days); for DDD pacing, it was 14 days (IQR 11-19 days); and for those with their pacers turned off, it was 16 days (IQR 11-18 days). Supplementary Material 2 shows a boxplot of the median hospital LOS after heart transplantation with extension from the first to the third IQR and the Kruskal-Wallis test *p*-value of 0.11. There were no pacemaker modes associated with a prolonged hospital LOS (Table 3). Patient characteristics associated with an increased hospital LOS were those of Black ethnicity (OR: 1.89 [95% CI: 1.02-3.55]), those with end-stage renal disease (ESRD) on dialysis (OR: 2.77 [95% CI: 1.33-6.01]) and those with a prolonged cardiac bypass pump time (OR: 1.01 [95% CI: 1.01-1.02]). Patients who received a single-organ transplant had significantly lower hospital lengths of stay: (OR: 038 [95% CI: 0.15-0.88]) (Figure 5).

Readmission within 30 days of discharge

Forty-one (28%) patients were readmitted within 30 days of discharge. Pacing modalities were distributed as 10 AAI pacing, 4 VVI pacing, 22 DDD pacing, and 5 with no requirement after the first 24 hours postoperatively. There were no specific factors strongly associated with increased readmission rates (Table 4).

Short-term adverse events

The composite of prolonged ICU LOS, prolonged hospital stay, and readmission within 30 days were compiled into a category referred to as short-term adverse events (STAE). A total of 128

Table 2 Odds of Prolonged ICU Length of Stay

Characteristic	N	OR	95% CI	*p*-value
Age at transplant	187	0.99	0.97, 1.02	0.6
Sex	187			
Female		—	—	
Male		0.95	0.52, 1.77	0.9
Race	187			
White		—	—	
Black		1.76	0.95, 3.31	0.076
Other		0.61	0.08, 3.25	0.6
Family Hx of heart disease	187	0.7	0.39, 1.24	0.2
Current or former smoker	187	1.15	0.65, 2.07	0.6
Obesity	187			
Not obese		—	—	
Obese		1.21	0.67, 2.16	0.5
Hypertension	187	0.76	0.18, 2.98	0.7
Diabetes	187	1.43	0.70, 2.98	0.3
Hyperlipidemia	187	0.4	0.08, 1.47	0.2
Atrial fibrillation/flutter	187	1.11	0.60, 2.06	0.7
Ventricular tachycardia	187	0.74	0.39, 1.38	0.3
Stroke/TIA	187	0.85	0.24, 2.93	0.8
CKD stages 1-3	187	0.5	0.10, 1.96	0.3
CKD stages 4 and 5	187	1.45	0.76, 2.81	0.3
ESRD on dialysis	187	2.23	1.07, 4.82	0.036
Reason for transplant	187			
Ischemic cardiomyopathy		—	—	
Nonischemic cardiomyopathy		0.83	0.45, 1.51	0.5
Dual-organ transplant	187			
Dual-organ transplant		—	—	
Single-organ transplant		0.56	0.23, 1.29	0.2
Type of induction agent used	187			
Basiliximab		—	—	
Thymoglobulin		0.89	0.50, 1.59	0.7
Total doses of induction agent	187	0.87	0.62, 1.22	0.4
MCS before transplant	187	2.06	1.15, 3.73	0.015
DCD or DBD	187			
DBD		—	—	
DCD		1.04	0.39, 2.78	> 0.9
Total ischemic time (minutes)	187	1	1.00, 1.01	0.6
Cardiac bypass pump time (minutes)	187	1.01	1.00, 1.02	0.016
Pacer mode	187			
Off		—	—	
AAI		0.57	0.19, 1.66	0.3
DDD		0.94	0.37, 2.39	0.9
VVI		2.11	0.67, 6.86	0.2

Abbreviations: AAI, atrially paced, atrially sensed, inhibit; CI, confidence interval; CKD, chronic kidney disease; DBD, donation after brain death; DCD, donation after circulatory death; DDD, dual chamber paced, dual chamber sensed, triger/inhibit sensed events; ESRD, end-stage renal disease; Hx, history; ICU, intensive care unit; MCS, mechanical circulatory support; OR, odds ratio; TIA, transient ischemic attack; VVI, ventricularly paced, ventricularly sensed, inhibit.

patients had an STAE. The median time to event was 7 days (IQR 5-12 days). The risk factor associated with an increased risk of STAE was a prolonged cardiac bypass pump time (OR: 1.01 [95% CI: 1.00-1.02]). No postoperative pacing modality was associated with an increased risk (Table 5). A Kaplan-Meier curve displaying event rates based on pacing modality was not significant (Figure 2). This was also confirmed via the Cox proportional hazards model: AAI (HR: 0.59 [95% CI: 0.16-1.91]), DDD (HR: 0.55 [95% CI: 0.17-1.54]), VVI (HR: 0.88 [95% CI: 0.23-3.27]).

Long-term adverse events

Seventy-one patients met the criteria for long-term adverse events. Ten developed coronary artery vasculopathy (median time of 17 months), 49 patients had grade 2 or worse rejection on endomyocardial biopsy (median time of 3 months), 15 patients developed malignancy (median time of 18 months), and 14 patients died (median time of 18.5 months). A Kaplan-Meier model confirmed no significant relationship between pacing mode and long-term adverse events (Figure 3). This was also

Table 3 Odds of Prolonged Hospital Length of Stay

Characteristic	N	OR	95% CI	*p*-value
Age at transplant	187	0.99	0.97, 1.01	0.4
Sex	187			
Female		—	—	
Male		0.74	0.40, 1.37	0.3
Race	187			
White		—	—	
Black		1.89	1.02, 3.55	0.046
Other		0.75	0.10, 4.00	0.7
Family Hx of heart disease	187	1.01	0.56, 1.80	>0.9
Current or former smoker	187	1.2	0.67, 2.15	0.5
Obesity	187			
Not obese		—	—	
Obese		1.25	0.70, 2.24	0.5
Hypertension	187	0.39	0.08, 1.53	0.2
Diabetes	187	1.01	0.49, 2.09	>0.9
Hyperlipidemia	187	0.33	0.07, 1.23	0.12
Atrial fibrillation/flutter	187	0.95	0.51, 1.77	0.9
Ventricular tachycardia	187	0.96	0.51, 1.80	0.9
Stroke/TIA	187	2.25	0.66, 8.85	0.2
CKD stages 1-3	187	0.98	0.24, 3.82	>0.9
CKD stages 4 and 5	187	2.06	1.07, 4.01	0.031
ESRD on dialysis	187	2.77	1.33, 6.01	0.008
Reason for transplant	187			
Ischemic cardiomyopathy		—	—	
Nonischemic cardiomyopathy		0.77	0.42, 1.42	0.4
Dual-organ transplant	187			
Dual-organ transplant		—	—	
Single-organ transplant		0.38	0.15, 0.88	0.028
Type of induction agent used	187			
Basiliximab		—	—	
Thymoglobulin		0.87	0.49, 1.55	0.6
Total doses of induction agent	187	0.97	0.69, 1.36	0.9
MCS before transplant	187	1.79	1.00, 3.24	0.051
DCD or DBD	187			
DBD		—	—	
DCD		1.6	0.60, 4.40	0.3
Total ischemic time (minutes)	187	1	1.00, 1.01	0.11
Cardiac bypass pump time (minutes)	187	1.01	1.01, 1.02	0.002
Pacer mode	187			
Off		—	—	
AAI		0.75	0.25, 2.16	0.6
DDD		0.52	0.20, 1.33	0.2
VVI		1.11	0.36, 3.45	0.9

Abbreviations: AAI, atrially paced, atrially sensed, inhibit; CI, confidence interval; CKD, chronic kidney disease; DBD, donation after brain death; DCD, donation after circulatory death; DDD, dual chamber paced, dual chamber sensed, triger/inhibit sensed events; ESRD, end-stage renal disease; Hx, history; MCS, mechanical circulatory support; OR, odds ratio; TIA, transient ischemic attack; VVI, ventricularly paced, ventricularly sensed, inhibit.

confirmed with Cox proportional hazards modeling: AAI (HR: 0.1.10 [95% CI: 0.47-2.58]), DDD (HR: 0.97 [95% CI: 0.46-2.08]), VVI (HR: 0.71 [95% CI: 0.26-1.97]). More long-term events were noted in recipients of single-organ heart transplants (OR: 3.92 [95% CI: 1.42-13.9]), and those with a prolonged cardiac bypass pump time (OR: 1.01 [95% CI: 1.00-1.02]) (Table 6).

Duration of pressor or inotropic support

Vasoactives investigated during this study were Dobutamine, Milrinone, Epinephrine, Norepinephrine, and Vasopressin. The median time for all vasoactive support needs was 13 days. Despite known denervation after heart transplantation and concern for intrinsic rhythm absence (e.g., asystole after cardiopulmonary bypass), there was no associated duration of support with vasoactive medications that correlated to any pacing modality (Figure 4, $p > 0.05$ overall).

Discussion

After reviewing our data and understanding the role of postheart transplant pacing-related outcomes in our population, we found

Table 4 Odds of Readmission Within 30 Days

Characteristic	N	OR	95% CI	*p*-value
Age at transplant	187	0.97	0.94, 1.00	0.02
Sex	187			
Female		—	—	
Male		0.52	0.25, 1.06	0.069
Race	187			
White		—	—	
Black		0.93	0.42, 1.98	0.9
Other		7.6	1.40, 57.1	0.023
Family Hx of heart disease	187	1.01	0.50, 2.04	>0.9
Current or former smoker	187	1.55	0.77, 3.12	0.2
Obesity	187			
Not obese		—	—	
Obese		0.74	0.36, 1.50	0.4
Hypertension	187	0.98	0.23, 6.77	>0.9
Diabetes	187	0.62	0.28, 1.43	0.2
Hyperlipidemia	187	0.64	0.17, 3.07	0.5
Atrial fibrillation/flutter	187	0.99	0.48, 2.14	>0.9
Ventricular tachycardia	187	1.08	0.51, 2.37	0.8
Stroke/TIA	187	1.36	0.29, 4.97	0.7
CKD stages 1-3	187	1.84	0.38, 7.33	0.4
CKD stages 4 and 5	187	2.11	1.00, 4.38	0.047
ESRD on dialysis	187	2	0.88, 4.40	0.088
Reason for transplant	187			
Ischemic cardiomyopathy		—	—	
Nonischemic cardiomyopathy		0.74	0.36, 1.54	0.4
Dual-organ transplant	187			
Dual-organ transplant		—	—	
Single-organ transplant		0.73	0.29, 1.99	0.5
Type of induction agent used	187			
Basiliximab		—	—	
Thymoglobulin		0.9	0.44, 1.80	0.8
Total doses of induction agent	187	0.98	0.64, 1.46	>0.9
MCS before transplant	187	0.76	0.38, 1.53	0.4
DCD or DBD	187			
DBD		—	—	
DCD		1.02	0.28, 3.04	>0.9
Pacer mode	187			
Off		—	—	
AAI		1.31	0.39, 4.81	0.7
DDD		0.95	0.33, 3.13	>0.9
VVI		0.57	0.12, 2.44	0.4
Total ischemic time (minutes)	187	1	1.0, 1.00	0.8
Cardiac bypass pump time (minutes)	187	1	1.0, 1.01	0.5

Abbreviations: AAI, atrially paced, atrially sensed, inhibit; CI, confidence interval; CKD, chronic kidney disease; DBD, donation after brain death; DCD, donation after circulatory death; DDD, dual chamber paced, dual chamber sensed, triger/inhibit sensed events; ESRD, end-stage renal disease; Hx, history; MCS, mechanical circulatory support; OR, odds ratio; TIA, transient ischemic attack; VVI, ventricularly paced, ventricularly sensed, inhibit.

that safety remains acceptable within our single-center practice. Despite the high-risk nature of organ transplantation, immunotherapy induction, and vasoactive support needs, the overall mortality was 7.49% within our cohort. Our data add significant knowledge to an area within the field of transplant medicine that may allow for early weaning of vasoactive support and better tolerance for lower thresholds, early pacemaker weaning trials, and shorter lengths of ICU stay.

We demonstrate that there was no significant association between the mode of temporary pacing and any adverse short-term or long-term events after heart transplantation. This finding also extended to the time-to-event analyses and duration of pressor or inotropic therapy. None of the patients included in our study needed to have a permanent pacemaker implanted during their hospital stay or on long-term follow-up. Analysis of baseline characteristics showed that patients with an MCS device before transplant, patients on dialysis, and those who had a prolonged intraoperative cardiopulmonary bypass time were significantly more likely to have a prolonged ICU LOS. Prolonged bypass time and ESRD on dialysis were associated with increased hospital LOS while heart-only transplantation was associated with decreased hospital LOS. There was 1 episode of mediastinitis (AV pacer wires present) and 3 episodes of primary graft dysfunction (2 patients with AV wires

Table 5 Odds of a Short-Term Adverse Event

Characteristic	N	OR	95% CI	*p*-value
Age at transplant	187	0.98	0.95, 1.00	0.12
Sex	187			
Female		—	—	
Male		0.49	0.23, 0.97	0.048
Race	187			
White		—	—	
Black		1.87	0.94, 3.89	0.08
Other		1.12	0.21, 8.29	>0.9
Family Hx of heart disease	187	0.71	0.38, 1.32	0.3
Current or former smoker	187	1.02	0.55, 1.92	>0.9
Obesity	187			
Not obese		—	—	
Obese		1.1	0.59, 2.07	0.8
Hypertension	187	0.61	0.09, 2.60	0.5
Diabetes	187	1.16	0.54, 2.45	0.7
Hyperlipidemia	187	0.23	0.01, 1.26	0.2
Atrial fibrillation/flutter	187	1.05	0.53, 2.01	0.9
Ventricular tachycardia	187	0.79	0.39, 1.55	0.5
Stroke/TIA	187	2.16	0.53, 14.4	0.3
CKD stages 1-3	187	1.65	0.38, 11.3	0.5
CKD stages 4 and 5	187	1.91	0.92, 4.23	0.093
ESRD on dialysis	187	1.87	0.83, 4.65	0.2
Reason for transplant	187			
Ischemic cardiomyopathy		—	—	
Nonischemic cardiomyopathy		1.01	0.52, 1.93	>0.9
Dual-organ transplant	187			
Dual-organ transplant		—	—	
Single-organ transplant		0.47	0.15, 1.23	0.2
Type of induction agent used	187			
Basiliximab		—	—	
Thymoglobulin		0.92	0.49, 1.71	0.8
Total doses of induction agent	187	0.93	0.65, 1.34	0.7
MCS before transplant	187	1.62	0.87, 3.04	0.13
DCD or DBD	187			
DBD		—	—	
DCD		0.7	0.26, 1.99	0.5
Total ischemic time (minutes)	187	1	1.00, 1.01	0.4
Cardiac bypass pump time (minutes)	187	1.01	1.00, 1.02	0.013
Pacer mode	187			
Off		—	—	
AAI		0.59	0.16, 1.91	0.4
DDD		0.55	0.17, 1.54	0.3
VVI		0.88	0.23, 3.27	0.9

Abbreviations: AAI, atrially paced, atrially sensed, inhibit; CI, confidence interval; CKD, chronic kidney disease; DBD, donation after brain death; DCD, donation after circulatory death; DDD, dual chamber paced, dual chamber sensed, triger/inhibit sensed events; ESRD, end-stage renal disease; Hx, history; MCS, mechanical circulatory support; OR, odds ratio; TIA, transient ischemic attack; VVI, ventricularly paced, ventricularly sensed, inhibit.

and 1 patient with V wires). Patients with prolonged bypass time were found to have higher odds of STAE. Those who had heart-only transplantations had lower hospital LOS but higher odds of adverse long-term events.

The 2022 ISHLT guidelines note that temporary epicardial pacing wires should be inserted into the newly transplanted heart regardless of the underlying rhythm and set to maintain a heart rate greater than 90.[1] This guideline also notes that there are no specific recommendations for temporary pacing early after transplantation from any of the major international guideline committees. To date, there have not been significant large-scale randomized controlled trials investigating the impact of different pacemaker settings in this population. Much of the data regarding temporary epicardial pacemakers is extrapolated from patients undergoing cardiac surgery for other purposes with benefits seen most often in those with low ejection fractions.[3-5] Contrary to these prior studies, ours failed to show any meaningful differences between any one mode of pacing and short- or long-term outcomes. This may be secondary to significant differences between the study populations, pacing settings, and outcomes of interest.

There were a variety of patient factors that appeared to be linked to prolonged ICU LOS, hospital LOS, hospital

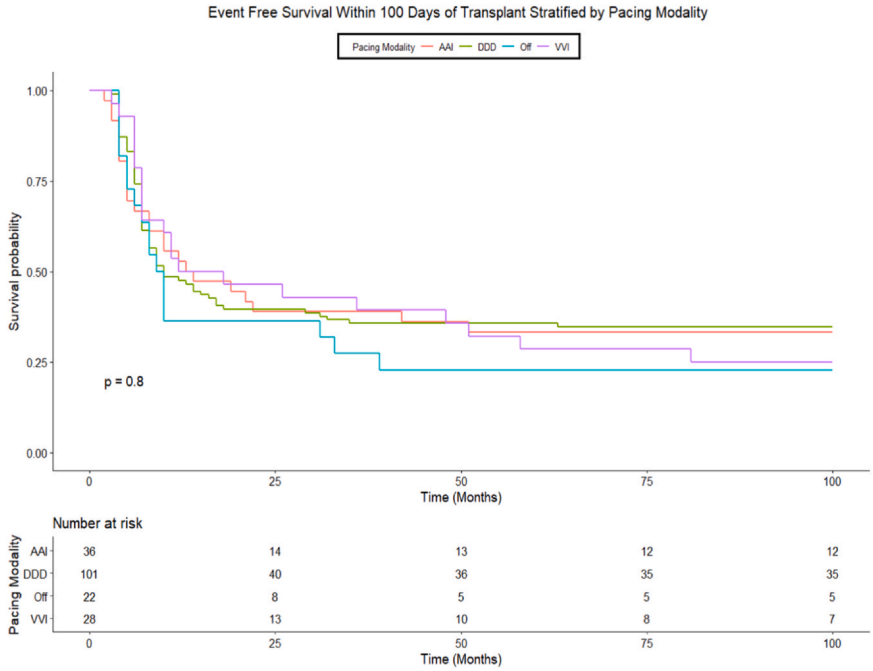

Figure 2 Event-free survival within 100 days of transplant stratified by pacing modality.

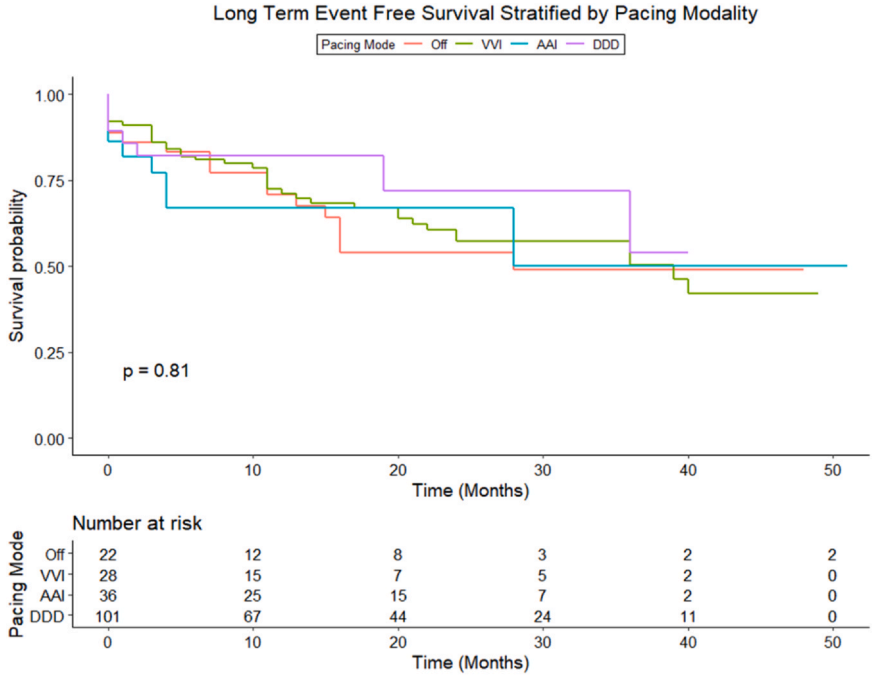

Figure 3 Long-term event-free survival stratified by pacing modality.

readmission, and the culmination of all 3 short-term adverse events. Most consistently, however, the use of a temporary MCS device as a bridge to transplant was linked to these adverse short-term events. The utilization of MCS devices before transplant is often done in patients who are on maximally tolerated medical therapy yet systemic hypoperfusion remains a problem. As a result, the prolonged ICU course may be a consequence of phenotypically sicker patients rather than a reflection of the actual device therapy. One study by Massad et al noted that patients with a left ventricular assist device (LVAD) have similar hospital LOS as those without an LVAD after heart transplantation.[6] On the other hand, a more contemporary study by Crawford et al found that patients who had an intra-aortic balloon pump, LVAD, or extracorporeal membrane oxygenation before transplant were more likely to have a prolonged hospital LOS.[7] Additionally, prolonged cardiopulmonary bypass times and the need for dialysis were also consistently found to be associated with adverse short-term outcomes.

The only factor found to be associated with a statistically significant reduction in adverse long-term events was dual-

Table 6 Odds of Long-Term Adverse Events

Characteristic	N	OR	95% CI	*p*-value
Age at transplant	187	1	0.98, 1.03	0.9
Sex	187			
Female		—	—	
Male		1.21	0.64, 2.31	0.6
Race	187			
White		—	—	
Black		0.71	0.37, 1.34	0.3
Other		0.72	0.10, 3.86	0.7
Family Hx of heart disease	187	0.76	0.42, 1.38	0.4
Current or former smoker	187	1.06	0.58, 1.92	0.8
Obesity	187			
Not obese		—	—	
Obese		1.59	0.88, 2.90	0.13
Hypertension	187	0.75	0.19, 3.14	0.7
Diabetes	187	0.92	0.45, 1.95	0.8
Hyperlipidemia	187	2.56	0.62, 17.3	0.2
Atrial fibrillation/flutter	187	0.76	0.41, 1.44	0.4
Ventricular tachycardia	187	1.19	0.63, 2.31	0.6
Stroke/TIA	187	2.05	0.59, 7.36	0.3
CKD stages 1-3	187	3.48	0.89, 16.9	0.085
CKD stages 4 and 5	187	0.7	0.35, 1.38	0.3
ESRD on dialysis	187	0.63	0.28, 1.35	0.3
Reason for transplant	187			
Ischemic Cardiomyopathy		—	—	
Nonischemic cardiomyopathy		0.9	0.48, 1.68	0.7
Dual-organ transplant	187			
Dual-organ transplant		—	—	
Single-organ transplant		3.92	1.42, 13.9	0.016
Type of induction agent used	187			
Basiliximab		—	—	
Thymoglobulin		1.03	0.57, 1.87	>0.9
Total doses of induction agent	187	1.04	0.74, 1.47	0.8
MCS before transplant	187	1.54	0.85, 2.81	0.2
DCD or DBD	187			
DBD		—	—	
DCD		1.73	0.64, 4.64	0.3
Pacer mode	187			
Off		—	—	
AAI		1.4	0.48, 4.28	0.5
DDD		1.15	0.45, 3.10	0.8
VVI		0.58	0.17, 1.98	0.4
Total ischemic time (minutes)	187	1	1.00, 1.01	0.049
Cardiac bypass pump time (minutes)	187	1.01	1.00, 1.02	0.011

Abbreviations: AAI, atrially paced, atrially sensed, inhibit; CI, confidence interval; CKD, chronic kidney disease; DBD, donation after brain death; DCD, donation after circulatory death; DDD, dual chamber paced, dual chamber sensed, triger/inhibit sensed events; ESRD, end-stage renal disease; Hx, history; MCS, mechanical circulatory support; OR, odds ratio; TIA, transient ischemic attack; VVI, ventricularly paced, ventricularly sensed, inhibit.

organ transplantation. This finding is in line with several other studies that suggest that survival with a combined heart-kidney transplant is at least comparable to those with only a heart transplant.[8-12] There also is a trend toward decreased rates of graft rejection and coronary artery vasculopathy with combined heart-kidney transplantation.[9-11,13-17] Regarding long-term events in patients with heart-liver transplants, a study by Rizvi et al noted that cardiac allograft rejection was approximately 24.7% within the first year.[18] No patients in our cohort had rejection during the follow-up interval which may reflect low absolute numbers of combined heart-liver transplants in our population. Mortality among patients with heart-liver transplants has been reported to be comparable to heart-only transplantation.[18] Only 1 patient in our cohort had a heart-lung transplant which makes it difficult to extrapolate any meaningful conclusions. The 1-year survival rate of heart-lung transplant recipients is approximately 63% to 66%.[19,20] While there appear to be favorable long-term outcomes with dual-organ transplantation, our results may be skewed due to the high number of heart-kidney transplants and low number of heart-lung transplants.

Several other limitations exist for this study which deserve mention. One major limitation of our study was the

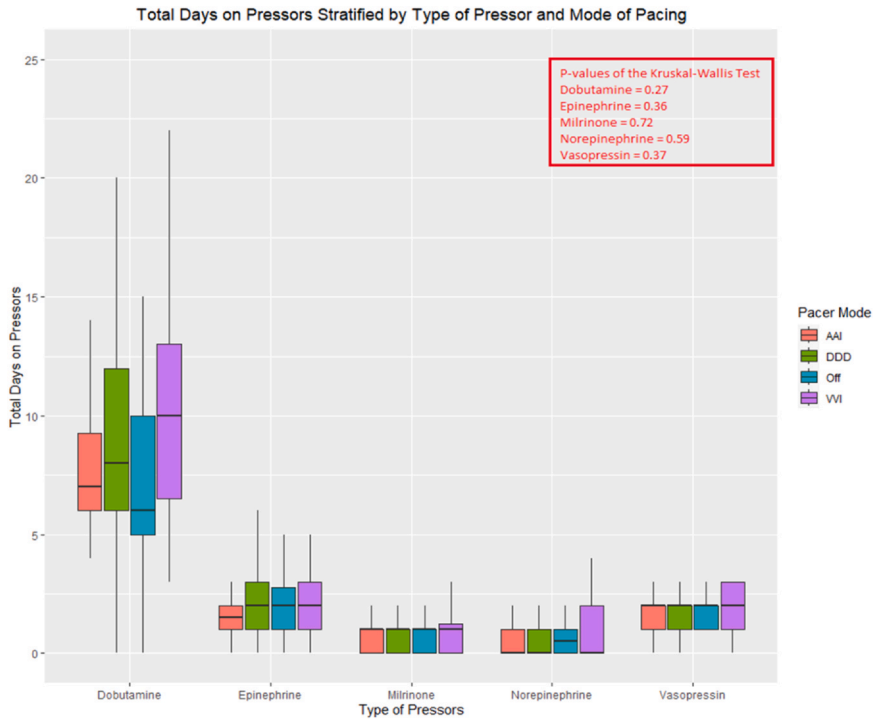

Figure 4 Total days on pressors stratified by type of pressor and mode of pacing.

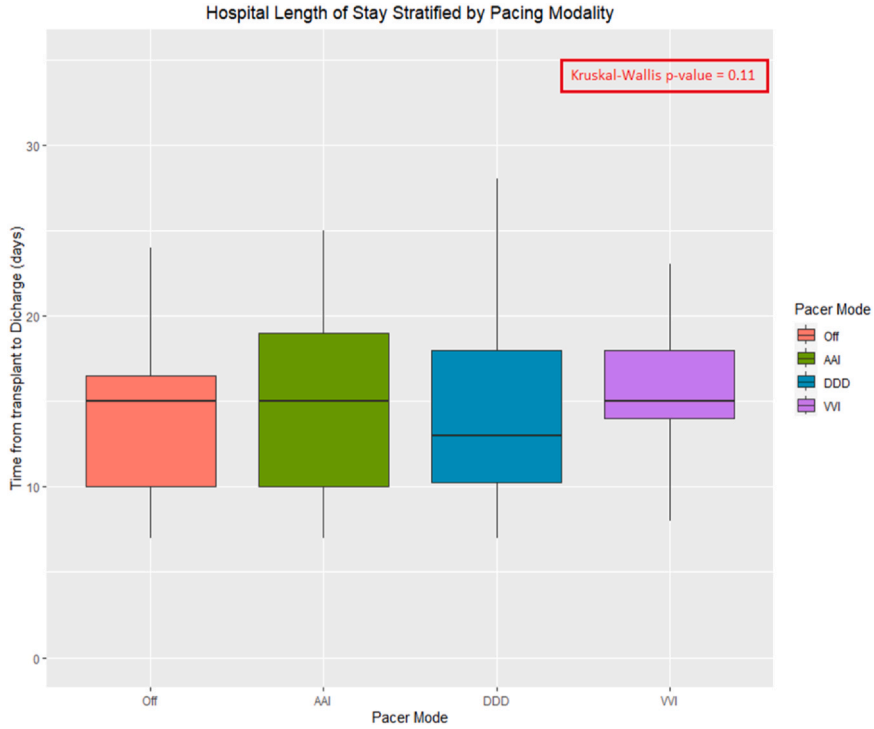

Figure 5 Hospital length of stay stratified by pacing modality.

inability to quantify the duration and frequency of pacing for each modality. Despite patients being assigned a particular pacing setting, if their inotropic support kept them at a higher heart rate, then their pacemaker would not need to function decreasing their overall pacing burden. This may explain why there was no difference noted between patients who had a specific modality selected for their device and those who had theirs turned off. Additionally, the doses of medications were not collected or analyzed during this study. Given the significant heterogeneity among dosing and frequent changes in this critically ill population, it would be difficult to break down each dosage into its category while maintaining enough patients to draw any significant conclusions. Lastly, the decision to group numerous variables into the category of "long-term variables" was made due to the small absolute number of patients who experienced each outcome. By grouping them a more robust association could be found generally but at the cost of lower specificity.

Conclusion

No mode of temporary epicardial pacing was associated with an increase in short- or long-term adverse events in patients receiving heart transplants. The use of an MCS device as a bridge to transplant, the need for dialysis, and prolonged cardiopulmonary bypass time were linked to a prolonged ICU LOS. Patients who underwent dual-organ transplants had a lower incidence of adverse long-term events.

Author contributions

G. Umadat: Participated in research design, data collection, analysis, and the writing of the paper. J. Lee: Participated in research design, data collection, analysis, and the writing of the paper. B. Rice: Participated in research design, data collection, analysis, and the writing of the paper. S. Gharacholou: Participated in research design, analysis, and the writing of the paper. P. Patel: Participated in research design and the writing of the paper. R. Goswami: Participated in research design, data collection, analysis, and the writing of the paper.

Disclosure statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jhlto.2024.100129.

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