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Slater, TA orcid.org/0000-0001-9213-5559, Cupido, B, Parry, H et al. (10 more authors) (2020) Implantable cardioverter-defibrillator therapy to reduce sudden cardiac death in adults with congenital heart disease: A registry study. Journal of Cardiovascular Electrophysiology, 31 (8). pp. 2086-2092. ISSN 1045-3873

https://doi.org/10.1111/jce.14633

Implantable Cardioverter-Defibrillator Therapy to Reduce Sudden Cardiac Death in Adults with Congenital Heart Disease: A Registry Study

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Disclosures: CBP has received honoraria from Medtronic for provision of training and advisory board attendance. The other authors have no relevant conflict of interest.

Funding: (None)

Abstract

Introduction

The Adult Congenital Heart Disease (ACHD) population is rapidly expanding. However, a significant proportion of these patients suffer sudden cardiac death. Recommending implantable cardioverter-defibrillator (ICD) insertion requires balancing need for appropriate therapy in malignant arrhythmia against the consequences of inappropriate therapy and procedural complications. Here we present long-term follow up data for ICD insertion in patients with ACHD from a large level 1 congenital cardiac centre.

Methods and Results

All patients with ACHD undergoing ICD insertion over an 18 year period were identified. Data were extracted for baseline characteristics including demographics, initial diagnosis, ventricular function, relevant medication and indication for ICD insertion. Details regarding device insertion were gathered along with follow up data including appropriate and inappropriate therapy and complications.

A total of 136 ICDs were implanted during this period: 79 for primary and 57 for secondary prevention. The most common congenital cardiac conditions in both groups were tetralogy of Fallot and transposition of the great arteries. Twenty-two individuals in the primary prevention group received appropriate anti-tachycardia pacing (ATP), 14 underwent appropriate cardioversion, 17 received inappropriate ATP and 15 received inappropriate cardioversion. In the secondary prevention group, 18 individuals received appropriate ATP, 8 underwent appropriate cardioversion, 8 received inappropriate ATP and 7 were inappropriately cardioverted. Our data demonstrate low complication rates, particularly with leads without advisories.

Conclusions

ICD insertion in the ACHD population involves careful balance of the risks and benefits. Our data show a significant proportion of patients receiving appropriate therapy indicating that ICDs were inserted appropriately.

Keywords: Adult congenital heart disease; implantable cardioverter-defibrillator; sudden cardiac death; ACHD; ICD

Introduction

The management of congenital heart disease has evolved significantly in recent decades and increasing numbers of affected individuals now survive into adulthood [1,2,3]. Data collected by the German Heart Registry suggest sudden cardiac death (SCD) may account for up to 23% of mortality in patients with ACHD, although this is partially dependent on the nature of the original cardiac lesion [4]. The decision to implant a cardioverter-defibrillator (ICD) is challenging and current guidance on the subject relies heavily on registry data and consensus. The most up to date European guidelines are not dedicated to the ACHD population and a recent study implied that these, and the US guidelines, have limited ability to predict sudden death [5,6,7].

A recent systematic review and meta-analysis of ICD outcomes in ACHD patients suggested a reassuringly high rate of appropriate ICD therapy (24%). However, even within a relatively short duration of follow up, these benefits were balanced against a similar prevalence of inappropriate therapy and complications [8,9]. Another prior study highlighted the higher risk of patients with Tetralogy of Fallot receiving inappropriate therapy compared to patients with ICD indication due to dilated cardiomyopathy [10]. A more recent study showed 57% received appropriate therapies compared with 33% receiving inappropriate therapies over long-term follow up. However, this study followed up 30 patients only [11]. As such, it is possible that clinicians could be concerned about implanting devices with high complication rates and a low incidence of appropriate therapy in patients who are so young and with such complex cardiac anatomy. Prognosis can be difficult to predict in ACHD and many young patients with borderline device indications could be exposed to many years of device therapy in which to experience inappropriate therapies and complications.

In the current analysis, we present long-term follow-up data from a large, quaternary referral congenital cardiac centre comprising a patient population with varied cardiac lesions

and disease phenotypes. Our objective was to gather data on the consequences of ICD implantation, including appropriate and inappropriate therapy, as well as the rate of complications over a long duration of follow-up.

Methods

The patient cohort was derived from a large, single, quaternary congenital cardiac centre with dedicated electrophysiological, interventional and surgical services. All ACHD patients with an ICD implanted between March 2002 and March 2020 were included. Data were extracted from patients' electronic and written records. Ventricular systolic dysfunction at the time of device implantation was defined as "significant" when there was an ejection fraction < 35% in the sub-systemic ventricle, or a description given of "moderate" or "severe" systolic impairment. Residual disease was deemed significant in the following circumstances: moderate or greater post-operative valvular stenosis or regurgitation; when part of the original structural anomaly had not been fully corrected (for example, incomplete closure of a septal defect); or a complication in the post-operative anatomy, such as a baffle leak. Use of medical therapy (beta-blockers or other anti-arrhythmic agents) was also documented. For the purposes of follow-up, patient records were accessed until the date of death or last follow-up appointment in those who moved to other centres. Otherwise, data analysis was censored on 21 April 2020. For those who moved to other hospitals, the ACHD team at the receiving centre was contacted to obtain follow-up data wherever possible.

Standard secondary prevention indications for ICD implantation comprised: cardiac arrest due to ventricular arrhythmia or sustained ventricular tachycardia (VT) with symptoms or other evidence of haemodynamic compromise, in line with established guidelines[5]. The remaining patients were classified as requiring an ICD for primary prevention.

Device insertion and follow-up records were used to ascertain the rates of therapy and device-related complications. Data were gathered by four investigators splitting up the overall cohort (AS, BC, HP and TS) and any disagreements regarding indication and appropriateness of therapy were resolved by discussion with a senior ACHD cardiologist (KE).

The sample size was determined by the registry. Normally distributed continuous data were presented as mean +/- standard deviation in the text and tables whilst non-normally distributed continuous variables were presented as median (interquartile range, IQR). Categorical data were described as numerical counts and percentages. Kaplan-Meier curves were used to plot survival and compared using log-rank tests using IBM SPSS statistics version 21 (IBM Corporation, NY).

Results

A total of 136 individuals were included in the study: 79 with primary prevention device indications and 57 with secondary prevention ICDs. The median follow-up was 8.3 years in the primary group and 9.6 years in the secondary group, with individual follow-up durations up to 18 years in some patients. Table 1 describes baseline variables in each cohort, whilst Figure 1 presents the distribution of underlying congenital heart lesions. Tetralogy of Fallot was the predominant diagnosis in both groups.

Table 2 shows the outcomes in both groups with respect to appropriate and inappropriate therapy, complications and mortality. Overall survival was high at 89%. Appropriate therapies occurred in 30 individuals (38%) in the primary prevention group and 21 individuals (37%) in the secondary prevention group (see Table 2 for a breakdown of the type of therapy). Inappropriate therapies were recorded in 24 (30%) of the primary prevention patients; almost all of these were due to the device interpreting atrial arrhythmia as VT/ VF, although one patient received an inappropriate shock due to T-wave oversensing. Inappropriate

therapies occurred in comparatively few secondary prevention patients (11; 19%). Complications included those related to: the generator site; peri-procedural access (such as pneumothorax and bleeding); infection and endocarditis; and lead malfunction. A substantial proportion (36%) of recorded complications occurred in patients who had a lead(s) carrying an advisory, despite devices with these leads accounting for only 19% of total devices implanted.

The Kaplan-Meier plots in Figure 2 demonstrate long-term follow-up data with respect to mortality (2A) and time to first shock (2B). With a median follow-up of nine years, overall survival was 89%. In the primary prevention group, 63% were free of shocks at ten years and secondary prevention patients had fewer shocks with 75% shock-free at ten years.

Discussion

This observational study of a real world cohort of patients with ACHD incorporates a longer average follow-up period than previous similar studies: 8.3 and 9.6 years in our respective primary and secondary cohorts compared with a maximum of 4.6 years in existing literature [9,12]. The largest studies have focused specifically on tetralogy of Fallot and transposition of the great arteries, though a large meta-analysis included rarer conditions as seen in our cohort [13,14,15,16].

Over this time period, appropriate therapies occurred in 38% of the full cohort, equally balanced in each group. This must be balanced against a rate of inappropriate therapy of 26% (30% for primary prevention and 19% for secondary prevention). These figures are broadly comparable to those in previous studies. A relatively low proportion received appropriate defibrillation compared to other publications: 18% in the primary prevention group and 14% in the secondary prevention group, giving an overall rate of appropriate shock therapy of 16%. This should be taken in the context of the wide variation in appropriate shock rates in current literature: Santharam et al quoted 14.3% [17], while other studies report rates between 25-35%

[12,16,18]. These differences could reflect small sample sizes, inconsistent criteria and thresholds for ICD implantation and variation in local practice regarding device programming. Nearly 30% of our cohort received appropriate ATP, which may be a factor in limiting the requirement for defibrillation. It is interesting that similar proportions received appropriate defibrillation in the primary and secondary prevention groups, and in fact, some patients with primary prevention ICDs had appropriate shocks earlier. It would be challenging to draw firm conclusions from these observational data and the explanation could be as simple as wide and unpredictable variation in the natural history of these complex anatomical lesions and their arrhythmic consequences. Possible alternative reasons include a longer median time from corrective surgery to device implant, and therefore more time in which to develop complicated post-operative anatomy that could predispose to arrhythmia. There were also more patients with significant systemic ventricular systolic dysfunction in the primary prevention group and it is possible that arrhythmias developed earlier in such individuals.

Risks and benefits of ICD insertion are carefully balanced, particularly in the relatively young group of patients with ACHD. Both inappropriate and appropriate shock therapies have been associated with increased rates of anxiety, depression, reduced social function and vitality[19,20]. In our primary prevention group, 1 person had 79 appropriate shocks and 1 person had 20 inappropriate shocks. Almost all inappropriate shocks in the primary prevention group were due to the device interpreting atrial arrhythmia as VT/ VF although one patient received an inappropriate shock due to T wave over sensing. There were fewer inappropriate shocks in the secondary prevention group, which correlated with fewer episodes of atrial tachycardia being misread as VT. However, 1 person had 11 inappropriate shocks, which has led to the data appearing skewed. The causes of inappropriate shocks in the secondary prevention group were divided between sinus tachycardia, atrial arrhythmia and T wave over sensing.

Efforts to reduce inappropriate shocks in both groups were made by programming high detection rates and drug therapies including therapeutic beta blockade or addition of flecainide or amiodarone. This is in accordance with previous studies recommending high detection rates and long duration to reduce inappropriate shocks in patients with congenital heart disease and ICDs [21].

Overall, 16% of our patients received inappropriate shock therapy. This compares well with the overall proportion of 25.2% of patients receiving inappropriate cardioversion/defibrillation in the meta-analysis by Vehmeijer *et al* [8]. This is in the context of the huge variation seen between studies included in this meta-analysis ranging from 11% to 75% of patients receiving inappropriate shock therapy [22,23]. Possible explanations for this may include variation in programming between centres and in the leads used. Many of the patients in our study who experienced complications had ICD leads with advisories applied to them (e.g. Fidelis and Riata leads). Patients with advisory leads accounted for 38% of all complications in the primary prevention cohort and 33% in the secondary prevention cohort. Hence, it is possible that future cohorts, with more reliable ICD hardware, may be exposed to lesser risk from inappropriate therapies and device revisions. It should also be noted that all therapies and complications occurred across a longer median follow up period than the other studies discussed, and so reflect even lower incidence than direct comparison would suggest.

Our study was limited by its retrospective nature and, in absence of prospectively collected, randomised data, it is difficult to make specific recommendations, although trends can be identified. Our sample size was comparable to previous studies but larger studies have also been published [12,15,17]. Furthermore, the use of electronic records provided the potential for loss to follow up and therefore lack of recognition of late complications.

Conclusion

The data presented reflect the experience of a large UK centre where ICDs are implanted in patients with adult congenital heart disease with prolonged follow up. The rates of appropriate and inappropriate therapies demonstrated, along with overall complication rate, add to the literature informing clinicians and patients in making the decision regarding whether ICD insertion should be performed.

We propose that, in a specialist centre with combined ACHD and targeted electrophysiology clinics, the ability to monitor and optimise treatment for such patients can result in a favourable benefit-risk profile once ICDs are implanted. Whilst this study does not influence case selection, clinicians may derive a degree of reassurance regarding device therapy in patients with equivocal indications.

Contributorship Statement

The study was devised by KE, AS, HP and BC. Study subjects were identified by LB and data collection was performed by AS, BC, HP and TS. The manuscript was drafted by AS, BC and HP. Statistical analysis was performed by MD and KW. Manuscript revisions were contributed to by TS, KW, JO, DC, DH, MB, and CP. KE is responsible for the overall content.

Acknowledgements: George Ballard

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Table 1: Baseline Characteristics

IQR=interquartile range

% quoted to nearest integer

	Primary Prevention (n=79)	**Secondary Prevention (n=57)**
Male (%)	50 (63)	35 (61)
Median age at censorship (IQR)	40.8 (36.1-48.4)	40.0 (34.1-48.8)
Median age at initial repair (IQR)	3.3 (1.0-5.9) (n=67)	4.8 (3.0-10.7) (n=42)
Median age at implant (IQR)	32.9 (24.3-41.1)	29.5 (21.6-40.3)
Median time from initial surgery to device implant (IQR)	30.3 years (21.5-34.2)	20.0 years (15.7-30.6)
Primary prevention indication: Severe LVSD (%) Induced ventricular arrhythmia (%) Non sustained VT (%) Syncope (%) Palpitations/pre-syncope (%) Unclear (%)	 22 (28) 17 (22) 26 (33) 6 (8) 6 (8) 2 (3)	 N/A
Secondary prevention indication: Cardiac arrest due to ventricular arrhythmia (%) Sustained VT (%)	 N/A	 12 (21) 45 (79)
Device type:		

Single chamber (%)	5 (6)	6 (11)
Dual chamber (%)	56 (71)	46 (81)
Subcutaneous (%)	4 (5)	1 (2)
Cardiac resynchronisation (%)	14 (18)	4 (7)
Significant systemic ventricular systolic dysfunction (%)	37 (47)	26 (46)
Residual structural disease (%)	45 (57)	37 (65)
Current beta-blocker therapy (%)	73 (92)	54 (95)
Other anti-arrhythmic therapy (%)	15 (19)	8 (14)
Ablation:		
VT (% of total)	3 (4)	9 (16)
Supraventricular (%)	5 (6)	1 (2)
AV node (%)	2 (3)	1 (2)
Lead with advisory (%)	16 (20)	10 (18)
Median years of follow-up since implant (IQR)	8.3 (3.8-12.0)	9.6 (4.8-13.3)

Table 2: Outcomes

ATP = anti-tachycardia pacing.

* = Each group includes one patient with an undocumented number of repeated therapies

	Primary Prevention (n=79)	Secondary Prevention (n=57)
Appropriate ATP (%)	22 individuals (28) 329* episodes	18 individuals (32) 709 episodes
Appropriate defibrillation (%)	14 individuals (18) 41+ episodes*	8 individuals (14) 26 episodes
Inappropriate ATP (%)	17 (22) 61 episodes	8 (14) 65+ episodes*
Inappropriate defibrillation (%)	15 (19) 47 episodes	7 (12) 24+ episodes*
Patients experiencing complications (%)	29 (37)	15 (26)
Complications necessitating hardware revision/extraction (% of total patients)	18 (23)	11 (19)
Complications: Generator site (%) Pneumothorax (%) Infection and endocarditis (%) Lead malfunction (%)	 4 (5) 3 (4) 3 (4) 16 (20)	 3 (4) 0 3 (5) 5 (9)

Complications in leads with advisory (% total complications)	11 (38)	5 (33)
Death (%)	10 (13)	5 (9)
Median time from implant to death, years	3.6	1.1

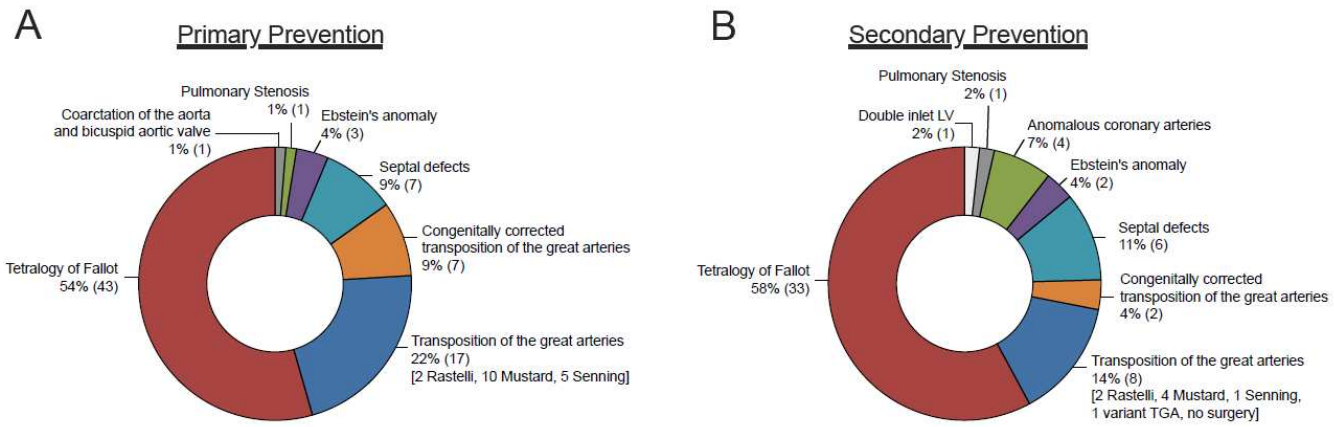

Figure 1: Congenital cardiac anatomy in patients with primary and secondary indications for implantable cardioverter defibrillators. Left panel: primary prevention devices (n=79). Right panel: secondary prevention devices (n=57).

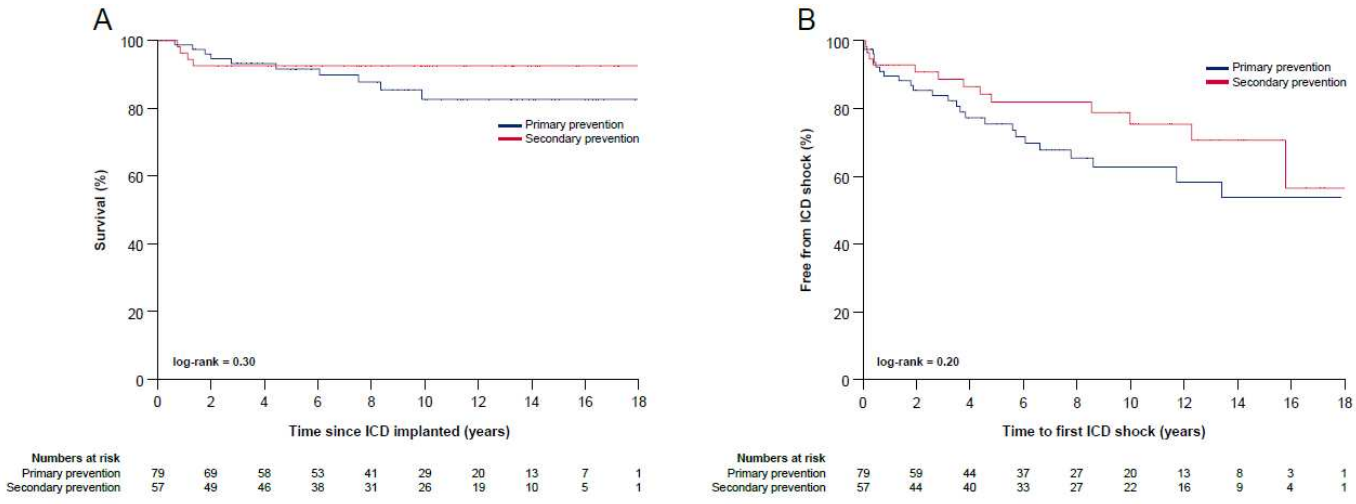

Figure 2a: Kaplan-Meier plot comparing time from ICD implantation to death between the primary and secondary prevention groups

Figure 2b: Kaplan-Meier plot comparing time from ICD implantation to first shock across the primary and secondary prevention groups