Ventricular pacing in single ventricles—A bad combination

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BACKGROUND Chronic ventricular pacing (VP) is associated with systolic dysfunction in a subset of pediatric patients with heart block and structurally normal hearts. The effect of chronic VP in congenital heart disease is less well understood, specifically in the single-ventricle (SV) population.

OBJECTIVE To determine the longitudinal effect of VP in SV patients.

METHODS SV patients with heart block and dual-chamber pacemakers requiring >50% VP were compared with nonpaced (controls) SV patients matched for age, sex, and SV morphology. Patients were excluded if a prepacing echocardiogram was not available. Echocardiogram and clinical parameters were compared at baseline (prepacing) and at last follow-up in the paced group, and in controls when they were at ages similar to those of their paced-group matches.

RESULTS Twenty-two paced and 53 control patients from 2 institutions were followed for similar durations (6.6±5 years vs 7.6±7.6 years; $P = .59$). There was no difference between groups regarding baseline ventricular function or the presence of moderate-to-severe atrioventricular valvar regurgitation (AVVR). Paced patients were more likely to develop moderate-to-severe systolic dysfunction (68% vs 15%; $P < .01$) and AVVR (55% vs 8%; $P < .001$) and require heart failure medications (65% vs 21%; $P < .001$). Chronic VP was also associated with a higher risk of transplantation or death (odds ratio, 4.9; 95% confidence interval, 1.05–22.7; $P = .04$).

CONCLUSIONS SV patients requiring chronic VP are at higher risk of developing moderate-to-severe ventricular dysfunction and AVVR with an increased risk of death or transplantation compared with controls. New strategies to either limit VP or improve synchronization in this vulnerable population is imperative.

KEYWORDS Congenital heart disease; Heart block; Pacemaker; Pediatrics; Single ventricle

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Introduction

Chronic ventricular pacing has been associated with poor systolic function in a subset of pediatric patients with complete heart block and structurally normal hearts.[1–6] The effect of chronic ventricular pacing in congenital heart disease is less well understood, especially in patients with single-ventricle physiology. To date, there has been no study in the literature specifically evaluating the effects of chronic ventricular pacing in this complex population. The objective of this study is to determine the longitudinal effect of ventricular pacing in children with single-ventricle congenital heart disease. We hypothesized that single-ventricle patients requiring chronic ventricular pacing would have worse outcomes than single-ventricle patients who did not require ventricular pacing.

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Methods

Study cohort

This was a retrospective cohort study across 2 institutions from 1990 to 2015 that investigated patients with single-ventricle congenital heart disease and dual-chamber epicardial pacemakers who had ≥50% ventricular pacing (based on the most recent pacemaker interrogation). Dual-chamber pacemaker modes DDD, DDI, DDIR, and DDDR were included. Patients with ventricular pacing were compared with a control group of single-ventricle patients without pacemakers who were matched for age, sex, and single-ventricle morphology and had similar follow-up periods; there was a 1:2 ratio of paced-group participants to controls. Patients were excluded if a prepacing

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echocardiogram was not available for review or if the follow-up period was <1 year. Clinical and echocardiographic parameters were compared at baseline, defined as prepacing in the pacing group and at similar ages in controls, as well as at last follow-up. This research protocol was approved by the Stanford University and Advocate Children's Heart Institute institutional review boards.

Patient characteristics such as age, gender, type of single-ventricle morphology, pacing indication (surgical vs nonsurgical advanced second- or third-degree heart block), date of pacemaker implantation, date of last follow-up echocardiogram, and follow-up duration (defined as the time period between the prepacemaker echocardiogram date and the last follow-up postpacemaker echocardiogram date) were collected. Primary study outcomes included patient disposition (alive, transplanted, dead) and necessity for heart failure medications as a surrogate marker for development of heart failure. Secondary study outcomes included ventricular function and atrioventricular valvar regurgitation (AVVR). Ventricular function was defined qualitatively as normal, mild dysfunction, moderate dysfunction, or severe dysfunction, as documented in the echocardiogram report. AVVR was defined as none/trivial, mild, moderate, or severe.

Statistical analysis

Continuous variables that were normally distributed were reported as mean plus or minus standard deviation and were compared using the *t* test. Categorical variables were reported as counts (percentage) and compared using the Fisher exact test. Logistic regression models were used to determine the influence of categorical variables on the primary outcome variable for cardiac transplantation or death. Stata version 12.0 (StataCorp, College Station, TX) was used to perform all statistical analyses. *P* values less than .05 were considered statistically significant.

Results

Baseline characteristics

A total of 75 patients were included in this study, of which 22 (29%) were paced and 53 (71%) were controls. Demographic and clinical characteristics are summarized in Table 1. Patients in both paced and control groups were of similar age and ventricular morphology and had similar follow-up duration. In addition, baseline ventricular systolic function and AVVR were similar between the paced and control groups. The distribution of single-ventricle anatomy among paced and control patient cohorts is illustrated in Figure 1. The indication for ventricular pacing was equally split between surgical complete heart block and nonsurgical advanced second- or third-degree heart block.

Longitudinal outcome of ventricular pacing in paced and control patients

The incidence of moderate-to-severe ventricular systolic dysfunction and AVVR at follow-up was higher in the paced group compared with the control group, despite having similar baseline characteristics (Table 2 and Figure 2). The paced group was more likely to be on heart failure medications at follow-up, as well as have a significantly higher incidence of transplantation or death, than the control group was.

Table 1 Baseline patient characteristics

	Paced (n = 22)	Control (n = 53)	*P* value
Age (years)	11 ± 1.6	13 ± 1.2	.15
Follow-up time (y, mean)	6.6 ± 5	7.6 ± 7.6	.59
Systemic ventricle			
Right	13	31	.96
Left	9	22	
Ventricular function			
Normal	20	45	.62
Mild dysfunction	2	4	
Moderate dysfunction	0	2	
Severe dysfunction	0	2	
AVVR			
None/trivial/mild	19	49	.18
Moderate/severe	3	4	

Data are presented as absolute numbers; age is presented as mean ± 2 standard deviations.

AVVR = atrioventricular valvar regurgitation; SD = standard deviation.

Univariate analysis for heart transplantation or death

A univariate logistic regression model found chronic ventricular pacing >50% to be a risk factor for heart transplantation or death, with an odds ratio of 4.9 (95% confidence interval (CI), 1.1–22.7; $P = .04$). As expected, moderate-to-severe ventricular systolic dysfunction and moderate-to-severe AVVR were also identified as risk factors for heart transplantation or death, with odds ratios of 25 (95% CI, 4.7–131; $P < .001$) and 9.45 (95% CI, 1.6–54; $P = .01$), respectively. A systemic left ventricle showed a trend toward being protective against risk of heart transplantation or death but did not reach statistical significance (Table 3).

Discussion

In this cohort of single-ventricle congenital heart disease patients across 2 institutions, we found that patients with dual-chamber pacemakers requiring ≥50% ventricular pacing were more likely to develop moderate-to-severe systolic dysfunction and AVVR compared with matched controls. These patients also had an approximately 5 times higher risk of heart transplantation or death compared with matched controls.

These results differ from an earlier published report by Fishberger et al[7] showing similar survival between paced and nonpaced patients. In that series, 28 patients required pacemaker implantation for ventricular pacing, 9 receiving VVI pacing and 19 dual-chamber DDD pacing. The long-term survival in the VVI paced patients showed a trend toward poorer survival (4 of 9) compared with DDD-paced patients (15 of 19); however, the survival in the