Efficacy of Implantable Cardioverter Defibrillators in Young Patients With Catecholaminergic Polymorphic Ventricular Tachycardia
Success Depends on Substrate

Christina Y. Miyake, MD; Gregory Webster, MD; Richard J. Czosek, MD; Michal J. Kantoch, MD; Anne M. Dubin, MD; Kishor Avasarala, MD; Joseph Atallah, MD, CM, SM

Background—The effectiveness of implantable cardioverter-defibrillator (ICD) therapy for the management of catecholaminergic polymorphic ventricular tachycardia (VT) in young patients is not known. ICD discharges are not always effective and inappropriate discharges are common, both resulting in morbidity and mortality.

Methods and Results—This is a multicenter, retrospective review of young patients with catecholaminergic polymorphic VT and ICDs from 5 centers. ICD discharges were evaluated to determine arrhythmia mechanism, appropriateness, efficacy of therapy, and complications. A total of 24 patients were included. Median (interquartile range) ages at onset of catecholaminergic polymorphic VT symptoms and ICD implant were 10.6 (5.0–13.8) years and 13.7 (10.7–16.3) years, respectively. Fourteen patients received 140 shocks. Ten patients (42%) experienced 75 appropriate shocks and 11 patients (46%) received 65 inappropriate shocks. On actuarial analysis, freedom from appropriate shock at 1 year after ICD implant was 75%. Of appropriate shocks, only 43 (57%) demonstrated successful primary termination. All successful appropriate ICD discharges were for ventricular fibrillation. No episodes of polymorphic VT or bidirectional VT demonstrated successful primary termination. The adjusted mean (95% confidence interval) cycle length of successful discharges was significantly shorter than unsuccessful discharges (168 [152–184] ms versus 245 [229–262] ms; adjusted P=0.002). Electrical storm occurred in 29% (4/14) and induction of more malignant ventricular arrhythmias in 36% (5/14). There were no deaths.

Conclusions—ICD efficacy in catecholaminergic polymorphic VT depends on arrhythmia mechanism. Episodes of ventricular fibrillation were uniformly successfully treated, whereas polymorphic and bidirectional VT did not demonstrate successful primary termination. Inappropriate shocks, electrical storm, and ICD complications were common. (Circ Arrhythm Electrophysiol. 2013;6:579-587.)

Key Words: arrhythmia ■ catecholaminergic polymorphic ventricular tachycardia ■ electrical storm ■ implanted cardioverter defibrillator ■ pediatric ■ ventricular tachycardia

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a rare but highly malignant disease with an estimated prevalence of 1:10,000.1 Early onset of symptoms has been associated with a more malignant clinical course and sudden death rates have been reported to be as high as 25% to 50% by the age of 30 years.2–4 Arrhythmias associated with CPVT are classically polymorphic or bidirectional VTs triggered by adrenergic stimulation; however, ventricular fibrillation (VF) and atrial arrhythmias can also be seen.5,7–9 Although antiarrhythmic therapy has been the first-line approach to managing these patients, implantable cardioverter-defibrillators (ICDs) are also used as a treatment strategy.

Clinical Perspective on p 587

Information on the use of ICDs in this patient population is limited and conflicting. High rates of appropriate shocks have been reported but deaths have occurred, despite appropriate therapy.5,6,10,11 On the basis of small case reports, it seems that ICD discharges are sometimes but not always effective and, therefore, ICD implantation may not necessarily be life-saving.12 In fact, ICD implantation may potentially increase mortality risk. Death secondary to lethal arrhythmias triggered by inappropriate discharges has occurred.9 Despite these concerns, there have been no previous studies evaluating appropriate and effective therapy in these patients.

Received September 25, 2012; accepted April 9, 2013.

From the Department of Pediatrics, Lucile Packard Children’s Hospital, Stanford University, Palo Alto, CA (C.Y.M., A.M.D.); Department of Pediatrics, Lurie Children’s Hospital, Northwestern University Feinberg School of Medicine, Chicago, IL (G.W.); Department of Pediatrics, The Heart Center, Cincinnati Children’s Medical Center, Cincinnati, OH (R.J.C.); Department of Pediatrics, Children’s Hospital Oakland, Oakland, CA (K.A.); and Department of Pediatrics, Stollery Children’s Hospital, University of Alberta, Edmonton, Alberta, Canada (M.J.K., J.A.).

The online-only Data Supplement is available at http://circep.ahajournals.org/lookup/suppl/doi:10.1161/CIRCEP.113.000170/-/DC1.

Correspondence to Christina Y. Miyake, MD, Texas Children’s Hospital, 6621 Fannin St, MC 19345-C, Houston, TX 77030. E-mail cymiyake@texaschildrens.org or christinamiyake@gmail.com

© 2013 American Heart Association, Inc.

Circ Arrhythm Electrophysiol is available at http://circep.ahajournals.org DOI: 10.1161/CIRCEP.113.000170
This study aimed to describe the appropriateness and effectiveness of ICD therapy in young patients with CPVT, with an emphasis on factors associated with effective ICD therapy.

Methods

Study Population
We performed a multicenter retrospective review of young patients with CPVT from 5 centers in the United States and Canada who had an ICD placed between January 1999 and September 2011. This study was conducted under institutional review board approval obtained separately at each participating institution (Stanford University, Northwestern University, University of Alberta, Cincinnati Children’s Medical Center, Oakland Children’s Hospital). Inclusion criteria included (1) onset of CPVT symptoms before the age of 21 years, (2) diagnosis of CPVT made by genetic testing or clinical history as determined by a pediatric electrophysiologist, and (3) presence of an implanted ICD.

Patient and ICD Characteristics
Data collection included demographics, symptoms, dates of presentation and therapy, medical management, length of follow-up, and family history. Details on exercise testing, genetic testing, and electrophysiology studies were collected. An exercise test or electrophysiology study was considered positive for the purpose of the CPVT diagnosis if it documented a ≥3 beat run of bidirectional VT (BDVT) or polymorphic VT (PMVT). Indication for primary or secondary prevention ICD was recorded. Secondary prevention was defined as documented sustained or hemodynamically unstable VT, VF, or resuscitated cardiac arrest. All ICD-related complications were recorded.

ICD Discharge Data
Each center submitted all available electrograms for each ICD discharge. Electrograms were available for 119 (85%) of all discharges. A blinded committee reviewed and classified all ICD discharge tracings and each tracing was independently reviewed by ≥2 pediatric electrophysiologists. If electrograms were not available for an event, the event was classified as reported by the patient’s treating electrophysiologist. Electrical storm was defined as appropriate ICD discharges within 24 hours.

Appropriate therapy was defined as ICD discharges for VT (PMVT or BDVT) or VF. Discharges were classified as inappropriate if a shock was delivered for noise, oversensing, sinus, or other forms of supra-VT, ventricular ectopy, or after spontaneous termination of an arrhythmia (Figure 1A and 1B). A discharge was defined as effective if it resulted in primary termination of the arrhythmia (Figure 2A). For the purposes of this study, shock events without electrical storm were classified as primary termination if the clinical record demonstrated constant amplitude but shift in morphology or axis and a mean cycle length (CL) >200 ms. BDVT was defined as VT with a consistent pattern of alternating QRS axis and morphology. VF was defined as an irregular VT with a mean CL <200 ms or if 75% of recorded CLs were <260 ms. Mean CL was measured by averaging all CLs used by the device to meet VF detect criteria. If electrograms were not available, mean CL was calculated using the average ventricular rate reported by the device and description of the tachyarrhythmia by the patient’s electrophysiologist was used to make the best determination of the arrhythmia.

Appropriate therapy was defined as ICD discharges for VT (PMVT or BDVT) or VF. Discharges were classified as inappropriate if a shock was delivered for noise, oversensing, sinus, or other forms of supra-VT, ventricular ectopy, or after spontaneous termination of an arrhythmia (Figure 1A and 1B). A discharge was defined as effective if it resulted in primary termination of the arrhythmia (Figure 2A). For the purposes of this study, shock events without electrical storm were classified as primary termination if the clinical record demonstrated constant amplitude but shift in morphology or axis and a mean cycle length (CL) >200 ms. BDVT was defined as VT with a consistent pattern of alternating QRS axis and morphology. VF was defined as an irregular VT with a mean CL <200 ms or if 75% of recorded CLs were <260 ms. Mean CL was measured by averaging all CLs used by the device to meet VF detect criteria. If electrograms were not available, mean CL was calculated using the average ventricular rate reported by the device and description of the tachyarrhythmia by the patient’s electrophysiologist was used to make the best determination of the arrhythmia.

Statistical Analysis
Continuous variables are presented as mean with SD or median with interquartile ranges (IQRs), depending on the normality of their distribution. Categorical variables are expressed as counts and percentages. Continuous variables were compared using analysis of variance (ANOVA) for normally distributed variables and a Kruskal-Wallis test for non-normally distributed variables. Categorical variables were compared using chi-square tests or Fisher’s exact test as appropriate. A P-value <0.05 was considered statistically significant.

Figure 1. A, Inappropriate shock caused by atrial tachycardia resulting in a more malignant ventricular arrhythmia. Top electrogram (EGM): RVtip to RVring, bottom EGM: HVA to RVring. B, Inappropriate shock caused by spontaneous termination before implantable cardioverter-defibrillator discharge. Top EGM: RVtip to RVring, bottom EGM: Can to RV coil. C, Appropriate but unsuccessful shock for polymorphic ventricular tachycardia. Top EGM: RVtip to RVring, bottom EGM: Can to RV coil.
distribution, and were analyzed using the t test or the Wilcoxon rank-sum test. Categorical variables are presented as counts with percentages and were analyzed using the Fisher Exact test or the χ² test. A Kaplan–Meier survival curve was constructed to examine the time-dependent freedom from a first appropriate shock after ICD implantation. The 1-year data are reported with 95% confidence intervals (CIs). The observed means and CI for successful versus unsuccessful shock CI ignoring repeated measures, as well as the predicted population means and 95% CI from a repeated measures mixed effects model considering multiple measurements for each subject are reported. Data are reported as adjusted 𝑃 value. Statistically significant data were defined as a 𝑃<0.05. Data analysis was performed using SAS version 9.3 (SAS Institute, Inc, Cary, NC).

Results

Patient Characteristics
A total of 24 patients (11 men, 13 women), each from different families, were included in this study. The majority of patients were probands (23/24; 96%). No affected family members met inclusion criteria for this study. Demographic data and presenting symptoms are listed in Table 1. Median (IQR) age at onset of symptoms consistent with CPVT was 10.6 (5.0–13.8) years. The majority of patients (67%) presented with a history of exertional or emotionally triggered syncope consistent with CPVT, whereas 6 patients (25%) presented with aborted sudden cardiac arrest. The median (IQR) time from initial symptoms to diagnosis was 4.0 (0.4–6.4) years. None of the patients had a history of left sympathetic cardiac denervation.

Diagnostic Testing
Diagnostic testing varied by center. Exercise stress tests and electrophysiology studies were not performed on all patients before initiation of β-blocker therapy or ICD implant. In total, 14 of 24 patients (58%) underwent exercise stress testing before initiation of antiarrhythmic medications and 13 patients (93%) had positive results. The remaining patient had single premature ventricular contractions during exercise. A total of 9 patients underwent an electrophysiology study before initiation of any antiarrhythmic medication and 7 (78%) had spontaneous induction of PMVT after infusion of isoproterenol or epinephrine. None of these patients had a pace-inducible ventricular arrhythmia, but in 2 patients AT was pace induced.

Genetic testing was performed in 16 of 24 patients (67%) and a probable candidate gene mutation was identified in the ryanodine receptor (RyR2) in 10 patients (63%; Tables 1 and 2). Among the remaining 6 patients who tested negative for ryanodine receptor defects, 3 patients underwent further testing for Calsequestrin defects and each tested negative. Five patients (21%) had a family history of CPVT.

Antiarhythmic Medications
Seventeen patients (71%) were on β-blocker therapy before ICD placement. Patients not receiving β-blocker medications at implant either had an initial presentation of aborted cardiac arrest (4) or the specific diagnosis of CPVT was made after ICD implantation (3). None of the patients were on flecainide before ICD implant. All patients received β-blocker therapy after ICD implant. Antiarrhythmic therapy before and after ICD implantation is shown in Table 2.

ICD Data
The median (IQR) age at ICD implant was 13.7 (10.7–16.3) years. Indications for implantation included aborted cardiac arrest (8 patients), syncope or VT on medical therapy (12 patients), and history of syncope with documented sustained or nonsustained VT before medical therapy (4 patients). In total, indication for ICD implantation was primary prevention in 12 patients and secondary prevention in 12 patients.

Single-chamber devices were implanted in 14 patients (58%), whereas the remainder had dual-chamber systems. A total of 20 patients (83%) had transvenous and 4 (17%) had epicardial systems. There were no subcutaneous systems. The majority (17 patients; 71%) received single coil ICD leads. All patients underwent successful defibrillation threshold testing without complication. Over a median (IQR) follow-up time of 3.3 (1.1–5.8) years, 8 patients (33%) had a total of
15 ICD-related complications (8 lead failures/fractures or lead dislodgements, 1 device recall, 1 improper setscrew, 4 pocket revisions, and 1 subclavian vein stenosis).

ICD Shocks
Among 24 patients, 14 (58%) experienced a total of 140 ICD discharges during a median (IQR) follow-up time of 3.3 (1.1–5.8) years (Figure 3). Median (IQR) number of discharges per patient was 8 (1–29). Three patients received only appropriate discharges and 4 patients received only inappropriate discharges. The remaining 7 patients received both appropriate and inappropriate discharges. Median (IQR) time to first appropriate shock was 1.3 (0.9–3.3) years and inappropriate shock 1.7 (0.8–2.6) years.

Appropriate Versus Inappropriate Shocks
Of 140 shocks, 75 (54%) were appropriate and involved 10/24 patients (42%), whereas the remaining 65 inappropriate discharges (46%) involved 11/24 patients (46%; Figure 4). The first appropriate ICD discharge was delivered for VF (mean±SD CL, 164±17 ms) in 7 patients and PMVT (mean±SD CL, 251±34 ms) in 3 patients. All appropriate shocks, including multiple shocks per patient, were delivered for 43 VF (mean±SD CL, 155±21 ms), 29 PMVT (mean±SD CL, 252±21 ms), and 3 BDVT (mean±SD CL, 245±5 ms). On actuarial survival analysis, freedom from the first appropriate shock per patient was 75% (95% CI, 49.6–88.8) at 1 year after ICD implantation (Figure 5). The most common reasons for inappropriate discharges were AT (24 events; 36%) and spontaneous termination of a ventricular arrhythmia before ICD discharge (22 events; 34%). Spontaneous termination of 3 VF (mean±SD CL, 153±25 ms), 14 PMVT (mean±SD CL, 277±36 ms), 2 BDVT (mean±SD CL, 269±22 ms), and 5 ventricular ectopy (mean±SD CL, 286±19 ms) resulted in inappropriate discharges.

A total of 24 shocks for AT (mean±SD CL, 269±29 ms) occurred among 8 patients, 3 of whom had dual-chamber devices. Of the 18 shocks with available electrograms for review, there was spontaneous AT termination before shock delivery in 2, primary termination in 5, secondary termination in 3, spontaneous termination after an unsuccessful shock in 4, and in 4 patients subsequent shocks were delivered. Primary termination of 5 AT episodes occurred in 3 patients with
single-chamber devices; electrograms demonstrated a regular rhythm in 3 episodes and an irregular rhythm in 2 episodes.

**Mechanism of Arrhythmia and Pattern of Termination**

Arrhythmia mechanism resulting in ICD detection and discharge included 46 episodes of VF, 43 PMVT, 5 BDVT, 5 ventricular ectopy, and 24 AT. The remaining 17 ICD discharges occurred because of lead fracture and noise (Figures 3 and 4).

Among 75 appropriate discharges, effective primary termination occurred in discharges (57%, 7 patients). All 43 episodes were for VF and, therefore, 100% of VF episodes that persisted to defibrillation demonstrated primary termination. Electrograms were available for 39 of the 43 VF episodes. In the 4 episodes without electrogams, the primary electrophysiologist reported VF and the mean arrhythmia CL range was 130 to 160 ms. The remaining 3 VF episodes were classified as inappropriate shocks because VF terminated before ICD discharge.

Ineffective ICD discharges were seen in 32 of the 75 (43%) appropriate discharges (3 patients). All 32 episodes were for PMVT (29) or BDVT (3). Of these 32 ineffective discharges, 5 (16%) demonstrated secondary termination within 3 s, 15 (47%) demonstrated spontaneous termination after 3 s, and 12 (37%) required 1 or more subsequent shocks. The adjusted mean (95% CI) CL of ventricular arrhythmias resulting in successful termination was significantly shorter than in those that did not primarily terminate (168 [152–184] ms versus 245 [229–262] ms; adjusted \( P=0.002 \)). The observed mean and CI for successful versus unsuccessful shocks, not taking into account repeated measures, were 163 ms (95% CI, 153–173 ms) and 251 ms (95% CI, 244–260 ms), respectively. Details on appropriate, inappropriate, effective, and ineffective discharges are listed in Figure 4. One patient exhausted ICD therapy but survived after the VT eventually spontaneously terminated.

Interestingly, reported compliance with medical therapy, per shock, was higher in the successful (36/43; 84%) versus the unsuccessful shock group (11/32; 34%).

**Primary Versus Secondary Prevention**

Two of 12 (17%) patients in the primary prevention group and 8 of 12 (67%) patients in the secondary prevention group

---

**Table 2. Patient Data: ICD Indication, Antiarrhythmic Therapy, Shock History, Genetic Testing, and Follow-Up**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age at First Sx, y</th>
<th>Reason for ICD</th>
<th>Meds Pre-ICD</th>
<th>Meds Post-ICD</th>
<th>Follow-up Since ICD, mo</th>
<th>Total No. of Shocks</th>
<th>Types of Shocks</th>
<th>Gene Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>5</td>
<td>P</td>
<td>Bisoprolol</td>
<td>Bisoprolol</td>
<td>13</td>
<td>0</td>
<td>—</td>
<td>RYR2</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>14</td>
<td>S</td>
<td>Nadolol, propranolol, mexiletine, sotalol</td>
<td>Nadolol</td>
<td>68</td>
<td>4</td>
<td>Both</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>9</td>
<td>S</td>
<td>Nadolol</td>
<td>Nadolol</td>
<td>30</td>
<td>8</td>
<td>App</td>
<td>Neg</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>10</td>
<td>S</td>
<td>—</td>
<td>Metoprolol</td>
<td>68</td>
<td>8</td>
<td>Both</td>
<td>RYR2</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>12</td>
<td>P</td>
<td>Nadolol</td>
<td>Nadolol, verapamil</td>
<td>56</td>
<td>2</td>
<td>Inapp</td>
<td>—</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>14</td>
<td>P</td>
<td>Metoprolol</td>
<td>Metoprolol</td>
<td>97</td>
<td>18</td>
<td>Both</td>
<td>—</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>16</td>
<td>P</td>
<td>—</td>
<td>Atenolol</td>
<td>37</td>
<td>8</td>
<td>App</td>
<td>Neg*</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>5</td>
<td>P</td>
<td>Atenolol</td>
<td>Atenolol</td>
<td>11</td>
<td>0</td>
<td>—</td>
<td>RYR2</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>6</td>
<td>P</td>
<td>Atenolol</td>
<td>Atenolol</td>
<td>4</td>
<td>0</td>
<td>—</td>
<td>RYR2</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>11</td>
<td>P</td>
<td>Metoprolol, nadolol, diltiazem, verapamil, digoxin</td>
<td>71</td>
<td>5</td>
<td>Inapp</td>
<td>Neg*</td>
<td></td>
</tr>
</tbody>
</table>

App indicates appropriate shocks; Both, appropriate and inappropriate shocks; F, female; Inapp, inappropriate shocks; M, male; Neg, negative; P, primary prevention; S, secondary prevention; sx, symptoms.

*Calsequestrin was tested and result was negative.
received an appropriate discharge. Although none of the primary prevention group had VF or an effective discharge, 7 of 12 patients (58%) who received an ICD for secondary prevention had VF and received an effective shock.

**Electrical Storm and Induction of More Malignant Arrhythmias**

Twelve discharges (in 5 patients) or 8.5% of total shocks resulted in a more malignant ventricular arrhythmia. The arrhythmias responsible for these ICD discharges included 3 PMVT, 8 AT, and 1 ventricular ectopy. In 11 of the 12 discharges, the shock-induced ventricular arrhythmia eventually spontaneously terminated; however, 5 discharges resulted in the patient receiving ≥1 inappropriate shock secondary to committed device therapy. In 1 patient, shock for an AT resulted in induction of PMVT and 3 subsequent shocks were delivered with eventual secondary termination. Four of 14 patients (29%) who received ICD therapy had electrical storm events secondary to ICD discharges. There were no patient deaths.

**Compliance With Medications**

Patients were thought to be noncompliant with medications at the time of 61 ICD discharges (44%). In 54 ICD discharges (38%), patients were thought to be compliant with medications. In the remaining 25 ICD discharges (18%), compliance with medications could not be determined by medical chart review.

**Discussion**

Young patients with CPVT are at high risk for life-threatening arrhythmias and sudden death.2-4,6,10,11,15 β-blockers are not always effective,2-3,6,10,12,16 and in some patients, ICD and left cardiac sympathetic denervation are being used as management strategies.17 However, death can occur, despite ICD implantation.9,11 Reports have shown that ICD therapy can be ineffective or dangerous,9,11,12 but no mechanism for this phenomenon has been established. Furthermore, previous studies have suggested that inappropriate discharges are secondary to supraventricular arrhythmias3,5,6 (Table 1; online-only Data Supplement). Our study found that (1) the rate of appropriate therapy is high, but only half are effective, (2) effective therapy is likely related to arrhythmia mechanism, and (3) inappropriate therapy is because of both supraventricular arrhythmias and spontaneous termination of arrhythmia before ICD discharge.

---

**Figure 3.** Arrhythmia mechanisms resulting in 140 implantable cardioverter-defibrillator discharges. AT, atrial tachycardia; BDVT, bidirectional ventricular tachycardia; Noise, noise on electrogram secondary to lead fracture; PMVT, polymorphic ventricular tachycardia; VE, ventricular ectopy; and VF, ventricular fibrillation.

**Figure 4.** Appropriate versus inappropriate shocks and successful versus unsuccessful termination. AT indicates atrial tachycardia; BDVT, bidirectional ventricular tachycardia; CI, confidence interval; CL, cycle length; PMVT, polymorphic ventricular tachycardia; Noise, noise on electrogram secondary to lead fracture; Spont Term, spontaneous termination of arrhythmia before implantable cardioverter-defibrillator discharge; Sub shock, subsequent shock; VEctopy, ventricular ectopy; and VF, ventricular fibrillation.
Patients with VF that persisted to defibrillation demonstrated 100% effective primary termination. No episodes of PMVT or BDVT successfully terminated. Previous studies have demonstrated the mechanism of arrhythmia origination for BDVT and PMVT in CPVT to be abnormal calcium regulation and delayed after depolarizations (DADs). Modeling studies suggest that origination and alternation of premature beats between the right and the left bundle branches of the purkinje system (the Ping-Pong mechanism) result in BDVT. When DADs arise from multiple purkinje sites, PMVT ensues. PMVT may spontaneously terminate, possibly explaining the high incidence of secondary or spontaneous termination seen after ICD therapy in this cohort, or may degenerate into VF, the arrhythmia that is likely responsible for sudden cardiac death in patients with CPVT. BDVT and PMVT arise from focal DADs and catecholamine surges after ICD discharge can increase further DADs. We, therefore, speculate that BDVT and PMVT are less amenable to defibrillation, whereas VF is a large wavefront of myocardial depolarization that will respond to ICD therapy. Arrhythmia substrate and mechanism in CPVT patients may explain our findings of (1) successful defibrillation for VF, (2) unsuccessful therapy for BDVT and PMVT, and (3) the incidence of more malignant arrhythmias after ICD discharges.

Patients with CPVT are known to have atrial tachyarrhythmias, but therapy for these supraventricular arrhythmias has not been studied. Studies have demonstrated DADs in atrial myocytes and decreased conduction velocities because of defects in RYR2, which can lead to atrial arrhythmias and potential atrial fibrillation. A total of 8 patients received 24 shocks for AT. Interestingly, 5 of these episodes (in 3 patients) demonstrated primary termination, 2 of which were irregular tachycardias and 3 regular tachycardias. Primary termination seen in irregular ATs may be explained by atrial fibrillation. Reasons for primary termination of regular AT seen in this cohort are not clear and further studies are needed. Because each of these 3 patients had single-chamber devices, we cannot exclude the possibility of a reentrant supra-VT.

A high rate of inappropriate therapy caused by spontaneous rhythm termination before ICD discharge was seen throughout this cohort. Overall, 46% of patients experienced an inappropriate discharge, a significantly higher percentage than the published rates of 25% to 30% in other pediatric device patients. Our study confirmed high rates of inappropriate discharge for supraventricular arrhythmias, as previously reported, however, we also found that spontaneous termination of ventricular arrhythmias accounted for an equally high rate of inappropriate discharge. This has not been previously reported and is an important consideration in terms of ICD programming for these patients.

Changes in ICD programming may help prevent unnecessary discharges and specific ICD programming details (which vary among devices) need to be considered in this patient population. In this study, all inappropriate shocks caused by spontaneous termination before ICD discharge may have been avoided. To avoid shocks secondary to ventricular ectopy and nonsustained brief runs of PMVT after VT/VF termination, setting a single VF zone to a substantially shorter CL (range, 200–260 ms) would have decreased reconfirmation intervals and along with increasing redetect duration may have also helped limit shocks to sustained VF episodes. Although in this cohort of patients, the above programming adjustments may have limited inappropriate shocks, device selection and programming should be individualized to each specific patient.

Preventing inappropriate ICD shocks may particularly be important among patients with CPVT as we found that device therapy may be harmful. Among the 14 patients who received device therapy, 5 (36%) had more malignant arrhythmias and 4 (29%) had electrical storm. We suspect that ICD discharge results in catecholamine surges that potentiate further DADs. These findings are quite concerning, as patients with CPVT are sensitive to catecholaminergic surges and hypothetically these surges could result in death. Despite these potential concerns, as well as relatively high rates of defibrillation failure and inappropriate device therapies, none of these events led to death in this cohort.

ICD therapy, although potentially life-saving, comes at a heavy cost in this patient population. Compliance with medications is paramount and use of flecainide and left sympathetic
cardiac denervation may decrease the need for ICDs in the future; however, if ICDs are implanted, programming needs to be adjusted to reduce the risks of inappropriate shocks and mortality from therapy exhaustion. Extending detection times and altering reconfirmation rates (to account for frequent spontaneous termination and ventricular ectopy), as well as adjusting ICD detection rates to shorter CLs (for detection of VF rather than VT) may improve outcomes for these patients. Specific rates and detection periods will need to be individually adjusted. The authors found atrial arrhythmias to be frequently (57%) among patients who received shocks and that dual-chamber devices were often helpful in discriminating atrial versus ventricular arrhythmias; however, further studies are needed to better understand atrial arrhythmias in this population and determine whether there is evidence to support the extra atrial lead burden.

Limitations
This is a retrospective study with a small patient population. Although 63% of patients who underwent genetic testing were positive, only 42% of our patients had genetic confirmation of their CPVT diagnosis. Electrograms at the time of ICD discharge were not available for all events. Because some unknown electrograms were classified as successful on the basis of the treating electrophysiologist’s note, without independent review of the tracings, we may have overestimated the rate of successful discharges. The clinical definitions of arrhythmia mechanism (VF, PMVT, and BDVT) were based on prior published ICD studies, but there may be a continuum in these mechanisms, and this classification may not accurately reflect the cellular arrhythmia substrate. Alternatively, the rate of the tachycardia may be important to successful defibrillation. Although a mean CL of 163 ms during tachycardia could be rapid PMVT susceptible to defibrillation, we felt that the electrograms and rate of tachycardias were most consistent with VF. Rhythms suspected to be AT were based on identical electrograms in arrhythmia and during sinus rhythm but a majority of patients had single-chamber ICDs. This limited our ability to distinguish atrial from VTs and we may have misclassified certain arrhythmia mechanisms.

Conclusion
ICD efficacy in young patients with CPVT depends on arrhythmia substrate or tachycardia CL. ICD therapy, although potentially life-saving for VF, may be ineffective for PMVT or BDVT and proarrhythmic in a significant subset. Atrial arrhythmias and spontaneous termination of ventricular arrhythmias before ICD discharge contribute to high rates of inappropriate discharges. The risks and benefits of ICD therapy in patients with CPVT should be carefully considered before implantation, particularly for primary prevention. Identifying those at highest risk, as well as optimizing ICD configuration and programming may help improve effectiveness and decrease related comorbidities. Left sympathetic cardiac denervation may also be an important and alternative treatment strategy for these patients. A comparative evaluation of such different strategies may prove to be clinically valuable.

Disclosures
Drs Miyake and Dubin receive fellowship-funding support from Medtronic, Inc. No direct or indirect support was provided for this study. The other authors have no conflict to report.

References
CLINICAL PERSPECTIVE

Catecholaminergic polymorphic ventricular tachycardia is rare but represents one of the most malignant inheritable arrhythmia syndromes. Optimal treatment strategies are not clear. Implantable cardioverter-defibrillators (ICD) are being used, despite limited and conflicting data on their efficacy. ICDs may not always terminate arrhythmias and deaths have occurred, despite an implanted ICD. This study highlights potential risks of ICD implantation and may shed some light on optimizing ICD programmability in patients with catecholaminergic polymorphic ventricular tachycardia. We report a high rate of ineffective appropriate discharges, as well as a high rate of inappropriate discharges, both related to the underlying arrhythmia mechanism. Although the hallmark arrhythmia in catecholaminergic polymorphic ventricular tachycardia is bidirectional ventricular tachycardia, effective appropriate shocks were only observed for ventricular fibrillation. Shocks for ventricular tachycardias, monomorphic or polymorphic, were ineffective. As expected, the cycle length was significantly shorter for arrhythmias receiving effective shocks. These findings are important for practicing clinicians treating young patients with catecholaminergic polymorphic ventricular tachycardia who have an ICD or in those patients in whom an ICD is being contemplated. The data may help physicians better anticipate the therapeutic potential of ICDs in this patient population. Our results suggest that specific programming settings for detection zones and rates may help decrease inappropriate and potentially harmful shocks.
Efficacy of Implantable Cardioverter Defibrillators in Young Patients With Catecholaminergic Polymorphic Ventricular Tachycardia: Success Depends on Substrate Efficacy

Christina Y. Miyake, Gregory Webster, Richard J. Czosek, Michal J. Kantoch, Anne M. Dubin, Kishor Avasarala and Joseph Atallah

_Circ Arrhythm Electrophysiol_. 2013;6:579-587; originally published online May 11, 2013; doi: 10.1161/CIRCEP.113.000170

_Circulation: Arrhythmia and Electrophysiology_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Copyright © 2013 American Heart Association, Inc. All rights reserved.

Print ISSN: 1941-3149. Online ISSN: 1941-3084

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://circep.ahajournals.org/content/6/3/579

Data Supplement (unedited) at:

http://circep.ahajournals.org/content/suppl/2013/05/11/CIRCEP.113.000170.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation: Arrhythmia and Electrophysiology_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation: Arrhythmia and Electrophysiology_ is online at:
http://circep.ahajournals.org/subscriptions/
### Table 1. Previous studies of CPVT patients with ICDs

<table>
<thead>
<tr>
<th>Study</th>
<th># pts with ICD</th>
<th>Age at onset of symptoms</th>
<th># pts with appropriate shocks</th>
<th># pts with inappropriate shocks</th>
<th>Reason for inappropriate shocks</th>
<th># pts with ineffective shocks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celiker et al</td>
<td>4</td>
<td>All children</td>
<td>3/4 (75%)</td>
<td>3/4 (75%)</td>
<td>TWO</td>
<td>Not reported</td>
</tr>
<tr>
<td>Cardiol Young 2009</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Incr HR</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lead fracture</td>
<td></td>
</tr>
<tr>
<td>Marai et al</td>
<td>6</td>
<td>Not reported</td>
<td>4/6 (67%)</td>
<td>Not reported</td>
<td>-</td>
<td>2/4 (50%)</td>
</tr>
<tr>
<td>Am J Cardiol 2009</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Priori et al</td>
<td>12</td>
<td>7 pts &lt;21 yrs, 4 pts &gt;21 yrs</td>
<td>6/12 (50%)</td>
<td>Not reported</td>
<td>-</td>
<td>Not reported</td>
</tr>
<tr>
<td>Circulation 2002</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sy et al</td>
<td>15</td>
<td>Not reported</td>
<td>4/15 (27%)</td>
<td>5/15 (33%)</td>
<td>SVT</td>
<td>Not reported</td>
</tr>
<tr>
<td>Heart Rhythm 2011</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hayashi et al</td>
<td>16</td>
<td>20 +/- 11 yrs</td>
<td>4/16 (25%)</td>
<td>6/38 (38%)</td>
<td>Sinus tach</td>
<td>Not reported</td>
</tr>
<tr>
<td>Circulation 2009</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lead fracture</td>
<td></td>
</tr>
<tr>
<td>Miyake et al</td>
<td>24</td>
<td>10 yrs (2-16 yrs)</td>
<td>10/24 (42%)</td>
<td>11/24 (46%)</td>
<td>Atrial tach</td>
<td>8/14 (57%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Spont term</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Vectopy</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lead fracture</td>
<td></td>
</tr>
</tbody>
</table>

TWO – T wave oversensing; Incr HR – increase heart rate; tach – tachycardia; spont term – spontaneous termination of arrhythmia prior to ICD discharge