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Incidence and clinical characteristics of sudden cardiac death in adult congenital heart disease

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ABSTRACT

Background: The life expectancy of adults with congenital heart disease (CHD) has significantly improved in recent decades, with non-cardiovascular causes of death now competing with traditional cardiovascular causes. The risk of sudden cardiac death (SCD), a devastating event, still remains elevated above that of the general population.
Methods: We reviewed 2935 patients in our adult CHD database (age ≥ 16 years, seen at least once in our centre) and documented all cases of SCD between 2000–2015. Incidence and characteristics of SCD cases by congenital defect and complexity of disease were determined.
Results: We documented 35 cases of SCD, with an incidence of 0.4 deaths/1000 patient years (py). Incidence in simple, moderate and complex congenital categories was 0.04/1000 py, 0.57/1000 py and 2.0/1000 py respectively. The highest risk category was Eisenmenger syndrome, with an incidence of 4.8 deaths/1000 py. Moderate risk lesions included transposition of the great arteries (atrial switch surgery or congenitally corrected) and Fontan circulations. Repaired tetralogy, atrial septal defect and left ventricular outflow tract lesions were all relatively low risk. We observed a high prevalence of atrial arrhythmias (43%) and QRS prolongation (mean 132 ms) in our SCD cases.
Conclusions: The adult CHD population remains at an elevated risk for SCD, particularly in the setting of complex underlying defects. Moderate to high risk lesions include Eisenmenger syndrome, transposition of the great arteries (atrial switch or congenitally corrected) and Fontan circulations.

1. Introduction

The adult congenital heart disease (ACHD) population is steadily growing as a result of advances in their paediatric medical and surgical care [1]. Unsurprisingly mortality patterns in this group are changing, with a diminishing proportion of cardiovascular death and rising non-cardiovascular causes such as malignancy or infection [2]. Sudden cardiac death (SCD) is an often unpredictable tragedy in these younger patients, historically accounting for 20–25% of all ACHD deaths [2–6]. Absolute incidence in *repaired* CHD is estimated to be 25–100 times greater than the general population [7]. Lesions implicated as "high risk" include transposition of the great arteries (TGA), Fontan circulations, repaired Tetralogy of Fallot (rTOF), aortic stenosis and coarctation of the aorta (CoA) [4,8–11].

In the context of changing mortality patterns, this study aimed to determine the incidence of SCD in a contemporary ACHD cohort, classified by underlying congenital lesion and complexity of defect. Clinical characteristics of SCD cases are described in detail.

2. Methods

A retrospective single centre review was performed at a quaternary ACHD referral centre in Sydney, Australia. Ours is the only ACHD centre state-wide with a catchment of 6–7 million people. 2935 patients aged ≥16 years old and seen at least once between January 2000 and December 2015 were included. All cases of SCD in this period were identified from the National Death Index Survey (NDIS), with cause of death verified by review of clinical records; 35 cases were included for analysis. Acquired cardiac lesions or small atrial septal defect (ASD)/patent foramen ovale was excluded. Patient years followed was calculated by multiplying the number of patients by the total years between their 16th birthday (age at referral to our ACHD centre) and last known vital status. Last known vital status was taken either as time of death, or if alive, the date of our last NDIS verification (31st December 2015). Incidence of SCD was calculated by dividing the number of SCD cases by total patient years followed, then multiplying by 1000 (expressed in deaths / 1000 patient years). This was calculated for specific congenital lesions and by Bethesda level of complexity of underlying CHD [12].

SCD cases were divided into diagnostic categories as follows: Eisenmenger syndrome, Fontan circulation, TGA with atrial switch (Mustard and Senning), congenitally corrected TGA (CCTGA), repaired Tetralogy of Fallot (rTOF), other complex biventricular repair, atrio-ventricular septal defect (AVSD), coarctation of the aorta (CoA), Ebstein's anomaly, ventricular septal defect (VSD), atrial septal defect (ASD), left ventricular outflow tract lesion (LVOT) or other. Eisenmenger syndrome was defined as the presence of systemic pulmonary artery pressures or high pulmonary vascular resistance with reversed or

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bidirectional shunts [13]. In the case of >1 diagnosis applying to the one patient, the most haemodynamically significant lesion (assessed at last follow up) was used to categorise the patient. SCD was defined in this study as 1) death due to cardiovascular causes within 1 h of symptom onset or worsening of symptoms or 2) unwitnessed death during sleep. Cases were included if classified as definite or probable SCD based on available clinical data. Patients with non-sudden cardiac death or non-cardiac cause of death were excluded.

Some of the patients included in this report have previously been included in lesion-specific papers from our group, including a subset of those with CCTGA [14] and atrial switch repairs for TGA [15].

Previous surgical, arrhythmic and heart failure history as well as echocardiographic and electrocardiographic parameters were extracted from clinical records and taken from the most recent review prior to death. Rhythm, QRS width and QTc interval were analyzed manually from standard 12 lead ECG with QT correction via Bazett's formula [16]. Heart failure symptoms were defined as dyspnoea and/or peripheral oedema. Ventricles were defined as systemic or subpulmonary and function was assessed by 2D echocardiography; classified as normal (EF ≥ 50%), mildly impaired (40–49%), moderately impaired (30–39%) or severely impaired (<30%). Where available, autopsy reports were reviewed from the State Coroner's office.

Statistical analysis was performed using Statistical Package for Social Services V.22.0 (SPSS, Chicago Illinois). Continuous variables are presented as mean ± standard deviation (SD) or median with range. Categorical variables are presented as frequencies and percentages. Kaplan–Meier curves for freedom from SCD were constructed.

Table 1
Patient years followed and absolute numbers of sudden cardiac deaths by congenital lesion.

Lesion	No. patients in database	Total follow up (patient years)	No. SCD	SCD events/1000 patient years
Eisenmenger	61	1467	7	4.8
TGA atrial switch	88	1676	4	2.4
Fontan	115	1944	4	2.1
CCTGA	43	1017	2	2.0
Complex biventricular repair	45	755	1	1.3
Other			2	
AVSD	37	565	1	1.8
rTOF	333	7091	7	1.0
Ebstein	49	1488	1	0.7
CoA	208	4706	2	0.4
LVOT lesion	815	32,763	1	0.0
VSD	243	6129	1	0.2
ASD	338	12,515	2	0.2

SCD = sudden cardiac death, TGA = transposition of the great arteries, CCTGA = congenitally corrected transposition of the great arteries, rTOF = repaired Tetralogy of Fallot, AVSD = atrioventricular septal defect, CoA = coarctation of the aorta, VSD = ventricular septal defect, ASD = atrial septal defect.

3. Results

3.1. Incidence

Overall there were 35 sudden cardiac deaths in 2935 patients (1.2%) within the study period. These patients were followed for a combined total of 85,276 years, corresponding to an event rate of 0.4 deaths/1000 patient years (py). LVOT lesion patients (predominantly bicuspid aortic valves) contributed 1 SCD in 32,763 py; if these were excluded the incidence of SCD was 0.7/1000 py. The majority of deaths occurred in men (n = 24, 69%), at a mean age of 39 (±16) years old. Fig. 1 shows the incidence of SCD in events per 1000 patient years for specific congenital defects. The highest incidence was seen in Eisenmenger syndrome patients, followed by other complex defects (Fontan, TGA atrial switch and other complex repaired defects). Table 1 displays the overall number of patients in each congenital diagnostic class along with total patient years followed and SCD events. The "complex biventricular repair" group included 1 patient post-Rastelli for TGA. There were 2 deaths in the "other" category, both cyanotic (non-Eisenmenger) complex defects. A relatively low incidence was seen in ASD and VSD patients. When considered by complexity of ACHD, there were 2 SCDs in the simple group (0.1% or 0.04 events/1000 py), 13 SCDs in the moderate group (1.4% or 0.57 events/1000 py) and 20 deaths in the complex group (3.8% or 2.0 events/1000 py). Fig. 2 shows the Kaplan–Meier curves for freedom from SCD arranged by complexity of CHD.

3.2. Clinical characteristics of SCD cohort

Clinical characteristics of the overall cohort are shown in Table 2, with data available in 30/35 patients (86%). Twenty-six patients had undergone surgical repair or palliation in childhood; the average total number of surgeries was 1.6 (±1.4). The average time from definitive repair or palliation to death was 27 years (4–61, SD 13). Nine patients had not undergone any operative interventions. In this relatively young cohort, coronary angiography had only been performed in 4; in 3 cases minor irregularities only were found and in 1 rTOF patient an

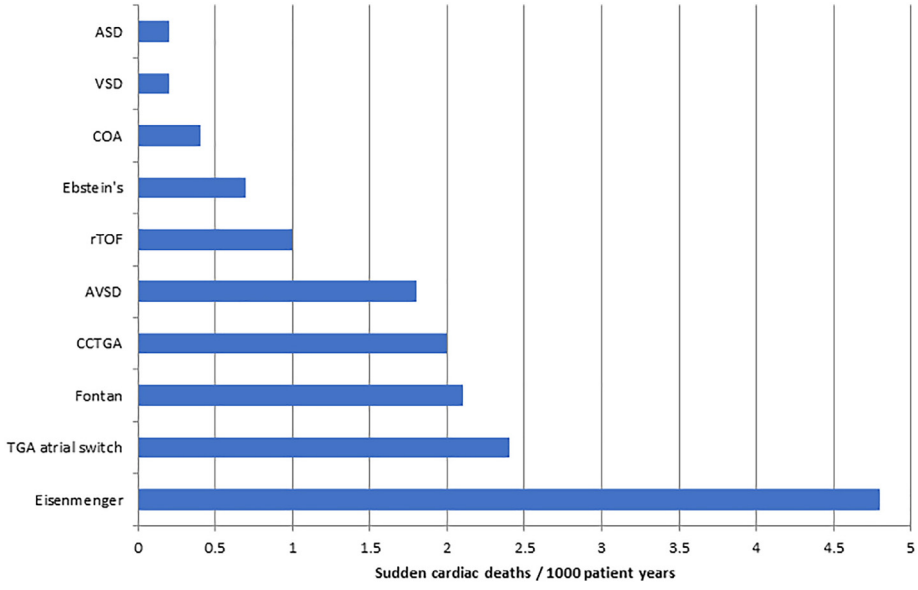

Fig. 1. Incidence of sudden cardiac death by underlying congenital lesion. Left ventricular outflow tract lesion SCDs are not included in this figure. ASD = atrial septal defect, VSD = ventricular septal defect, COA = coarctation of the aorta, rTOF = repaired Tetralogy of Fallot, AVSD = atrio-ventricular septal defect, CCTGA = congenitally corrected transposition of the great arteries, TGA = transposition of the great arteries.

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