Implantable Cardioverter Defibrillator Outcomes in Pediatric and Congenital Heart Disease: Time to System Revision

Short Title: ICD system revision in pediatrics

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Abstract

Background: Implantable cardioverter-defibrillators (ICDs) are intended to prevent sudden cardiac death yet also impose a risk of morbidity. This study describes the outcomes of ICDs in a pediatric and congenital heart disease (CHD) population from a single center.

Methods: Retrospective cohort study of all patients with an ICD followed at the University of Michigan Congenital Heart Center from 2005 – 2013. The primary outcome was ICD system revision for any reason excluding routine generator change for battery depletion.

Results: There were 191 ICD systems in 131 patients, including 57 with CHD, 24 with hypertrophic cardiomyopathy (HCM) and 45 with structurally normal hearts. Median age was 16 years at initial implant. Total follow-up was 850 patient-years; median 4.9 years/patient. There were 43 (33%) patients that required 60 ICD revisions; 70 revisions/1000 patient-years of follow-up. Revisions included 25 lead extractions with replacement, 21 lead additions, 5 lead repositions, and 4 full system revisions. Kaplan-Meier (K-M) median time to appropriate shock was similar to the median time to system revision. K-M time to system revision was significantly affected by recalled lead performance.

Conclusions: The need for ICD system revision is high in this pediatric and CHD population and occurs at a rate similar to the rate of receiving appropriate therapy. These results highlight the need for judicious implant criteria and improved device longevity.

Keywords: Pediatric; Congenital Heart Disease; Implantable cardioverter-defibrillator; Complications

Abbreviations:
ICD=implantable cardioverter defibrillator
CHD=congenital heart disease
HCM=hypertrophic cardiomyopathy

Introduction:

Implantable cardioverter defibrillators (ICD) are a widely used therapy to prevent sudden cardiac death. Despite the life-saving potential of ICDs, they may impose significant morbidity. Device complications occur in up to 32% of pediatric and congenital heart disease (CHD) patients. (1-3) A recent study of primary prevention ICDs in this population showed that the risk of complication was greater than the risk of receiving an appropriate shock. (3)

The most highlighted complication in many studies is inappropriate shocks which occur in 19-46% of pediatric and CHD patients compared to only 12% in the adult population. (2, 4-8) Inappropriate shock risk may be attenuated with programming whereas complications such as lead failure may require system revision - increasing morbidity and the risk of mortality. (1, 9) Many pediatric patients have been affected by failures of recalled high voltage lead models implanted between

2005-2008. (1,10-11) Even for non-recalled leads, the failure rate in pediatric patients is higher (2.3% per year) than in adult patients (0.6% per year). (1, 10-11) In some cases, lead extraction is necessary which imposes additional risk of major complications, including perforation and death. (9) In other cases, failed leads may be abandoned and an additional lead placed, increasing the risk of vessel occlusion, a particular concern in younger children requiring a lifelong device.

The goal of this study is to describe the outcomes of ICDs in a single center population of pediatric and CHD patients focusing on complications, specifically the need for system revision.

Methods:

This is a retrospective cohort study of all patients with an ICD followed at the University of Michigan Congenital Heart Center from 2005-2013 (including ICDs implanted prior to 2005). Patients were excluded if they had less than 6 months of follow up. The primary outcomes were ICD system revision for any reason, defined as any operative procedure for device management, excluding routine generator changes for battery depletion; and first appropriate shock. Data was collected from the electronic medical record, hospital device database, and industry remote monitoring databases (Medtronic Carelink, St Jude Merlin and Boston Scientific Latitude). The study was approved by the institutional review board. In order to adequately describe the study population, patients were categorized into 4 groups based on type of heart disease: 1) congenital heart disease, 2) structurally normal heart, 3) hypertrophic cardiomyopathy (HCM) and 4) non-HCM cardiomyopathies. Patients with structurally normal hearts were those with diagnosed primary arrhythmia syndromes or idiopathic malignant ventricular arrhythmias. Recalled leads were defined as those with a current recall: Medtronic Sprint Fidelis and St Jude Riata. Appropriateness of ICD delivered therapy was confirmed by review of device electrograms by pediatric electrophysiology providers. Secondary prevention was defined as ICD implanted for aborted sudden cardiac arrest or documented arrhythmic syncope. Statistical analysis included Kaplan-Meier time to event analysis

for the primary outcomes. Deaths were censored. Subgroup comparison included analysis of variance for continuous variables and chi-square or Fisher exact test for categorical variables; continuous variables by the GLM procedure (SAS 9.3, Cary, NC). Patient specific analyses were limited to the first ICD revision only and for system specific analyses, ICD system revision was considered to result in a distinct ICD system, regardless of the amount of hardware replacement.

Results:

There were 191 ICD systems implanted in 131 patients; 43 patients (33%) required 60 ICD revisions. Device manufactures included 116 patients with Medtronic, 11 with Boston Scientific and 4 with St Jude; only 5% had epicardial or transvenous / epicardial hybrid devices. Total follow up time was 850 patient-years; median 4.9 (IQR 2.1-8.2) years per patient. Clinical data by subgroup are presented in Table 1. Of the 45 patients with structurally normal hearts, 37 had primary arrhythmia syndrome and 8 had an unknown cause of cardiac arrest. Subgroups were similar with the exceptions that patients with CHD were older at ICD implant, patients with HCM were more likely to have a primary prevention ICD and patients with structurally normal hearts were more likely to receive an inappropriate shock. There was no difference in risk of ICD revision in those less than 18 years compared to those 18 years and older at the time of initial implant. Patients with a secondary prevention ICD were more likely to have appropriate shocks ($p = 0.4$) and inappropriate shocks ($p = <0.001$) compared to those with primary prevention ICD. There was no difference when comparing primary versus secondary devices and risk of system revision ($p=0.14$). There were 3 known deaths during follow-up, all documented as unrelated to device function based on post-mortem interrogation.

For the entire cohort, Kaplan-Meier median time to ICD revision (first system only) was 9.3 years, whereas median time to appropriate therapy, including ICD shock or anti-tachycardia therapy was >15.1 years (log rank p value = 0.42; Figure 1). The rate of ICD revisions was 70 per 1000 patient-

years of follow up. Median time to ICD revision for those devices implanted prior to 2012 (n=165) was stratified by year of implant (log rank p value = 0.0026) (Figure 2). Time to device revision was similar for those implanted pre-2005 and those implanted 2009-2011 (log-rank p=0.5). Devices implanted from 2005-2008 had a significantly shorter time to revision compared to those implanted pre-2005 (log rank p=0.001). Time to revision was not statistically different between devices implanted 2005 – 2008 vs those implanted 2009-2011 (log rank p = 0.2); however this may be due to the limited follow-up of the latter device group and the high number of censored observations in this group. To assure that old components (IE:leads) were not implicated in new implant revision rates during the most recent era, an additional Kaplan-Meier analysis was completed on only the first implanted device. This also showed no era effect (log-rank p = 0.8).

Due to the potentially significant impact that recalled leads may have had on the outcome, a second survival analysis was performed removing those lead models that had been recalled (n=116). Kaplan-Meier median time to ICD revision (first system only) was 10.4 years and median time to appropriate therapy was >15.2 years (log rank p value = 0.7; Figure 3). There was no longer a significant difference in time to system revision by era when recalled leads were removed (Figure 4, n=157).

Table 2 shows the indication for system revision. There were 29 recalled leads in the study population - 16 (27% of total revisions) were implicated in revisions for lead fracture or malfunction and 3 functioning yet recalled leads were revised because of parent request. Revisions included 25 lead extractions with replacements, 21 lead additions, 5 lead repositions, 4 full system revisions, and 5 others (recalled generator replacement, placement of azygous or other coil for inadequate DFT). Comparing indications for early (<3 years) versus late (>5 years) revisions revealed lead malfunction or fracture accounting for 14 (42%) of early revisions and 15 (62%) of late revisions. Lead malposition or dislodgement was the indication for 6 (18%) of the early revisions and none of the late revisions.

Discussion:

This study presents a unique perspective on ICD complications in a population of pediatric and congenital heart disease patients – namely, the risk of requiring ICD system revision after initial implant. In this population, the median time to system revision was similar to the median time to appropriate therapy indicating that these patients were as likely to require a revision for device complication as they were to need the device's life-saving capabilities. The rate of system revision in this study was 7% per year. This rate is twice that reported in a recent adult study showing a 3.5% per year rate of ICD revisions. (12)

Most studies on ICD complications in pediatric and congenital heart disease patients assess all complications and typically highlight inappropriate shocks or other complications such as infection. (2-7) A recent study shows that 26% of pediatric patients with primary prevention ICDs required re-intervention but did not elaborate on indication or timing. (3) System revision is a major complication of ICD implantation, as it requires a surgical procedure which imposes morbidity and increases the risk of mortality. In addition, system revision in young patients and patients with abnormally structured hearts can be more difficult due to distorted anatomy, small size and difficult venous access making the risk of mortality even higher. (1, 3) Revisions are costly, requiring anesthesia, surgical costs, and hospital admission. Notably, death is not an equivalent outcome to the temporary morbidity of most device complications. However, the anticipated need for additional unplanned procedures is an important risk to discuss with patients and their families prior to ICD implantation, especially in those cases where the indications for implantation is primary prevention and definitive risk of sudden cardiac death may be unclear.

To evaluate for any era effect in risk of system revision, time to revision was evaluated based on the year the device was implanted. The system revision rate was significantly higher for those devices implanted from 2005-2008, related to the implantation of now recalled lead models used during this

time frame. (1) Repeat analysis without including recalled leads reveals no era influence on time to revision. This suggests that despite having improvement in technology of ICDs, and increased experience in ICD implantation, the risk of complications requiring system revision in this population is similar to 10 years ago. Ideally, one might expect improved outcomes over time as technology and experience improve; however, this is not the observation in this study.

Solutions for decreasing complications may include design improvement to enhance performance and longevity in leads commonly used in pediatric and congenital heart disease patients. Specific design improvements targeted to this small portion of the device market may, in fact, have significant benefit to these patients. Use of the subcutaneous ICD in children and patients with congenital heart disease may reduce the need for system revisions, and when necessary, should be lower risk procedures. (13) Lastly, improved understanding of implant necessity, especially in those who do not meet a Class I indication may help to refine the target population. This, in return, may decrease the use of ICD therapy and avoid these types of complications.

This study was limited by its retrospective method. Data was only as complete as the documentation in the medical record. Complete follow-up would not have been captured for all patients who had changed medical systems. Center specific practices and procedural techniques may contribute significantly to outcomes and risk of needing revision making. During the study period, over 5 attending electrophysiologists and several advanced fellows participated in implantation of these patients. These data may not be optimally translated to other centers with different physicians and practices.

Conclusions:

The need for ICD system revision represents an important complication in the pediatric and CHD population; in this study, occurring at a rate similar to the rate of receiving appropriate therapy. More recently implanted systems did not show a significant improvement in rate of system revision

compared to earlier implanted devices. These data support further efforts to minimize complications related to ICDs. These risks should be clearly discussed with families prior to the decision to implant an ICD.

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Figure Legends

Figure 1: Combined graphic of Kaplan-Meier time to event analysis for first ICD system revision (group 1) and first appropriate therapy (group 2)
n= 131 patients (first system and first appropriate therapy only)

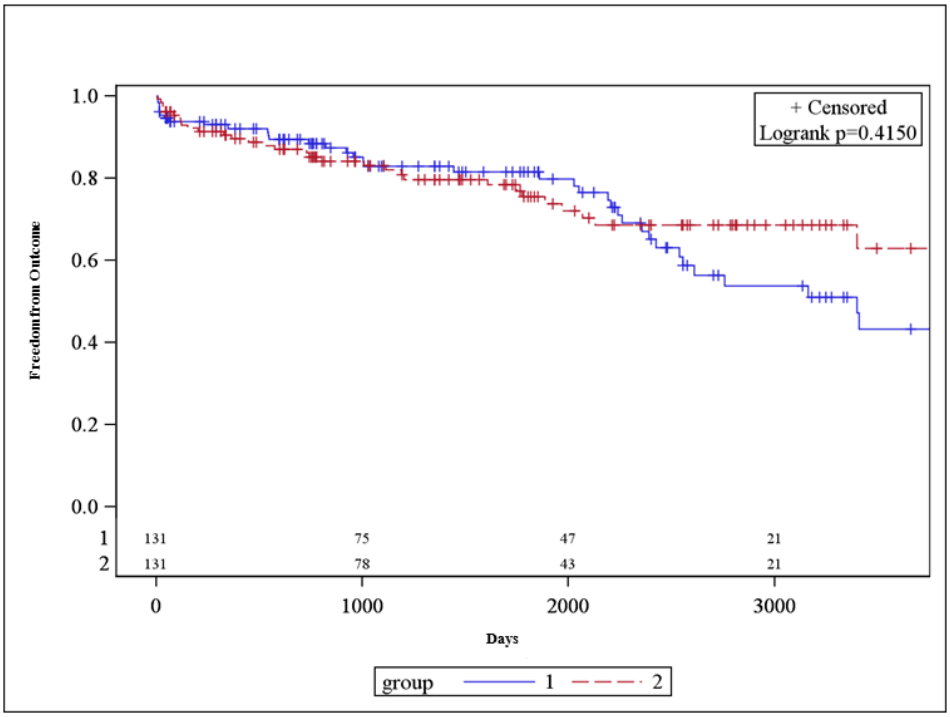

Figure 2:
Kaplan-Meier time to ICD revision for all ICD systems implanted prior to 2012 (n=165/191 systems included)
Group 1 = devices implanted before 2005
Group 2 = devices implanted 2005 – 2008
Group 3 = devices implanted 2009 – 2011

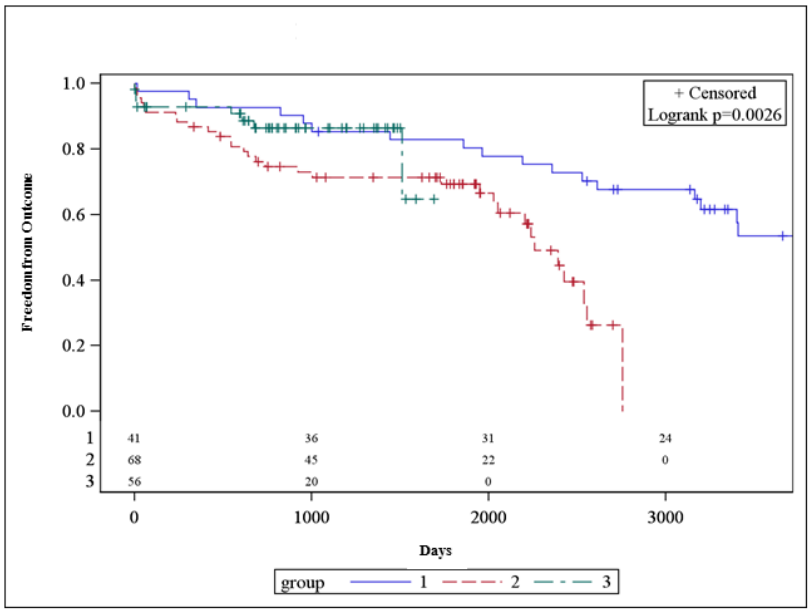

Figure 3: Combined graphic of Kaplan-Meier time to event analysis for first ICD system revision, excluding recalled leads (group 1) and first appropriate therapy (group 2)
n= 116 patients (first system excluding recalled leads and first appropriate therapy only)

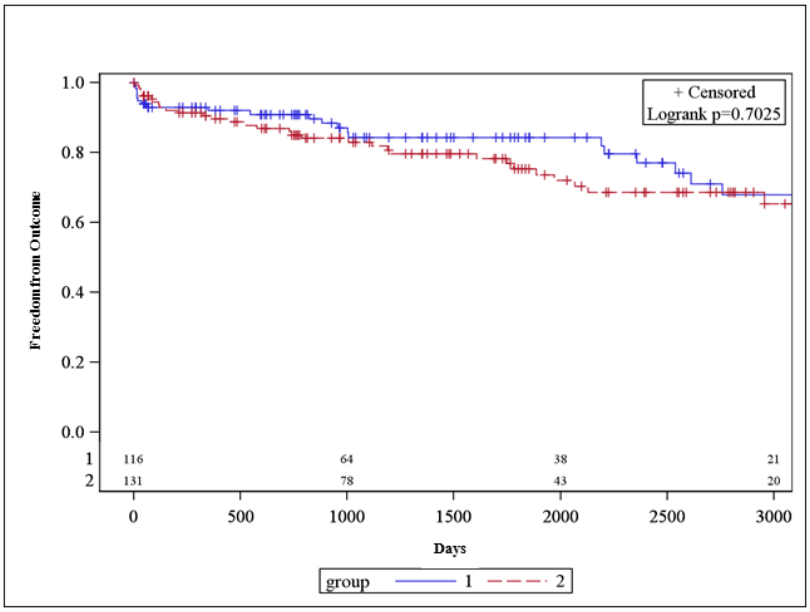

Figure 4:
Kaplan-Meier time to ICD revision for ICD systems implanted prior to 2012, excluding recalled leads (n=142-191 systems included)
Group 1 = devices implanted before 2005
Group 2 = devices implanted 2005 – 2008
Group 3 = devices implanted 2009 – 2011

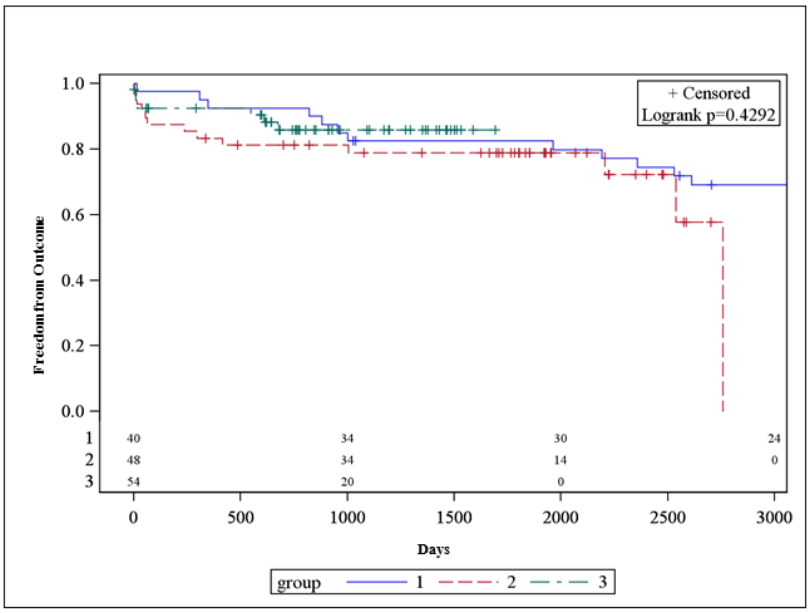

Table 1

	Total cohort n=131	CHD n=57	Structurally normal heart n=45	HCM n=24	Other CM n=5	p value
Age at implant (years)	16 (12.4-	26.3 (16.9-	13.7 (10.7-16.2)	12.3 (10.3-	17.6 (13.4-	<0.001
Primary prevention	76 (58%)	35 (57%)	13 (28%)	23 (96%)	5 (100%)	<0.001
Secondary prevention	55 (42%)	22 (35%)	32 (71%)	1 (4%)	0	<0.001
Follow up (years)	4.9 (2.1-8.2)	4.9 (2.1-8.2)	5.8 (3.5-8.9)	4.8 (2.1-	1.6 (1.1-1.2)	0.12
Appropriate ICD therapy	30 (23%)	17 (27%)	12 (27%)	3 (13%)	2(40%)	0.40
Time from implant to appropriate	1.6 (0.3-3.8)	2.1 (0.6-4.9)	1.0 (0.2-3.3)	2 (2-3.4)	0.4 (0.4-0.5)	0.37

Inappropriate shock	39 (30%)	15 (35%)	20 (45%)	4 (17%)	0	0.03
Patients w/ revision	42 (32%)	21 (34%)	16 (35%)	5 (21%)	0	0.23

Data presented as median (IQR) or count (%). †Data included only those who had appropriate therapy. HCM = hypertrophic cardiomyopathy. CHD = congenital heart disease. CM = cardiomyopathy.

Table 2

Indication for Revision	n= 60 (%)
Lead malfunction/lead fracture	32 (53)
Defibrillation failure†	7 (12)
Lead malposition/dislodgement	5 (8)
Elective lead replacement due to recall (per parents)	3 (5)
Add atrial lead for rhythm detection	3 (5)
Infection	3 (5)
Loose header	2 (3)
Lead perforation	2 (3)
Other	3 (5)

† Delivery of an appropriate device discharge that fails to convert the patient to a normal rhythm