Results of a Multicenter Retrospective Implantable Cardioverter-Defibrillator Registry of Pediatric and Congenital Heart Disease Patients

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Objectives
We sought to determine the implications of implantable cardioverter-defibrillator (ICD) placement in children and patients with congenital heart disease (CHD).

Background
There is increasing frequency of ICD use in pediatric and CHD patients. Until recently, prospective registry enrollment of ICD patients was not available, and children and CHD patients account for only a small percentage of ICD recipients. Therefore, we retrospectively obtained collaborative data from 4 pediatric centers, aiming to identify implant characteristics, shock frequency, and complications in this unique population.

Methods
Databases from 4 centers were collated in a blinded fashion. Demographic information, implant electrical parameters, appropriate and inappropriate shock data, and complications were recorded for all implants from 1992 to 2004.

Results
A total of 443 patients were included, with a median age of 16 years (range 0 to 54 years) and median weight of 61 kg (range 2 to 130 kg), with 69% having structural heart disease. The most common diagnoses were tetralogy of Fallot (19%) and hypertrophic cardiomyopathy (14%). Implant indication was primary prevention in 52%. Shock data were available on 409 patients, of whom 105 (26%) received appropriate shocks (mean 4 shocks/patient, range 1 to 29 shocks/patient). Inappropriate shocks occurred in 87 of 409 patients (21%), with a mean of 6 per patient (range 1 to 60), mainly attributable to lead failure (14%), sinus or atrial tachycardias (9%), and/or oversensing (4%).

Conclusions
Children and CHD ICD recipients have significant appropriate and inappropriate shock frequencies. Optimizing programming, medical management, and compliance may diminish inappropriate shocks. Despite concerns regarding generator recalls, lead failure remains the major cause of inappropriate shocks, complications, and system malfunction in children. Prospective assessment of ICD usage in this population may identify additional important factors in pediatric and CHD patients. (J Am Coll Cardiol 2008;51:1685–91) © 2008 by the American College of Cardiology Foundation

Implantable cardioverter-defibrillator (ICD) therapy was introduced in the 1980s, and over the past few decades, it has been used with increasing frequency in children and patients with congenital heart disease (CHD). Advances in technology have allowed downsizing of devices and leads, making them more suitable for application in children. Until recently, prospective enrollment of ICD patients in a national registry was not available, and children and CHD patients account for only a very small percentage (<1%) of all ICD recipients. Therefore, we sought to retrospectively obtain collaborative data from 4 pediatric ICD implanting centers, aiming to identify implant characteristics, shock frequency, and long-term complications in this unique patient population. There have been prior pediatric reports of ICD use in children, mainly involving either mining and subset extraction from manufacturers’ databases or relatively small single-center descriptive reports (Table 1) (1–14).
Methods

Databases from 4 centers were reviewed and collated in a blinded fashion for review by the investigators. Local investigational review board approval was obtained at each site. Two of the centers were combined because they had overlapping physician implanters and to allow adequate subgroup sample size. The databases were queried for pediatric and adult CHD patients with ICDs implanted between March 1992 and March 2004 to allow sufficient time after device implantation for observation of shocks and complications. Demographic information, implant electrical parameters, appropriate and inappropriate shock data, and complications were recorded for all implants occurring within the specified time frame. Demographics included patient age, weight, gender, anatomic diagnosis, and electrical diagnosis. The implant data included type of ICD, type of lead, indication for implant, electrical parameters, and defibrillation threshold when available. The indications for implantation and other implant data were determined contemporaneously at each center from available records at time of implant and were then retrospectively adjudicated by chart review. The shock data included the receipt of any shocks (whether appropriate or inappropriate), number of shocks per episode, number of episodes shocked, time of shock since ICD implanted, and whether the shock was successful at converting rhythm. Shock data were also assessed by era of implant, divided into 2 equal groups. In addition, shock data were subanalyzed by implanting center to investigate variances in implant indications. Complications were compiled by time since implant and divided into acute (within 30 days of ICD implant) and chronic complications.

Statistics. Continuous variables were expressed as medians and ranges. Comparisons between medians were made with the Wilcoxon rank-sum test. Event data (shock frequency) were analyzed using the chi-square or Fisher exact test depending on sample size. Multivariable analysis (comparisons between centers) used analysis of variance, with Scheffe’s subgroup testing where appropriate. A value of p < 0.05 was considered significant for individual comparisons.

Results

Demographics. Over the 12-year study period, a total of 443 patients were included, with a median age of 16 years (mean age 18 years, range 0 to 54 years) and median weight of 61 kg (mean 61.3 ± 22.9 kg, range 2 to 130 kg). The mean height of subjects at time of first ICD implant was 160.7 ± 21.3 cm, and mean body surface area was 1.64 ± 0.4 m². A total of 307 patients (69%) had structural heart disease, including various types of CHD (46%) or cardiomyopathy (23%) (Fig. 1). The most common structural diagnoses seen were tetralogy of Fallot (19%) and hypertrophic cardiomyopathy (14%). Primary electrical diseases with a structurally normal heart, such as long-QT syndrome, Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia, accounted for 31% of patients (Fig. 2). There were 7 infants who underwent first ICD implantation at <1 year of age (Table 2). Adult patients (age >21 years) accounted for 111 of 443 patients (25%) and, not surprisingly, were much more likely to have CHD (n = 96; 86%) compared with dilated or hypertrophic cardiomyopathies (n = 11) or primary electrical diseases (n = 4).

Implant characteristics. The indications for ICD implantation were primary prevention in 231 patients (52%) and secondary prevention in 212 patients (48%). There was some variation in implant indications between centers and over time, with primary prevention indications more prevalent in the recent era (years 2000 to 2004) compared with the first half of the study group (Fig. 3). The ICD generator type selected was single-chamber in 186 patients (42%) and dual-chamber in 257 patients (58%). The defibrillator lead type was overwhelmingly active-fixation (429 patients, 97%), with only 14 patients receiving passive-fixation ICD leads at initial implant. The leads were single-coil in 199 patients.
and dual-coil in 244 patients (55%). There were no implant procedure-related deaths.

**Shocks. APPROPRIATE SHOCKS.** Defibrillation therapy for a ventricular arrhythmia faster than the programmed detection criteria, and accurately detected by the ICD, was categorized as an appropriate shock. Information regarding shocks was available on 409 of 443 patients (92%) in the databases, of whom 105 patients (26%) received appropriate shocks, at a mean of 4 shocks per patient (median 2, range 1 to 29). Appropriate shocks were more common in patients who received an ICD for secondary prevention (32%) compared with primary prevention (18%, p < 0.001). Although most patients who received an appropriate shock did so within the first 5 years, 7 patients (7%) did not receive a shock until after receiving their second ICD generator at a mean of 5.5 years after their initial ICD implantation. When evaluation was between implant eras, appropriate shocks occurred more commonly among those implanted from 1992 to 1999 (35%) compared with 2000 to 2004 (20%, p < 0.05). Obviously, this difference is at least partially accounted for by the differences in length of follow-up between the 2 cohorts, as well as differences in implant indications and disease severity. These trends for implant indication and implant era were similar among all of the individual study centers (Fig. 4).

In an attempt to distinguish clinical differences between children and adult congenital ICD patients, the shock frequency was analyzed by age. Overall, appropriate shocks were observed in 66 of 290 (23%) pediatric patients (age < 18 years) and in 39 of 119 (33%) patients over age 18 years (p < 0.05, chi-square test). There were no differences seen in subgroup testing among different diagnostic categories (primary electrical diseases vs. congenital disease).
heart disease vs. cardiomyopathies) for either pediatric or adult patients.

**INAPPROPRIATE SHOCKS.** Defibrillation therapy received for anything other than a ventricular arrhythmia faster than the programmed detection criteria was categorized as an inappropriate shock. Inappropriate shocks occurred in 87 of 409 patients (21%), with a mean of 6 inappropriate shocks per patient (median 4, range 1 to 60), mainly attributable to lead failure (14%), sinus or atrial tachycardias (9%), and/or oversensing (4%). Inappropriate shocks occurred with similar frequency for primary versus secondary implant indications, and there were no differences when analyzed by centers. When analyzed by age groups, 70 of 290 (24%) pediatric patients (age <18 years) experienced at least 1 inappropriate shock, compared with only 17 of 119 (14%) adult patients over 18 years old (p < 0.05, chi-square test). In pediatric subgroup analysis, an inappropriate shock was less likely to have been received in cardiomyopathy patients (13%) compared with primary electrical disease (31%) or congenital heart disease (28%) patients (p < 0.01).

Following an inappropriate shock that was not related to lead problems, specific clinical interventions included 1) encouraging better compliance with medications such as beta-blockers; 2) initiation of an antiarrhythmic medication; 3) catheter ablation for atrial flutter; or 4) device reprogramming, such as tachycardia detection rates, R-wave sensing, blanking periods, and use of tachycardia discrimination algorithms. Multiple interventions were performed in some of these patients (sometimes simultaneously), precluding analysis of the effect of specific changes. However, following these overall clinical management strategies, there were less frequent shocks among the cohort, particularly for sinus tachycardia, and the inappropriate shock frequency was markedly reduced or eliminated for some individual subjects.

**Complications.** A total of 64 acute complications occurred in 55 patients during the first 30 days after implant (Table 3). Of these, most directly resulted from the initial implantation surgery, such as lead placement issues, infections, bleeding, and vascular problems. The chronic complications were more difficult to fully ascertain, but at least a lower boundary was identified, as not all follow-up complications may have been documented. The majority of chronic complications related to lead issues, including conductor fractures, insulation breaches, and changes in electrical characteristics. There was not any specific manufacturer or model of lead that had a higher failure rate in this series. In addition, there was no obvious trend toward a difference in lead failure rates by subgroup analysis for lead type or approach (transvenous vs. epicardial, subcutaneous, pericardial, or nonstandard implants), although the number of patients with nonstandard lead implant approaches was underpowered to determine statistical significance. There were no associations between specific manufacturers’ advisories and lead failures. Generator-related problems that necessitated reoperation were notably uncommon, occurring in only 3 of 443 patients (0.68%) over the 12-year study period.
Discussion

Large, prospective double-blinded trials to assess the safety and efficacy of ICD therapy in adults have proven the value of ICDs in a variety of disease substrates, including post-myocardial infarction, ischemia, and cardiomyopathies (15–18). Implant indications and guidelines have been developed to appropriately determine who is a good ICD candidate for both primary and secondary prevention (19,20). The sheer volume of adult patients in these studies dwarfs the pediatric ICD experience, where sudden cardiac death is fortunately relatively uncommon (except perhaps in untreated channelopathies and malignant myocarditis/cardiomyopathies). However, the rarity of diseases and cardiac events also makes determining the appropriate indications for therapy diagnostically challenging. The impact of receiving an ICD may be more substantial in a young patient, who may live for decades after initial device implantation and would be subject to multiple procedures for generator replacements and lead revisions/extractions (21,22). These additional procedures significantly increase the complexity of decision-making, increase costs, and likely increase psychosocial stressors related to ICD therapy (23,24). In addition, assessing the safety and efficacy is hindered by the sample size necessary to achieve adequate statistical power, which has previously limited the ramifications and conclusions of prior pediatric ICD series.

The small retrospective series in pediatrics do suggest a potential benefit to ICD therapy in children. Particularly in patients implanted for secondary prevention, there is a high reported rate of appropriate shocks, at least some of which can be presumed to be lifesaving. Silka et al. (1) surveyed members of the Pediatric Electrophysiology Society in the early 1990s regarding their ICD patients, and reported 125 patients under age 20 years implanted with an ICD, predominantly following resuscitated sudden death (76%), drug-refractory ventricular tachycardia (10%), or syncope in patients with structural heart disease and inducible sustained ventricular tachyarrhythmias. This relatively early series of pediatric ICD patients implanted before 1992 included a preponderance of epicardial ICD systems, and they had a high appropriate shock rate (68% over 31 ± 23 month follow-up). Interestingly, similar to recent adult studies, the main predictor of mortality among these patients was impaired ventricular function (1). Gradua et al. (7) reported a survival benefit in children with ICDs by comparing the difference between the curves for death versus the combined end point of death plus recurrences of fast symptomatic ventricular tachycardia. However, despite a high rate of appropriate shocks for ventricular arrhythmias, 2 of 25 children died (including 1 death from ICD patch electrode erosion), and they had a high rate of inappropriate shocks: 28% in the first year and 49% by 5 years of follow-up (7). Previous studies have shown a higher rate of complications and technical difficulties related to ICD implantation and management in the pediatric population. A comparison study by Link et al. (4) found a significantly higher complication rate in pediatric versus adult ICD recipients implanted at the same institution. In a smaller study, Goel et al. (8) reported their experience with ICD therapy for children with long-QT syndrome and observed appropriate therapies in 5 of 12 patients, inappropriate shocks in 4 of 12, 2 complications, and 1 death after electrical storm. Korte

Mortality. Among the study cohort, there was a total of 18 deaths (4% all-cause mortality) during follow-up, of which only 4 (1%) were known to be sudden cardiac death or documented fatal arrhythmia. The nonsudden deaths were attributed to progressive congestive heart failure, pulmonary embolism, cerebrovascular accident, or unknown (nonsudden) etiology. A total of 16 patients (3.6%) underwent orthotopic heart transplant at some point following their ICD implantation. They did not receive a new ICD system during or following transplant, and 3 of these 16 patients subsequently died after transplantation.

Table 3 ICD-Related Complications

<table>
<thead>
<tr>
<th>No. of Complications</th>
<th>Acute Complications (Perioperative or Within 30 Days of Implant)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead dislodgement</td>
<td>13</td>
</tr>
<tr>
<td>Inability to defibrillate or unacceptable DFT</td>
<td>9</td>
</tr>
<tr>
<td>Bleeding or pocket hematoma</td>
<td>8</td>
</tr>
<tr>
<td>Infection</td>
<td>7</td>
</tr>
<tr>
<td>Unsuccessful transvenous lead placement</td>
<td>6</td>
</tr>
<tr>
<td>Electrical storm</td>
<td>5</td>
</tr>
<tr>
<td>Hemorrhax or pneumothorax</td>
<td>4</td>
</tr>
<tr>
<td>EMD/PEA</td>
<td>4</td>
</tr>
<tr>
<td>Skin erosion</td>
<td>3</td>
</tr>
<tr>
<td>SVC syndrome</td>
<td>2</td>
</tr>
<tr>
<td>Skin burns</td>
<td>2</td>
</tr>
<tr>
<td>Pneumonia and ileus</td>
<td>1</td>
</tr>
<tr>
<td>Total acute complications</td>
<td>64 (in 55 patients)</td>
</tr>
<tr>
<td>Chronic Complications (More Than 30 Days After Implant)</td>
<td></td>
</tr>
<tr>
<td>Lead-related problems overall</td>
<td>68</td>
</tr>
<tr>
<td>Lead conductor fractures</td>
<td>20</td>
</tr>
<tr>
<td>Lead insulation breech</td>
<td>28</td>
</tr>
<tr>
<td>Lead late dislodgement</td>
<td>7</td>
</tr>
<tr>
<td>Lead-related change in capture, sensing, or DFT</td>
<td>13</td>
</tr>
<tr>
<td>Electrical storm</td>
<td>23</td>
</tr>
<tr>
<td>Inappropriate shocks (not related to lead failure)</td>
<td>22</td>
</tr>
<tr>
<td>Infection</td>
<td>13</td>
</tr>
<tr>
<td>Generator malfunction</td>
<td>2</td>
</tr>
<tr>
<td>Manufacturers’ advisories/FDA recalls – device failure</td>
<td>1</td>
</tr>
<tr>
<td>Total chronic complications</td>
<td>130 (in 116 patients)</td>
</tr>
</tbody>
</table>

| Mortality | |
| Periprocedural death | 0 |
| Death >30 days after implant | 18 (4 known SCD) |
| Orthotopic heart transplantation after ICD | 16 |
| Death after orthotopic heart transplantation | 3 |

DFT = defibrillation threshold; EMD/PEA = electromechanical dissociation/pulseless electrical activity; FDA = Food and Drug Administration; SCD = sudden cardiac death; SVC = superior vena cava; other abbreviations as in Table 2.
et al. (9) categorized shocks in pediatric ICD recipients as appropriate in 15 of 20 patients (75%) and inappropriate in 10 of 20 patients (50%), attributable mainly to supraventricular tachycardia, T-wave oversensing, or lead failure. Alexander et al. (6) reported a 38% complication rate over 2-year follow-up in 76 pediatric and young adult ICD patients (who are included in the present series), including infection, lead failure, and potential for electrical storm. In that study, growth was strongly associated with lead failure, with a change in body surface area having the highest hazard ratio. Eicken et al. (13) reviewed 16 patients who received an ICD and found 7 of the 16 (44%) received appropriate therapies, whereas 4 (25%) received inappropriate shocks. In a recent study including 22 children with hypertrophic cardiomyopathy who received an ICD (14), only 4 (18%) received appropriate shocks, and 4 also received 1 or more inappropriate shocks; complications were reported for 3 of 22 patients. Increased recognition of the risks of ICD lead fractures and inappropriate shocks have led to the development of novel implantation techniques and leadless ICD systems for small children and patients with complex congenital heart disease (25–27). Several investigators (27,28) have described subcutaneous coil placement around the heart, as well as in the pericardium.

The present multicenter retrospective study demonstrates the heterogeneity of pediatric and congenital heart ICD recipients and highlights important issues related to growth and development. The results from this study confirm that children and CHD patients who are ICD recipients have significant appropriate and inappropriate shock frequencies. With 105 patients (26%) receiving a mean of 4 appropriate shocks each, it is highly probable that at least some of these shocks were potentially lifesaving, although the study design does not allow a determination of hemodynamic compromise from the ventricular arrhythmias or the impact of ICDs on overall survival benefit. However, the overall all-cause mortality rate of 4% and sudden cardiac death rate of 1% over a relatively long follow-up period (mean 7.5 years, range 1 to 20 years) were strikingly low compared with similar adult ICD patient series (15–17). This finding substantiates the perceived concerns regarding the long-term impact of receiving an ICD and exposure to chronic device-related and procedure-related complications such as lead failure and extraction.

The relatively high rate of inappropriate shocks and complications, similar to that observed in smaller pediatric series, increases the morbidity of ICD therapy in children, balancing the risk–benefit ratio. The finding of higher inappropriate shock rates in children versus adults with congenital heart disease supports the hypothesis that continued growth and activity place increased strain on ICD leads, rather than the alternative that the congenital heart disease is a primary risk factor. Therefore, clarification of proper indications for implantation is critical for determining the optimal pediatric candidates for ICD therapy. We suggest that careful attention to optimizing device programming, medical management, and encouraging compliance with prescribed therapies and recommendations may diminish inappropriate shock frequency in this unique patient population.

**Study limitations.** The limitations of this retrospective multicenter study include practice variations between centers; differences in implant threshold and indications for ICD; variations between operators in implantation techniques and programming; and variances in case mix, ages, presence, and complexity of CHD. The follow-up design did not capture the time to each appropriate shock for all patients, limiting the ability to perform a time-dependent analysis of ICD therapies. Finally, although shock data was determined for 92% of subjects, the chronic follow-up and late complications are likely not comprehensively reported for all patients.

**Conclusions**

This is the largest series of pediatric and congenital heart ICD patients reported to date. It is a heterogeneous group with a wide age range (infant through adult) and broad mix of diagnoses. The threshold for prescribing an ICD in the pediatric and congenital heart population appears to have lowered over time. The indications for implantation are clearly different from most adult ICD series, which have a preponderance of ischemic heart disease and post-infarction patients. Despite these differences, young ICD patients have a significant rate of shocks, both appropriate and inappropriate. However, although recent concerns regarding ICD generator recalls and manufacturers’ advisories have generated significant public concern (29,30), lead failure actually remains the dominant mode of inappropriate shocks, complications, and system malfunction in children. Future directions that may identify additional important factors include a prospective pediatric ICD registry and consensus development of guidelines and definitions in pediatric and congenital heart ICD recipients.

**Acknowledgments**

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**References**