

Implications of Implantable Cardioverter Defibrillator Therapy in Congenital Heart Disease and Pediatrics

MARK E. ALEXANDER, M.D., FRANK CECCHIN, M.D., EDWARD P. WALSH, M.D., JOHN K. TRIEDMAN, M.D., LAURA M. BEVILACQUA, M.D., and CHARLES I. BERUL, M.D.

From the Arrhythmia Service, Department of Cardiology, Children's Hospital, Boston, Massachusetts, USA; and the Department of Pediatrics, Harvard Medical School, Boston, Massachusetts, USA

ICD in Pediatrics and CHD. Introduction: The incidence of appropriate and inappropriate discharges, indicators of system failure, and clinical implications of implantable cardioverter defibrillator (ICD) therapy in children and young adults with heart disease is poorly defined.

Methods and Results: In a retrospective study at a single medical center, a total of 90 ICD procedures were performed in 76 patients younger than age 30 years (median 16 years, range 1–30): 42% with congenital heart disease, 33% with primary electrical disease, 17% with hypertrophic cardiomyopathy, and 8% with idiopathic dilated cardiomyopathy. Indications for ICD included arrest or sustained ventricular tachycardia (n = 27), and combinations of syncope (n = 32), palpitations (n = 17), spontaneous ventricular arrhythmia (n = 40), inducible ventricular tachycardia (n = 36), or severe hypertrophic cardiomyopathy. Transvenous dual-chamber ICDs were implanted in 29 patients. Subcutaneous arrays or epicardial patches were used in 9 patients. Over a median 2-year follow-up, 28% of patients received appropriate shocks for ventricular tachycardia (median 13 months to first shock) and 25% experienced inappropriate shocks for multiple causes (median 16 months). With multivariate analysis, growth strongly correlated with lead failure (odds ratio 73, 3.5–1530, P = 0.006). Complications occurred in 29 patients, including lead failure in 16 (21%), ICD “storm” with sequential shocks in 5, and infection in 2 patients. No deaths were attributable to ICD placement or subsequent device failure.

Conclusion: ICD therapy can effectively manage malignant arrhythmias in selected pediatric and congenital heart patients. Spurious shocks or ICD storm may increase morbidity and emphasize the need for concomitant medical and ablative therapy. ICD lead failure was relatively frequent in this population. (*J Cardiovasc Electrophysiol*, Vol. 15, pp. 72-76, January 2004)

congenital heart disease, implantable defibrillator, ventricular tachycardia, sudden cardiac death

Introduction

Sudden death is the number one cause of mortality in adolescent and adult survivors of congenital heart disease (CHD)¹ and a dominant concern in the management of younger patients with cardiomyopathy and primary electrical disease. The experience with implantable cardioverter defibrillators (ICDs) in these patients^{2,3} is limited compared with the extensive experience in older high-risk adults.

Based on prior series³⁻⁵ and personal clinical experience, we hypothesized that younger and smaller pediatric ICD patients would encounter a significantly higher incidence of lead-related problems and a relatively high proportion of inappropriate-to-appropriate shock therapy than would be the case in adults. In addition, we aimed to determine whether ICD system failures occurred more frequently in growing children than in fully grown patients under similar circumstances. Therefore, the aim of the present study was to determine the incidence of appropriate and inappropriate thera-

pies, indicators of lead failures, and related clinical outcomes in young ICD patients using multivariate analyses.

Methods

Patients

Data were collected in accordance with the policies and procedures of the hospital institutional review board. All patients managed with ICDs were retrospectively identified, and patients younger than age 30 years at implantation were included in the present analyses. Patient characteristics, procedural details, outcomes, and potential confounding diagnoses were extracted from the medical record. Follow-up clinical status was ascertained from a review of departmental records and contact with the referring cardiologist. The majority of implanted devices had stored intracardiac electrograms, which were carefully examined to classify events. Outcomes analyzed included time to first appropriate shock, first inappropriate shock, lead failure requiring revision, and death. Patients were censored at time of heart transplant. Defibrillation threshold testing was individualized by the implanting physicians and demonstrated an adequate safety margin.

Statistical Analysis

Continuous variables are summarized using means, medians, and standard deviations. The Kruskal-Wallis test was used to compare variables that were not normally distributed. Patient characteristics, indications, and appropriate and

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Address for correspondence: Mark E. Alexander, M.D., Arrhythmia Service, Department of Cardiology, Children's Hospital-Boston, 300 Longwood Avenue, Boston, MA 02115. Fax: 617-739-9058; E-mail: mark.alexander@cardio.chboston.org

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TABLE 1
Patient Characteristics and Therapy

Variable	Congenital Heart Disease [n = 32 (42%)]	Primary Electrical Disease [n = 25 (33%)]	Dilated Cardiomyopathy [n = 6 (8%)]	Hypertrophic Cardiomyopathy [n = 13 (17%)]†	Total [n = 76]
Age (years)					
Mean	18	12	16	17	16
Range	3–30	1–19	8–21	11–23	1–30
Weight (kg)	62 ± 26	49 ± 22	49 ± 15	64 ± 24	57 ± 24
Pre-ICD events					
Arrest	10 (31%)	12 (48%)	0	2 (15%)	24 (32%)
Syncope	13 (41%)	12 (48%)	4 (67%)	3 (23%)	32 (42%)
Spontaneous SMMVT	4 (13%)	1 (4%)	0	0	5 (7%)
Palpitations	9 (28%)	1 (4%)	1 (17%)	6 (46%)	17 (22%)
SVT	7 (22%)	4 (16%)	0	2 (15%)	13 (17%)
NYHA class ≥III	6 (19%)	0	5 (20%)	0	11 (14%)
None	0	0	4 (16%)	2 (15%)	6 (8%)
Programmed stimulation					
Performed	30 (94%)	18 (72%)	3 (50%)	3 (23%)	44 (58%)
Negative*	6 (20%)	9 (53%)	0	2 (67%)	17 (32%)
NSVT*	0	3 (17%)	1 (33%)	0	4 (8%)
SMMVT*	16 (53%)	2 (12%)	2 (67%)	0	21 (45%)
SPMVT*	7 (23%)	3 (18%)	0	1 (33%)	11 (21%)
Appropriate therapy					
No. of patients	7 (22%)	11 (44%)	2 (33%)	1 (8%)	21 (28%)
Time to first shock					
Median (months)	13	7	14	1	13
No. of shocks					
Mean (max)	6 (12)	5 (24)	5 (9)	3 (4)	5 (24)
Inappropriate therapy	8 (25%)	7 (28%)	1 (17%)	3 (20%)	19 (25%)

*Percentages of those who underwent programmed stimulation.

†There was a family history of sudden cardiac death in 5 of the 6 with familial hypertrophic cardiomyopathy. Maximal ventricular wall thickness ranged from 20 to 42 (median 31).

ICD = implantable cardioverter defibrillator; NSVT = nonsustained ventricular tachycardia, >5 beats of induced ventricular arrhythmia; NYHA = New York Heart Association; SMMVT = sustained monomorphic ventricular tachycardia, >30 seconds or requiring cardioversion; SPMVT = sustained polymorphic ventricular tachycardia requiring cardioversion; SVT = supraventricular tachycardia, including atrial reentry.

inappropriate ICD therapy results were coded and analyzed using univariate and multivariate logistic regression to identify predictors of outcome. Cox proportional hazard models were analyzed for survival to each defined outcome using patient characteristics and potential confounding variables. Patients without an event were censored at the date of most recent follow-up. Variables were removed from the final stepwise multivariate model if $P < 0.2$. Confidence intervals (CI) at 95% are presented for odds ratios (OR) following logistic regression, and for hazard ratios (HR) following Cox regression. $P < 0.05$ was considered statistically significant. All statistics were performed using Stata 8.0 software (Intercooled Stata, Austin, TX, USA).

Results

Patient Characteristics

The characteristics of the study population are summarized in Table 1 and Figure 1. From our database of 140 ICD procedures, 76 patients (61% male) underwent 90 implantation procedures at age ≤ 30 years (mean 16 ± 6 , range 1–30). The largest group had CHD (32 [42%]), including tetralogy of Fallot (19), d-transposition of great arteries (5), aortic valve disease and left ventricular outflow tract obstruction (4), and single patients with pulmonary atresia, isolated ventricular septal defect, and congenital left ventricular aneurysm. The next largest group (25) had primary electrical disease including long QT syndrome (11), catecholaminergic ventricular

tachycardia (VT), and idiopathic ventricular fibrillation. The remainder of patients had hypertrophic (13 patients) or idiopathic dilated cardiomyopathy (6 patients). Median follow-up duration was 1.4 years (mean 2.3 ± 1.9 , maximum 7.4).

Patients had combinations of symptoms with spontaneous and/or induced ventricular arrhythmias. Programmed ventricular stimulation was performed in 54 patients, including

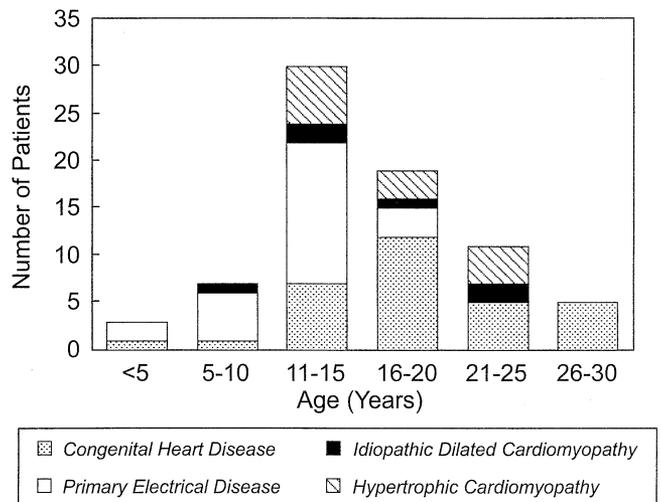


Figure 1. Diagnosis and age at initial implant of patients 30 years or younger at Children's Hospital-Boston through 2002.

94% of the CHD patients and 72% of the primary electrical disease patients. Supraventricular tachycardia (SVT) was present in 13 patients (17%), including 22% of the CHD patients. The majority of patients (65 [86%]) were New York Heart Association functional class I or II.

The general philosophy of the program is to recommend ICD placement in all patients with cardiac arrest or sustained ventricular arrhythmias requiring cardioversion/defibrillation. For other patients, the approach is dependent upon the underlying disease. For CHD, ICDs are recommended with syncope and nonsustained VT unexplained following evaluation that includes atrial and ventricular stimulation, whereas those with less severe symptoms will be stratified using programmed electrical stimulation. For hypertrophic cardiomyopathy, the indications are evolving and the patient characteristics noted below.* Those with primary electrical disease generally require recurrent syncope, failed therapy, malignant family history, or a severe episode on presentation.

Implantation Techniques

There were 90 implants of new hardware, the majority (93%) using standard tranvenous techniques. In the initial implant, 65 (72%) were in subclavicular positions and 25 (28%) in abdominal positions. Dual-chamber devices were used in 29 (32%) of the implants. Nine patients underwent placement of a subcutaneous array, either for reduction of defibrillation threshold or in 2 patients who had a novel technique using an epicardial pace/sense lead and a shock vector between an active can and the array.⁶

Overall Survival

Overall survival was 95% with 4 deaths. All deaths were in the CHD group, which had a 13% total mortality and a 5% annualized mortality rate. These same rates were seen in older CHD patients managed with ICDs at this center (data not shown). Of the 4 deaths, 2 were in the setting of end-stage heart failure, and 2 represented isolated sudden cardiac death. In one case, there were repeated episodes of VT, not terminated by ICD treatment. In the other case, ICD interrogation was not available. Six patients were censored after successful heart transplant. In this selected population, none of the variables analyzed predicted actuarial survival.

Appropriate Therapy

Overall, 28% of the patients had at least a single episode of appropriate therapy with a median time to first appropriate shock of 13 months (Table 1). Patients with primary electrical disease were significantly more likely to receive appropriate therapy (OR 3.2, 1.1–9.2, $P = 0.03$); however, there was no significant difference in time to first shock or in number of appropriate episodes. Smaller and younger patients were less likely to have appropriate therapy (OR 0.24, 0.06–0.87,

*Implant indications for hypertrophic cardiomyopathy were combinations of symptoms, arrhythmia, family history, and ventricular wall thickness. Prior cardiac arrest (3) and recurrent syncope (4) had occurred in 53% with the remainder having palpitations without clear arrhythmia or primary prevention as the primary goal. There was a family history of sudden cardiac death in 5 of the 6 with familial hypertrophic cardiomyopathy. Maximal ventricular wall thickness ranged from 20 to 42 mm (median 31).

TABLE 2
Causes of Inappropriate Therapy

Cause	No. of Patients	Median Time to First Shock (months)	No. of Shocks [Mean (max)]
Lead failure	7	35*	25† (60)
Sinus tachycardia	8	3	1.6 (4)
SVT/IART	4	4	2.3 (4)
T wave oversensing	2	22	1.5 (2)
Overall (patients)	19 (25%)	16	10 (60)

Two patients had inappropriate therapy both for lead failure and sinus tachycardia.

* $P = 0.028$; † $P = 0.038$, Kruskal-Wallis.

IART = intra-atrial reentry tachycardia; SVT = supraventricular tachycardia.

$P = 0.03$ for body surface area; OR 0.91, 0.82–0.99, $P = 0.038$ for age in years) by univariate analysis, although these findings did not persist with multivariate analysis.

Inappropriate Therapy

Twenty-five percent of the patients experienced inappropriate therapy, with a median time to first inappropriate shock of 16 months. Table 2 details inappropriate therapy that includes shocks delivered because of sustained sinus tachycardia, SVT (excluding the 2 patients with ICD therapy specifically targeting their SVT), and false sensing episodes secondary to T wave oversensing or lead failure. The most common cause of inappropriate therapy was lead failure that required lead revision. In 8 (43%) of the episodes of inappropriate therapy, electrogram review demonstrated sinus tachycardia or T wave oversensing that potentially could be managed with programming changes and drug adjustments. An additional 4 episodes resulted from SVT at rates where therapy would otherwise be appropriate for therapy. SVT discrimination had not been routinely activated in these patients.⁷ Inappropriate therapy resulting from lead failure occurred later (median time 35 months) than inappropriate therapy delivered for any other reason (4 months, HR 0.2, 0.075–0.77, $P = 0.017$). Patients who had inappropriate therapy experienced a mean of 7 ± 15 (median 2, maximum 60) inappropriate discharges. Lead failure resulted in more inappropriate shocks (mean 18 ± 24 , median 5, maximum of 60) than did other causes of inappropriate therapy (2 ± 1 , maximum 4, $P = 0.038$, Kruskal-Wallis test). None of the variables analyzed, including younger patient age and smaller patient size, were associated with inappropriate therapy.

Complications and Lead Failure

There were 11 (14%) acute complications that extended hospital stay and required a repeat procedure or repeat hospitalization. These included pocket infections (2), pocket hematoma (2), microdislodgment requiring lead manipulation, hemothorax, superior vena cava syndrome, pneumonia, electromechanical dissociation requiring cardiopulmonary resuscitation during defibrillation testing, second-degree burns from repeated external rescue shocks, and one lead failure <30 days after implant.

There were 38 chronic complications among 29 patients (Table 3). The most frequent complication was lead failure, which occurred in 16 patients (21%). There was a trend for

TABLE 3
Chronic Complications

Complication Type	Patients [n (%)]
Lead failure	16 (21%)
Inappropriate shocks (no lead failure)	14 (18%)
ICD storm	5 (7%)
Elevated pacing thresholds	1 (1%)
Diaphragmatic oversensing	1 (1%)
LSVC occlusion	1 (1%)
Overall complications	38
Total no. patients affected*	29 (38%)

*Patients may have had multiple complications.

ICD storm = repeated appropriate shocks with only transient termination of ventricular arrhythmia; LSVC = left superior vena cava.

fewer complications in devices placed in a subclavicular location. Age, growth, diagnosis, and other technical details did not predict chronic complications. The median time to lead failure was 1.6 years, resulting in inappropriate shocks in 7 of 16 patients (Fig. 2). Changing anthropometrics were a contributor to lead failure (Table 4). Although older/larger and younger/smaller patients had both lead failures and long-term lead survival, the youngest and smallest patients had a higher incidence of lead failure. The smallest patients, those $<1.2\text{M}^2$, had a 4.5-fold increased risk for lead failure (7/19 [36%], OR 4.5, 1.4–14.5, $P = 0.01$). Focusing on growth, an increase in size was associated with a higher risk for lead failure, as were increases in height and weight individually. With multivariate analysis, growth strongly correlated with lead failure (OR 73, 3.5–1530, $P = 0.006$). This general pattern of risk factors was the same when other chronic complications were analyzed.

There were 27 repeat procedures (5 patients having 2 repeat procedures), with a median time to repeat procedure of 2.8 years. Uncomplicated generator changes were performed in 8 patients; upgrades to transvenous dual-chamber systems or revisions to epicardial systems in 2, lead revision or repair in 14 (10 requiring laser lead extraction), and system removal

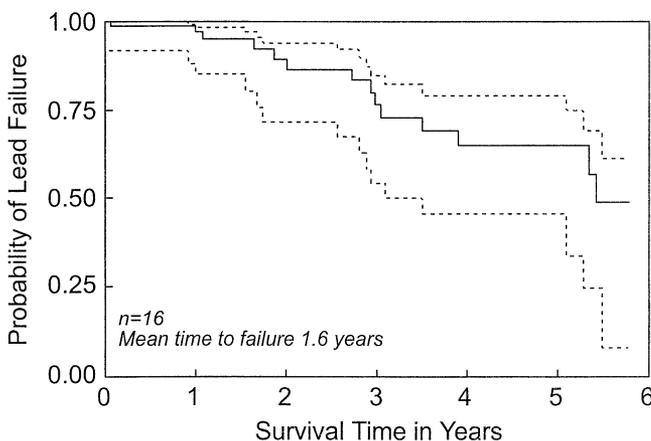


Figure 2. Kaplan-Meier survival with 95% confidence interval to lead revision or lead failure. There were 16 lead failures or revisions with a median time to failure of 1.6 years in patients who had lead failure. Data are more limited beyond 4 years. This includes all leads that required repositioning, repairs, extraction, and replacement or those that contributed to inappropriate therapy. Data truncated at 6 years.

TABLE 4
Predictors of Lead Failure

	Odds Ratio (95% CL)	P Value
Univariate Analysis		
Increase in body surface area	329.67 (8.61–12627.50)	0.002
Smallest patients	4.45 (1.37–14.46)	0.013
Subcutaneous array	4.04 (0.81–20.20)	0.089
Single-chamber device	4.02 (0.85–19.05)	0.079
Youngest patients	2.9 (0.95–8.87)	0.062
Change in height	1.09 (1.02–1.16)	0.007
Change in weight	1.06 (1.01–1.11)	0.028
Weight	0.99 (0.97–1.02)	0.62
Height	0.98 (0.95–1.01)	0.27
Age at implant	0.94 (0.88–1.02)	0.12
Year of implant	0.93 (0.80–1.09)	0.39
Generator manufacturer	0.76 (0.26–2.20)	0.60
Body surface area	0.55 (0.12–2.46)	0.44
Lead manufacturer	0.42 (0.12–1.48)	0.18
Subclavicular location	0.41 (0.13–1.27)	0.12
Multivariate Analysis		
Increase in body surface area	73 (3.5–1529)	0.006

in 2 (1 elective extraction, 1 for infection). Single-chamber systems were more likely to be revised (OR 4.0, 1.2–13, $P = 0.019$), as were systems in smaller patients. Growth was the only significant variable predicting reintervention necessity with multivariate analysis.

Discussion

This report analyzes the largest experience of a single center managing ICD patients with CHD and pediatric indications for device therapy. The overall survival of these patients is 97% at 2 years and 89% at 5 years, with a 5 year mortality of $\sim 2\%$ per year. Appropriate device therapy that potentially prolonged survival was delivered in 28%, whereas 25% experienced inappropriate therapy. Patients often received multiple inappropriate shocks, particularly with associated lead failure. With the exception of patients with CHD, the mortality rate was low. This continued survival in CHD and pediatric ICD patients highlights the importance of determining chronic follow-up data on these patients and developing strategies and technology that limit the adverse consequences of device therapy.

Younger age and smaller size, by themselves, did not predict complications or lead failure. Rather growth, measured as change in height, weight, or body surface area, was a strong predictor of lead failure. Within this cohort there was not a clear threshold for these effects. In other patient-specific outcomes, age and size were not associated with a higher incidence of technical difficulties or with appropriate or inappropriate device use. Multiple combinations of leads, devices, and approaches all appeared to have comparable risk and efficacy. This experience suggests that the technical challenges posed by these patients are manageable.

It might be expected that younger and smaller patients have a higher risk of lead complications, although this has not been reliably demonstrated. There were 16 lead failures in this cohort, which permitted statistical analysis that specifically included measures of growth. There is a wide range of patient sizes (9–120 kg) and ages (1–30 years). Although the influence of growth is statistically significant, with the

most inclusive multivariate model the sensitivity is only 26% and the positive predictive value 82%. Thus, there clearly are additional patient, device, and technical details that potentially contribute to lead failure but were not identified in this study. Stretching and distortion of the proximal coil have been shown to be present in children with lead fractures.⁸ Because single-coil leads were almost never used, this variable could not be examined. The use of single-coil leads or increased use of subcutaneous arrays each may decrease the risk of lead failure with growth.

An early survey of Pediatric Electrophysiology Society members identified 125 children with ICDs.² More recent reports are limited to smaller series^{3-5,9,10} and focused reports of specific details. In this current series, only 32% of the patients were survivors of aborted sudden death, compared with 76% in the Pediatric Electrophysiology Society's multicenter experience.² This present series also has a higher number of CHD patients than in other reports, although a limited number are truly in the pediatric age range. Despite these differences, there is nearly identical long-term survival: 85% in the multicenter experience and 89% in this series. The 25% incidence of inappropriate therapy also is comparable to other experiences.^{4,5,9,10}

Randomized controlled trials have demonstrated a survival advantage to ICD use in high-risk adults with several underlying conditions, most notably depressed ventricular function, spontaneous nonsustained VT, and inducible non-suppressible VT,¹¹ and those with prior myocardial infarction and depressed ventricular function.¹² Without the benefit of these trials, a clinical practice extrapolating to the distinctive details of CHD and pediatric myopathy patients has evolved, trying to identify a group that will benefit from appropriate ICD therapy. In the CHD population, much of the mortality relates to hemodynamic failure (2/4 deaths). Limiting the analysis to CHD patients 30 years or younger who did not die from hemodynamic failure or undergo transplantation, 6 (20%) of 30 received appropriate therapy for VT or ventricular fibrillation.

This report does not directly address the decision to implant an ICD. Although there is a clear consensus that survivors of aborted sudden cardiac death deserve ICD therapy, there is no consensus regarding prophylactic therapy in different combinations of lower-risk CHD or cardiomyopathy patients with nonsustained VT, induced VT, or syncope. These data do allow an estimate of the sample size required to identify survival benefit from ICD therapy. For 90% power to demonstrate a 5-year survival improvement from 85% to 90%, >950 ICD patients would need to be enrolled, with an equal number of historical or contemporary controls.

This is an uncontrolled retrospective study, with biases in selection and follow-up of patients assumed to be at increased risk for ventricular arrhythmias. Evaluating any therapy decision in this population has intrinsic limitations. This report

shares those limitations of heterogeneous patient selection, limited cohort size, and lack of a clear comparison group.

The variables analyzed are neither independent nor comprehensive. The presence of multiple potentially confounding variables and a relatively small number of competing outcomes increase the possibility of both false-positive and false-negative inferences. A larger, more homogeneous population, which may be underpowered even using prospective multicenter registry data, may allow higher precision.

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