Equivalent Performance of Epicardial Versus Endocardial Permanent Pacing in Children: A Single Institution and Manufacturer Experience

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The strategy for permanent pacing in pediatric populations is complicated by unique biologic constraints of growing children, limited vascular access and anomalies of systemic venous connection, complex congenital heart disease with structural defects requiring multiple surgical reinterventions for long-term survival, and changing pacemaker hardware technology. The universal transvenous approaches, customary in adults, may cause problems in children with limited endovascular domain, intracardiac right-to-left shunting, and other sundry complications, including valvular damage, endocarditis, and thromboembolism. With heart failure diagnoses further broadening indications for pacing therapy, the intracardiac foreign body load looms large in children requiring life-long pacing that may potentially complicate subsequent lead extraction if need arises. While avoiding these unique problems with transvenous leads the epicardial route requires more “invasive” approaches (subxiphoid, sternotomy, or thoracotomy) and is historically fraught with higher pacing and sensing thresholds, lead failure, and earlier battery depletion rates. With the advent of steroid-eluting epicardial leads we sought to test the hypothesis that steroid-eluting epicardial and endocardial leads now had equivalent outcomes.

Patients and Methods

A retrospective review of the medical records of all pediatric patients (<19 years) who underwent permanent pacemaker (PPM) implantation at our tertiary health care center from January 1990 through December 2003 was undertaken. Numerous pacing leads and pulse generators were used during this time period and this observational study restricted entry to children receiving hardware from Medtronic, Inc., a single manufacturer, to minimize potential confounders among differing hardware manufacturers. The study investigators have no conflict of interest disclosures with Medtronic, Inc., or any other pacemaker company and the study received University of California-Los Angeles (UCLA) Institutional Review Board (IRB) approval (UCLA IRB #G04-04-008-03) with waiver of patient consent.

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At the outset, one hundred and sixty children, mean age 7.4 ± 5.5 years (range, 0.4 to 18 years), with atrial and(or) ventricular leads meeting criteria, were identified and reviewed. These children were recipients of a PPM system with steroid eluting leads from a single manufacturer. The routes of PPM implantation in these children were transvenous, subxiphoid, sternotomy, or thoracotomy. The choice of either endocardial or epicardial system, transvenous or surgical approach, was dependent on cardiology and surgeon preference. One hundred and forty-eight of this group received both atrial and ventricular leads, while 11 received only ventricular leads and a single child only an atrial lead. The primary outcome focused on mortality, both short term (30 days postimplantation) and long term. Secondary outcomes analyzed included lead failure, lead reintervention, and lead functional parameters at time of implantation. For analysis, the patient pool, of 148 with dual-chamber pacemakers, was split into two groups: children with endocardial versus epicardial PPM leads. Outcome variables were compared between the two groups.

**Multivariable Analysis**

A multivariable Cox hazard model analysis was created to neutralize potential cofactors that may have precipitated lead failure and reintervention in the endocardial and epicardial subgroups. Because there were not enough comparable patients with only one lead placed either in the atria or ventricle, only patients with dual-chamber pacemakers (both atrial and ventricular leads) in endocardial or epicardial groups were compared with one another. The subpopulation for lead failure and reintervention analysis of the study was restricted to 148 (50 endocardial, 98 epicardial). Refer to Table 1 for demographic characteristics of this subpopulation.

**Cofactors**

Medical records for all children were examined for age, weight, diagnosis, and indication for PPM implantation. The typical indications for PPM implantation included postoperative atroventricular (AV) block, complete congenital AV block, and sick sinus syndrome. Children with single ventricle physiology (diagnoses of hypoplastic left heart syndrome [HLHS], double-inlet left ventricle [DILV], tricuspid atresia [TA], and s/p bidirectional cavo-pulmonary anastomosis or Fontan operation) were identified. Medical records were further screened for any history of congestive heart failure, coronary artery or valvular disease, arrhythmias, and prior implanted PPM. Refer to Tables 1 and 2 for a comparison of outcome variables for the endocardial and epicardial subgroups.

**Outcome Variables**

The primary endpoint of the study was early (within 30 days postoperation) and late mortality. Secondary outcomes included freedom from lead failure and pacemaker system reintervention. Lead failure was defined by loss of capture-sensing, lead displacement-fracture, exit block, and high thresholds. Reintervention included the need for lead revision or generator change (Tables 2 and 3).

**Statistical Analysis**

The two study groups were compared for continuous variables with the Student t test and χ² analysis for binary variables. The covariants were analyzed by a proportional hazards (Cox) model to adjust for the aforementioned covariants. Results are reported as relative hazard ratios between the two groups. Event occurrences are reported as total occurrences as well as rates/1,000 patient-months to indicate events over time. Kaplan-Meier plots were employed to visualize pacing lead survival and freedom from lead reintervention.

**Results**

**Mortality**

There was no early mortality in either epicardial or endocardial pacing groups. Late mortality occurred only

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**Table 1. Demographics for Lead Failure and Reintervention Analysis**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Endocardial</th>
<th>Epicardial</th>
<th>p Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± SD (year)</td>
<td>11.0 ± 4.3</td>
<td>5.5 ± 5.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean weight ± SD (kg)</td>
<td>38.1 ± 18.1</td>
<td>19.7 ± 17.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Postoperative third degree heart block</td>
<td>12 (24%)</td>
<td>59 (60%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Congenital third degree heart block</td>
<td>25 (50%)</td>
<td>16 (16%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sick sinus syndrome</td>
<td>13 (26%)</td>
<td>23 (23%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Concomitant cardiac surgery</td>
<td>3 (6%)</td>
<td>27 (28%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>17 (34%)</td>
<td>88 (90%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Single-ventricle physiology</td>
<td>8 (16%)</td>
<td>51 (52%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Prior pacemaker</td>
<td>16 (32%)</td>
<td>21 (21%)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

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once in the endocardial cohort for an overall death rate of 0.5 ± 0.5 deaths/1,000 patient-months. There were eight late deaths in the epicardial cohort for an overall mortality rate of 3.4 ± 1.2 deaths/1,000 patient-months. While there was a trend favoring greater survival in the endocardial group over 24 months the difference was not statistically significant (Fig 1).

There was no pacemaker-related mortality. Late mortality occurred after additional surgery for congenital heart disease, single ventricle pathophysiology, or after orthotopic transplantation. The mean follow-up period for endocardial and epicardial pacing groups was 32.5 ± 29.3 (range, 0–110 months) and 23.9 ± 22.8 (range, 0–89 months), respectively.

**Lead Failure**

The endocardial group had five lead failures (out of 50 patients) at a rate of 3.18 ± 1.42 failures/1,000 patient-months. By contrast, the epicardial group sustained 18 failures (among 98 children) for a rate of 7.79 ± 1.84 failures/1,000 patient-months. This represents a hazard ratio of 0.408 (p = 0.038). However, after adjusting for the covariates of concomitant surgery, congenital heart disease, single ventricle physiology, and age, using proportional hazards Cox model the adjusted hazard ratio for freedom from lead failure is 0.055 (p = 0.36) and thus any differences are now insignificant.

**Lead Reintervention**

Seven reinterventions occurred in the endocardial group (n = 50) for a rate of 4.34 ± 1.64 reinterventions/1,000 patient-months. In the epicardial group (n = 98), 16 reinterventions occurred for 6.91 ± 1.73 reinterventions/1,000 patient-months. The hazard ratio is 0.629 (p = 0.0023). The adjusted hazard ratio for freedom from lead reintervention is 0.157 (p = 0.045) for the endocardial versus epicardial group. The number of lead reinterventions is significantly lower in the endocardial group even after adjusting for covariates (Fig 2). The causes for reintervention in the endocardial group in five instances were generator change and in four other cases due to lead revision. This represents rates of 2.52 ± 1.13/1,000 patient-months and 2.02 ± 1.01/1,000 patient-months, respectively, for generator change and lead revision. In the epicardial group, generator change was the reason for 9 reinterventions and lead revision, 7. This represents rates of 3.82 ± 1.27/1,000 patient-months and 2.97 ± 1.12/1,000 patient-months for generator change and lead revision. There is no significant difference in generator changes or lead revisions between the two groups (Table 2).

**Stimulation Threshold**

The acute mean stimulation threshold for endocardial atrial leads at time of implantation was 0.74 ± 0.14 V. For the epicardial group, this threshold increased to 1.61 ± 1.09 V. The difference between the two groups at implantation was 0.87 ± 0.24 V (p = 0.0005). Similarly, for ventricular leads, the endocardial group recorded a mean acute stimulation threshold of 0.49 ± 0.07 V compared with 1.13 ± 0.17 V for the epicardial group (p = 0.0001).

**Sensing Threshold**

The mean acute sensing threshold of endocardial atrial leads at implantation was 4.26 ± 0.89 mV compared with 3.49 ± 0.60 mV for epicardial leads (p = 0.49). At the ventricular site, the mean sensing threshold at time of implant for the endocardial group was 13.0 ± 1.7 mV compared with 18.5 ± 7.7 mV for the epicardial group (p = 0.46).

**Lead Impedance**

The mean lead impedance for the atrial endocardial leads was 594 ± 27 Ω (ohms) compared with 386 ± 26 Ω for the epicardial group. The mean difference was 212 ± 39 Ω (p < 0.0001). The mean lead impedance for the ventricular position was 644 ± 38 and 449 ± 34 Ω for endocardial and epicardial groups, respectively (p = 0.0003).

**Table 2. Reason for Reinterventions**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Endocardial (rate/1,000 patient-months)</th>
<th>Epicardial (rate/1,000 patient-months)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generator replacement</td>
<td>5 (2.25 ± 1.13)</td>
<td>9 (3.82 ± 1.27)</td>
<td>0.57</td>
</tr>
<tr>
<td>Lead revisions</td>
<td>4 (2.02 ± 1.01)</td>
<td>7 (2.97 ± 1.12)</td>
<td>0.59</td>
</tr>
</tbody>
</table>

**Table 3. Electrophysiologic Lead Measurements at Implantation**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Endocardial (Value ± SE)</th>
<th>Epicardial (Value ± SE)</th>
<th>Mean Difference (Value ± SE)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial stimulation threshold (V)</td>
<td>0.74 ± 0.14</td>
<td>1.61 ± 1.09</td>
<td>0.87 ± 0.24</td>
<td>0.0005</td>
</tr>
<tr>
<td>Ventricular stimulation threshold (V)</td>
<td>0.49 ± 0.07</td>
<td>1.83 ± 0.17</td>
<td>1.34 ± 0.19</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Atrial sensing threshold (mV)</td>
<td>4.26 ± 0.89</td>
<td>3.49 ± 0.60</td>
<td>0.76 ± 1.09</td>
<td>0.49</td>
</tr>
<tr>
<td>Ventricular sensing threshold (mV)</td>
<td>13.0 ± 1.7</td>
<td>18.5 ± 7.7</td>
<td>5.5 ± 7.5</td>
<td>0.46</td>
</tr>
<tr>
<td>Atrial lead impedance (Ω)</td>
<td>594 ± 27</td>
<td>386 ± 26</td>
<td>212 ± 39</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ventricular lead impedance (Ω)</td>
<td>644 ± 38</td>
<td>449 ± 34</td>
<td>195 ± 51</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

Ω = ohms; SE = standard error of the mean; V = voltage.
Measurements we were unable to track lead performance between the two groups. Due to incomplete follow-up, there was no important difference in atrial and ventricular sensing acutely. This finding was correlated with significantly lower acute lead impedances at the atrial and ventricular epicardial sites. Of note, there was no important difference in atrial and ventricular stimulation thresholds at the epicardial site, steroid elution has exhibited better chronic pacing thresholds in the long run. Steroid-eluting leads reduce inflammation at the electrode-tissue interface leading to lower stimulation thresholds, and thus less depletion of battery life. Lead survival has proven significantly better for steroid-eluting versus nonsteroid-eluting lead. In our series there was no significant difference in mortality between the two pacing approaches in children despite epicardial lead recipients being younger, smaller in size, and with higher severity of cardiovascular disease and risk. There was a higher incidence of postoperative and congenital heart block in infants requiring permanent epicardial pacing. The overwhelming majority of the epicardial cohort had congenital heart disease with over half having some form of single ventricle anatomy and physiology and about a third undergoing concomitant open heart surgery; therefore, higher disease severity and risk. Conversely, in our experience, implantation of endocardial leads in comparatively healthier children may explain the statistical trend toward higher actuarial survival in the endocardial subgroup. There was no important difference in lead failure rate (loss of capture-sensing, lead displacement-fracture, exit block, and high pacing-sensing thresholds) between the two pacing sites. Thomson and colleagues recently found the major causes for lead failure were unreasonably increased pacing threshold and lead fracture. Suboptimal pacing, lead displacement, and infection also played an important contribution in their experience.

In our series, electrophysiologic lead measurements at the time of pacemaker implantation showed higher atrial and ventricular stimulation thresholds at the epicardial position acutely. This finding was correlated with significantly lower acute lead impedances at the atrial and ventricular epicardial sites. Of note, there was no important difference in atrial and ventricular sensing acutely between the two groups. Due to incomplete follow-up measurements we were unable to track lead performance long term. The literature supports improvement in stimulation threshold with time for the steroid-eluting epicardial leads. A comparison of steroid-eluting leads in endocardial and epicardial pacemakers has previously shown lower ventricular stimulation thresholds for endocardial leads than epicardial leads at the time of implant and at a two-year follow-up. However, there is insufficient evidence demonstrating important reductions of stimulation threshold in endocardial versus epicardial atrial leads. Furthermore, data showing important differences in impedance and sensing thresholds in epicardial and endocardial pacing in pediatric patients is lacking.

Lead reintervention (lead revision-replacement or generator change) occurred less frequently among the group receiving endocardial implants. Nine children as opposed to five required reintervention for generator change due to battery life depletion while seven as opposed to four (endocardial) underwent epicardial lead revisions. Significantly younger and smaller children with intrinsically higher heart rates and higher stimulation thresholds among recipients of epicardial implants partially explain increased battery depletion and higher generator change and reintervention rates in the epicardial group. Sachweh and colleagues found a similarly higher reoperation rate in individuals with epicardial leads due to higher acute and long-term pacing stimulation thresholds. Improvements in lead design technology and long-term stimulation thresholds may have neutralized these differences.

**Study Limitations**

The retrospective and observational study design limited the scope of data collection, particularly our inability to obtain complete and analyzable long-term chronic pacing parameters. During the study period there was no attempt to compare recently improved thin to thick diameter pacing leads as this feature may have influenced the acute sensing and stimulation thresholds reported in this series. Additional research and data gathering regarding long-term follow-up will be required to discern relative performances of various lead types within each lead design (epicardial or transvenous) for a
given manufacturer. We were not able to assess, in retrospect, complications of transvenous systems related to venous occlusion, thromboembolism, and AV valve damage. Some of these children remain asymptomatic with these subclinical events not detected in the absence of routine angiography or echocardiography.

Conclusions
Steroid-eluting epicardial pacing leads appear as safe and proficient as their endocardial counterparts in children. In light of expanding indications for pacing, biologic constraints of growing children, and limited endovascular domain, consideration of epicardial pacing systems remain an attractive alternative strategy. Continual refinement of pacemaker lead and battery technology may increase the attractiveness of the permanent epicardial pacing approach, particularly in light of complications of long-term endovascular pacing leads and potential needs for lead extraction.

References