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Sudden Death in Childhood Cardiomyopathy

Results From a Long-Term National Population-Based Study

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ABSTRACT

BACKGROUND Children with cardiomyopathy (CM) are at risk of sudden cardiac death (SCD), but the incidence and risk factors for this outcome are not clear.

OBJECTIVES This study sought to determine the incidence and risk factors for SCD in children with varying CM phenotypes from a long-term population-based study of childhood CM.

METHODS The NACCS (National Australian Childhood Cardiomyopathy Study) is an ongoing longitudinal cohort study including all children in Australia with primary CM who were diagnosed between January 1, 1987, and December 31, 1996, and were <10 years of age. The cumulative incidence and risk factors for SCD within individual CM phenotypes were explored using survival analysis.

RESULTS Of 289 eligible patients, 16 (5.5%) experienced SCD over a median follow-up of 11.9 years (interquartile range: 1.7 to 15.4). The risk of SCD varied according to CM phenotype ($p = 0.007$). The cumulative incidence of SCD at 15 years was 5% for dilated cardiomyopathy (DCM), 6% for hypertrophic cardiomyopathy (HCM), 12% for restrictive cardiomyopathy, and 23% for left ventricular (LV) noncompaction. Older age at diagnosis, positive family history of CM, and severity of LV dysfunction were related to increased risk of SCD in patients with DCM, and a higher posterior wall thickness Z-score was the sole risk factor identified for patients with HCM.

CONCLUSIONS Predictors of SCD include CM phenotype, family history of CM (DCM), severity of systolic dysfunction (DCM), and extent of LV hypertrophy (HCM). Continuing follow-up of this cohort into adulthood is likely to reveal an ongoing risk of SCD. (J Am Coll Cardiol 2015;65:2302–10) © 2015 by the American College of Cardiology Foundation.

Pediatric cardiomyopathies (CMs) are an uncommon and heterogeneous group of conditions, with multiple etiologies and varied outcomes. They are an important cause of morbidity and mortality in childhood (1–3). Children with CM are at risk of sudden cardiac death (SCD), but the

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incidence and risk factors for SCD in children with varying CM phenotypes have not previously been well defined (4–7). Better data regarding the incidence and risk factors for SCD in this population are required to deploy appropriate primary prevention strategies targeting high-risk individuals.

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The NACCS (National Australian Childhood Cardiomyopathy Study) is a population-based cohort study comprising all Australian children under the age of 10 years who were diagnosed with CM over a 10-year period (8). Using this cohort, we sought to describe the incidence of SCD in young children with different CM phenotypes and to explore risk factors for SCD in this population.

METHODS

STUDY DESIGN. The NACCS is an ongoing cohort study that includes all children in Australia with primary CM who were diagnosed between January 1, 1987, and December 31, 1996, and were younger than 10 years of age at diagnosis. The exclusion criteria included congenital heart disease, arrhythmia-induced cardiac dysfunction, Kawasaki disease, prior exposure to corticosteroids or anthracyclines, progressive systemic, metabolic, or neuromuscular disease resulting in other severe organ involvement, and maternal diabetes or prematurity for children who were diagnosed before 4 weeks of age. Full details of the methods, including enrollment and inclusion and exclusion criteria, have been detailed elsewhere (8). Local ethics committee approval was obtained in accordance with requirements from each participating center.

DATA COLLECTION. Prospective follow-up was arranged for enrolled study patients, using standardized data collection sheets to document uniform clinical and echocardiographic data at baseline and throughout follow-up. Echocardiographic measurements were normalized according to body surface area or age (9). The variables recorded for each patient are listed in the Online Appendix.

CLASSIFICATION OF CASES. A single observer assigned each case to a diagnostic category according to the World Health Organization's classification of CM (10) during site visits, after directly reviewing each medical record and all available data, including diagnostic cardiac imaging. The diagnostic criteria for dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), restrictive cardiomyopathy (RCM) and left ventricular noncompaction (LVNC) have previously been described (8). Patients were excluded from this analysis if they did not clearly meet the criteria for 1 of these 4 CM phenotypes. A single pediatric pathologist centrally reviewed all available cardiac histology and made a diagnosis of lymphocytic myocarditis on the basis of the Dallas criteria (11). The diagnosis of familial CM required a history of at least 1 affected first- or second-degree relative. SCD was defined as a sudden and unexpected death in a child within 4 h of new symptoms and was adjudicated by the same observer who reviewed each medical record. Congestive heart failure (CHF) was assessed on the basis of signs and symptoms recorded by the attending physician. Patients who died following abrupt deterioration in the setting of CHF or during hospitalization for heart failure management were considered to have died of CHF.

ABBREVIATIONS AND ACRONYMS

CHF = congestive heart failure
CM = cardiomyopathy
DCM = dilated cardiomyopathy
HCM = hypertrophic cardiomyopathy
ICD = implantable cardioverter-defibrillator
LVEDD = left ventricular end-diastolic dimension
LVFS = left ventricular fractional shortening
LVNC = left ventricular noncompaction
RCM = restrictive cardiomyopathy
SCD = sudden cardiac death

STATISTICAL METHODS. The cumulative incidence of SCD for each CM phenotype was assessed using survival analysis. Patients who died of other causes were censored at the time of death, and patients who are still alive were censored at the time of last follow-up. Patients who were not known to have CM until they experienced SCD and those who died within 24 h of diagnosis were excluded from the survival analysis because pre-death data were not available for this group. In patients with DCM, normalization of LV function was considered to have occurred on the first occasion when the left ventricular end-diastolic dimension (LVEDD) Z-score was $<+2.0$ and the left ventricular fractional shortening (LVFS) Z-score was >-2.0. Because implantable cardioverter-defibrillator (ICD) insertion may have modified the risk of SCD, a competing risk analysis was performed, with results presented as cumulative incidence of SCD, heart failure death/transplant, and ICD insertion, along with the corresponding survival curve.

Risk factors for SCD for each CM phenotype were assessed using Cox proportional hazards models. Patients who experienced either of the competing risks of heart failure death/transplant or ICD insertion were censored at the time of the event. Patients were censored at the time of last follow-up if no event was experienced. Potential risk factors (Online Appendix) included characteristics at the time of diagnosis, as well as the latest and rate of change of echocardiographic measurements (included as time-dependent covariates, for which rate of change was the difference between the 2 most recent measurements before the event divided by the time between the measurements). Echocardiographic measurements considered

were LVFS, LVEDD, posterior wall thickness, and interventricular septal thickness Z-scores. Risk factors were considered in univariable models to assess independent predictors. In view of the low event rates for SCD, multivariable analysis was not undertaken.

RESULTS

A total of 301 patients with a CM phenotype of DCM, HCM, RCM, or LVNC were recruited into the NACCS between January 1, 1987, and December 31, 1996. Nine patients with DCM had SCD as their first manifestation, and an additional 3 patients with DCM died within 24 h of diagnosis, leaving 289 for this analysis. The demographics of the study population are shown in Table 1. The majority of patients were diagnosed with CM during their first year of life (median age at diagnosis for all patients 0.56 years; interquartile range [IQR]: 0.15 to 1.91 years). Follow-up data were available for all patients. The median duration of follow-up was 11.9 years (IQR: 1.7 to 15.4 years) for all patients and 14.2 years (IQR: 12.5 to 17.4 years) for those who survived without transplantation. Nineteen percent of the cohort (n = 55) had familial CM.

INCIDENCE OF SCD. SCD occurred in 16 patients (Table 1). SCD accounted for 15% of all deaths in the study cohort and 24% of deaths among patients who died >1 year after diagnosis.

The cumulative incidence of SCD at 15 years after diagnosis (Central Illustration) was 5% (95% CI: 2% to 11%) for DCM, 6% (95% CI: 2% to 17%) for HCM, 23% (95% CI: 10% to 47%) for LVNC, and 12% (95% CI: 2% to 61%) for RCM (p = 0.007 for association of incidence and CM phenotype). The median LVEDD Z-score at the latest follow-up in patients with DCM who experienced SCD was +5.3 (range 4.2 to 8.6), and the median LVFS Z-score was −9.5 (range −13.0 to −6.2). There were no instances of SCD among those who had documented echocardiographic normalization of LV function. The median age at SCD was 8.6 years (ages of individual patients 1.5, 5.1, 6.9, 10.2, 11.2, and 15.2 years) for patients with DCM, 8.3 years (ages of individual patients 0.5, 7.1, 9.5, and 14.0 years) for HCM, 2.8 years (ages of individual patients 0.9, 2.6, 3.0, 3.1, and 3.3 years) for LVNC, and 2.8 years for the patient with RCM.

Figure 1 shows a breakdown of the outcomes by CM phenotype presented as competing risk curves. These indicate an ongoing risk of SCD beyond the first few years after diagnosis, especially for patients with DCM or HCM.

FAMILIAL CM. There were 55 patients with familial CM: 26 with DCM, 19 with HCM, 9 with LVNC, and 1 with RCM. Of these patients, 3 with DCM and 2 with LVNC experienced SCD. None of the 9 patients with familial HCM or the single patient with familial RCM died suddenly.

DEVICE THERAPY. During the study period, ICD insertion was performed in 19 patients (4 DCM, 13 HCM, and 2 LVNC): in 9 patients for primary prevention and in the remaining 10 due to syncopal symptoms or documented arrhythmias. During a 7.8 ± 4.5 years after ICD insertion, 1 patient with DCM died suddenly and the remaining 18 patients are alive. Appropriate defibrillator shocks were documented in 5 of 14 patients (35.7%) for whom this information was available. No cardiac resynchronization therapy devices have been implanted into any of the study patients.

RISK FACTORS FOR SCD IN DCM. Older age at diagnosis, presence of familial CM, and lower LVFS Z-score at the latest follow-up were associated with increased risk of SCD in patients with DCM (Table 2). A higher LVEDD Z-score was also associated with

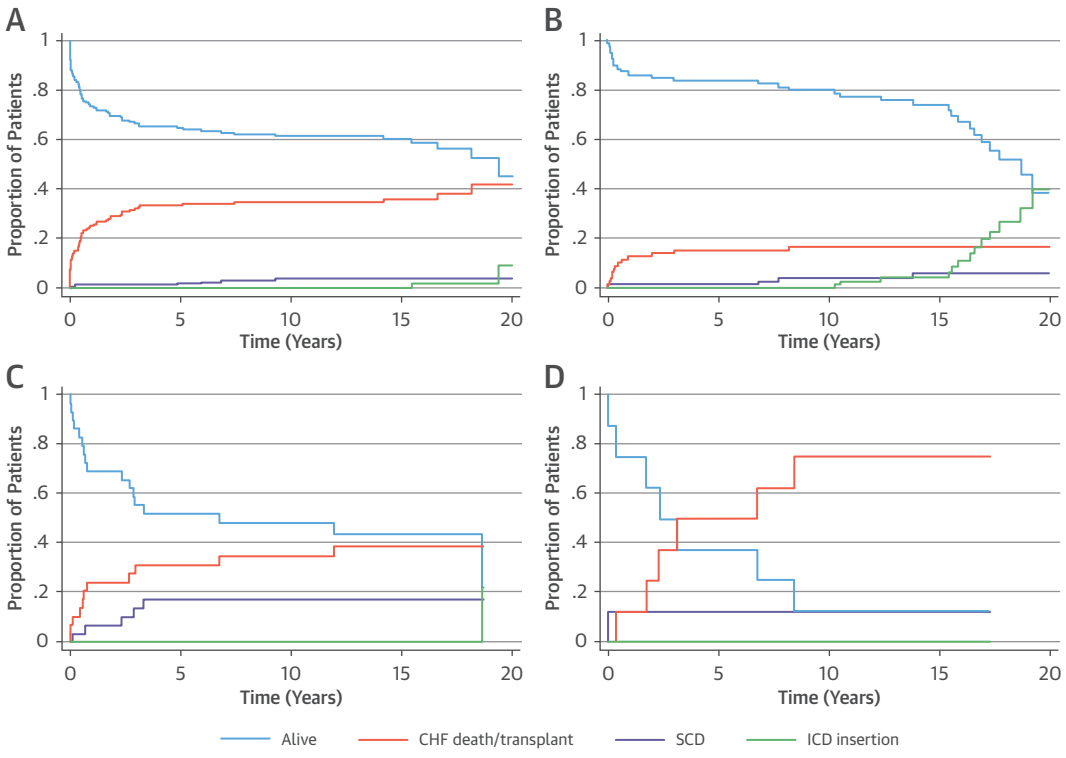
TABLE 1 Demographics of Study Population

	DCM (n = 172)	HCM (n = 80)	LVNC (n = 29)	RCM (n = 8)	All Patients (N = 289)
Age at diagnosis, yrs	0.65 (0.16–1.69)	0.45 (0.12–2.48)	0.34 (0.10–1.33)	3.03 (2.59–5.44)	0.56 (0.15–1.91)
Follow-up, yrs	12.5 (0.6–15.9)	14.0 (10.7–17.1)	6.8 (7.0–14.1)	2.8 (1.5–7.2)	11.9 (1.7–15.4)
Follow-up for survivors, yrs*	15.1 (13.0–17.3)	15.7 (12.9–17.7)	14.3 (12.2–14.7)	N/A (n = 1)	14.2 (12.5–17.4)
Positive family history of CM	26 (13.4)	19 (23.8)	9 (3.4)	1 (12.5)	55 (19.0)
Outcome					
SCD	6	4	5	1	16
HFD/transplant	62	13	11	6	92
Survivors	104	63	13	1	181

Values are median (IQR), n (%), or n. *Patients surviving without heart transplant.

CM = cardiomyopathy; DCM = dilated cardiomyopathy; HCM = hypertrophic cardiomyopathy; HFD = heart failure death; IQR = interquartile range; LVNC = left ventricular noncompaction; N/A = not applicable; RCM = restrictive cardiomyopathy; SCD = sudden cardiac death.

FIGURE 1 Outcomes for Patients With CM



Cumulative incidence for the competing risks of sudden cardiac death (SCD), death due to congestive heart failure (CHF) or transplantation, and implantable cardioverter-defibrillator (ICD) insertion. Event-free survival in patients with dilated cardiomyopathy **(A)**, hypertrophic cardiomyopathy **(B)**, left ventricular noncompaction **(C)**, and restrictive cardiomyopathy **(D)**.

increased risk of SCD but not in addition to LVFS Z-score. There were no patients with lymphocytic myocarditis diagnosed by endomyocardial biopsy who experienced SCD during the study follow-up, although lymphocytic myocarditis was found in 6 of 9 excluded patients whose initial symptom was sudden death.

RISK FACTORS FOR SCD IN HCM. The only variable that was identified as a predictor of SCD in patients with HCM was the LV posterior wall thickness Z-score at the latest follow-up (Table 3). The presence of familial HCM could also have been protective of SCD, but the magnitude of any effect could not be assessed because no one with familial HCM died suddenly.

RISK FACTORS FOR SCD IN LVNC. There was a trend toward a higher risk of SCD in patients with LVNC with deteriorating ventricular function measured by LVFS or LVEDD and greater severity of LVNC as measured by increased ratio of compacted to noncompacted myocardium (Table 4).

RISK FACTORS FOR SCD IN RCM. It was not possible to explore risk factors for SCD in patients with RCM because there was only 1 instance of SCD.

DISCUSSION

This national, population-based cohort study is unique because of its fully inclusive nature, the extended follow-up duration, and the availability of comparative data for different CM phenotypes. This study provided insight into the incidence of SCD in children with CM and identified potential predictors for this outcome. As seen in this study, SCD is an important cause of mortality, affecting between 5% and 25% of patients over a 15-year period according to CM phenotype (Central Illustration). These estimates are conservative due to the stringent definition of SCD and the exclusion of patients who deteriorated abruptly in the setting of CHF.

The identification of patients with CM who are at risk of SCD may facilitate modification of the natural history by allowing the clinician to target high-risk

TABLE 2 Risk Factors for SCD in Patients With DCM

	Univariable Analysis	
	HR (95% CI)	p Value
Sex (female vs. male)	0.41 (0.07–2.21)	0.30
Race (Aboriginal vs. other)	*	
Age at diagnosis, yrs	1.40 (1.11–1.77)	0.005
Congestive heart failure at diagnosis	*	
Family history of CM	7.19 (1.44–35.9)	0.02
Family history of CM with sudden death	*	
Myocarditis	†	
Latest end-diastolic dimension Z-score	1.61 (1.16–2.22)	0.004
Latest fractional shortening Z-score	0.75 (0.60–0.93)	0.009
Rate of change of end-diastolic dimension Z-score (per year)	1.01 (0.91–1.12)	0.87
Rate of change of fractional shortening Z-score (per year)	0.73 (0.49–1.07)	0.10

*Not possible to calculate an HR because all 6 events occurred in 1 category. †Not possible to calculate an HR because there were no SCD events in patients with biopsy-proven myocarditis.
HR = hazard ratio; other abbreviations as in Table 1.

patients for insertion of ICDs. These have proven efficacy in preventing SCD by terminating life-threatening ventricular arrhythmias in children and adolescents identified to be at high risk (12).

DILATED CM. Children with DCM make up the largest proportion of this cohort (59.5%) and have a lower incidence of SCD than children with other CM phenotypes. Late normalization of LV function has been noted in a high proportion of children with DCM (13) and may account for the generally lower rates of SCD in this CM phenotype.

In the current study, familial CM was an important risk factor for SCD in patients with DCM, a phenomenon that could potentially be explained by the presence of familial proarrhythmic genotypes (14,15). This finding is in contrast to a report from the PCMR (Pediatric Cardiomyopathy Registry), in which family history was not associated with SCD (16). In the PCMR study, sex, ethnicity, and etiology were also not associated with SCD, as in our study, and greater LV dilation, age at diagnosis <14.3 years, and lower LV posterior wall thickness to LVEDD ratio were predictive of SCD. The difference with respect to familial DCM between these 2 studies may be explained by the age difference of enrolled patients, the more severe presentation of familial DCM in our younger patients, and our exclusion criteria. In the NACCS registry, familial DCM was also associated with a higher risk of death or transplantation during follow-up (13).

In children with DCM, the highest risk of death or transplantation occurs in the first year after diagnosis (13). The risk of SCD, on the other hand, appears to be ongoing in individuals with persisting cardiac dysfunction. The association between severity of LV dysfunction and the risk of SCD is supported by studies in children and adults (5,17) and is consistent with observations from multiple studies showing that worse systolic function at diagnosis is associated with generally poorer short- and long-term outcomes (2,4,13).

In the present study, there were no patients with myocarditis who experienced SCD. A recent report from the PCMR study demonstrated that children with DCM secondary to biopsy-proven or clinically diagnosed myocarditis had generally better outcomes, with lower rates of both death and transplantation, and higher rates of normalization of ventricular function (18).

TABLE 3 Risk Factors for SCD in Patients With HCM

	Univariable Risk Factors	
	HR (95% CI)	p Value
Sex (female vs. male)	2.29 (16.31–0.32)	0.41
Race (Aboriginal vs. other)	*	
Age at diagnosis, yrs	0.68 (1.62–0.28)	0.38
Congestive heart failure at diagnosis	*	
Family history of CM	*	
Family history of CM with sudden death	*	
Noonan syndrome	1.38 (2.65–0.72)	0.34
Latest end-diastolic dimension Z-score	1.13 (1.73–0.74)	0.56
Latest fractional shortening Z-score	1.00 (1.29–0.77)	0.98
Latest posterior wall thickness Z-score	1.47 (2.03–1.06)	0.02
Latest interventricular septal thickness Z-score	1.05 (1.49–0.73)	0.81
Rate of change of end-diastolic dimension Z-score (per year)	0.90 (1.37–0.59)	0.62
Rate of change of fractional shortening Z-score (per year)	1.03 (1.51–0.70)	0.89
Rate of change of posterior wall thickness Z-score (per year)	1.01 (1.31–0.78)	0.94
Rate of change of interventricular septal thickness Z-score (per year)	0.93 (1.96–0.44)	0.85

*Not possible to calculate an HR because all events occurred in 1 category.
Abbreviations as in Tables 1 and 2.

HYPERTROPHIC CM. Pediatric HCM is characterized by a variety of metabolic, mitochondrial, and sarcomeric etiologies, some of which are not fully expressed until adult life. Risk factors for SCD in HCM previously reported in adult patients include family history of SCD, documented ventricular arrhythmias, and abnormal blood pressure response during exercise (19–21). Maron et al. (22,23) also found that approximately 40% of patients with HCM who die suddenly do so during, or just after, exertion. However, approximately 60% experience SCD while they are inactive or mildly active (24), with the majority being symptom free beforehand. Several studies have shown that severely increased LV wall thickness is an important marker of risk for SCD (25–27). In our study, the most important risk factor for SCD in patients with HCM was the magnitude of LV free wall hypertrophy. The potential protective effect of familial HCM in our cohort of pediatric patients may explain why isolated septal hypertrophy, typically associated

with sarcomeric mutations, did not confer an increased risk of SCD.

Family history of SCD in the setting of familial HCM has been suggested as a risk factor for SCD, particularly in association with syncope (28–30). Certain sarcomeric mutations are associated with higher-risk phenotypes (31,32). In our study, no patients with familial HCM died suddenly, although it is unlikely that these patients were truly protected from the risk of this outcome. These individuals may not yet have reached full phenotypic expression of the disease and may therefore remain at ongoing risk of SCD during adult life.

LV NONCOMPACTION. Other than the diagnosis itself, we were unable to identify individual risk factors for SCD in patients with LVNC. This disease is uncommon and has multiple subtypes; the small number of patients in our study may have limited our ability to quantify and detect risk factors for SCD. These patients have a variable, but generally poor, outcome overall, as has also been noted by other researchers (33,34). In a large study of 240 patients with LVNC (34), the risk of SCD was found to be 6%, compared with 23% in the present study. The unexpectedly high incidence of SCD in patients with LVNC may reflect the early onset of severe DCM physiology in our study. Children with LVNC have a high incidence of arrhythmias, and in the presence of ventricular dysfunction, they should be considered at risk of SCD (34).

RESTRICTIVE CM. We were unable to explore risk factors for SCD in RCM due to the small number of events in this population-based study; however, as suggested here and in previous studies, children with RCM have poor survival rates (35–37). In a reported series of 18 children with RCM, 5 (28%) experienced "sudden death events"; 1 of these children was successfully resuscitated and proceeded to transplant and 4 died (38). Our figures are in accord with this; although the absolute number of patients was small, the incidence rate of death was large. A high proportion of our patients with RCM underwent transplant; because there is no effective therapy for RCM, transplantation is the only therapeutic option that decreases mortality (39).

TIMING OF SUDDEN DEATH. In both LVNC and RCM, patients in our series experienced SCD relatively early; all SCDs in these 2 diagnostic groups occurred within the first 3 years following diagnosis. Conversely, patients with DCM or HCM have an ongoing risk, with a gradual increase in the cumulative incidence of SCD continuing many years after diagnosis and commencement of heart failure therapy.

TABLE 4 Risk Factors for SCD in Patients With LVNC

	Univariable Analysis	
	HR (95% CI)	p Value
Sex (female vs. male)	0.89 (8.20–0.10)	0.92
Race (Aboriginal vs. other)	*	
Age at diagnosis, yrs	0.94 (1.83–0.48)	0.85
Congestive heart failure at diagnosis	0.49 (2.92–0.08)	0.43
Family history of cardiomyopathy	0.89 (5.40–0.15)	0.90
Family history of sudden death	2.25 (20.29–0.25)	0.47
End-diastolic dimension Z-score	0.85 (1.22–0.59)	0.37
Fractional shortening Z-score	0.91 (1.16–0.71)	0.44
Rate of change of end-diastolic dimension Z-score (per year)	1.64 (2.92–0.92)	0.09
Rate of change of fractional shortening Z-score (per year)	1.10 (1.24–0.98)	0.11
Ratio of compacted to noncompacted myocardium		
Systole	3.89 (29.43–0.51)	0.19
Diastole	2.90 (9.68–0.87)	0.08

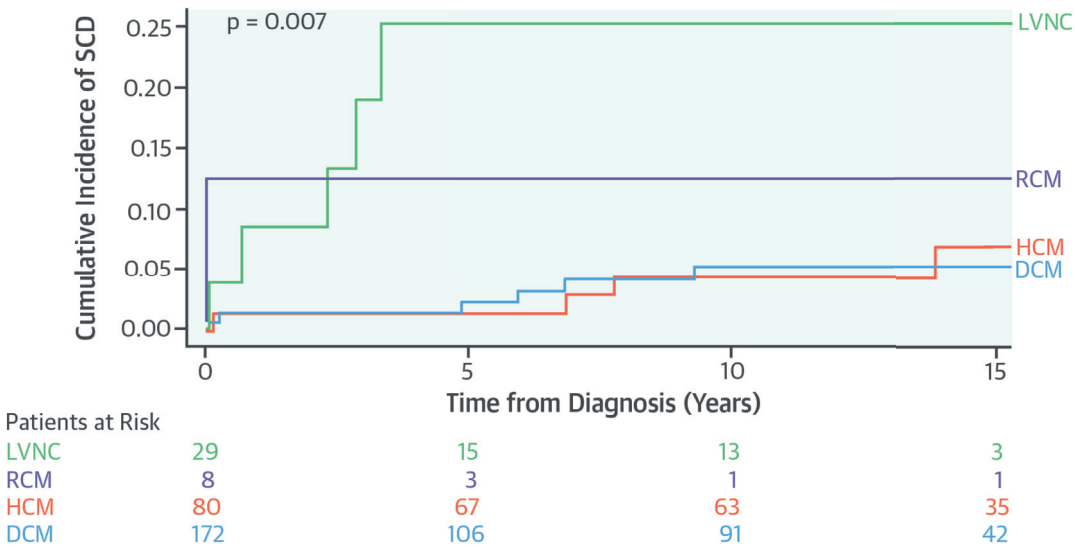
*Not possible to calculate an HR because all events occurred in 1 category.
Abbreviations as in Tables 1 and 2.

ICD THERAPY. Long-term follow-up data on children with ICDs are lacking, and it has not yet been precisely established which subgroup of children with CM warrants primary prevention of SCD with implantable defibrillators or at which age implantation is appropriate. Complications related to ICD leads remain a major problem in pediatric patients (40). A recent study that examined a mixed group of children and adults with HCM considered at high risk of SCD with ICDs inserted as primary prevention found no overall association between age of implantation and subsequent risk of appropriate ICD discharge (41). ICD discharge and SCD remain significant risks, even in the presence of antiarrhythmic drug therapy (41–43).

An unwanted complication of ICDs are inappropriate discharges, which are not uncommon in many reported series, being approximately 25% (41). Inappropriate shocks have been reported to be more common in younger patients (<30 years of age) (41,44). Only 1 of our study patients who received an ICD subsequently died, and none has been listed for heart transplant. However, uniform implantation of ICDs for primary prevention of SCD in pediatric patients awaiting transplant has been shown to be unlikely to improve survival (45).

Despite detailed guidelines (46) for adult patients, there is a lack of evidence-based guidelines for pediatric patients, and decisions to implant an ICD in a child are frequently difficult, with multiple individual considerations. The risk factors for SCD identified in this pediatric population may find a place in decision-making with regard to primary prevention in conjunction with traditional risk factors derived from adult studies.

CENTRAL ILLUSTRATION **Sudden Death in Childhood Cardiomyopathy: Cumulative Incidence by Cardiomyopathy Phenotype**



Bharucha, T. et al. J Am Coll Cardiol. 2015; 65(21):2302-10.

This graph shows the cumulative incidence of sudden cardiac death (SCD) by cardiomyopathy (CM) phenotype in children to 15 years from diagnosis. The incidence of SCD varied by CM type, with patients with left ventricular noncompaction (LVNC) being at highest risk. Patients with dilated cardiomyopathy (DCM) or hypertrophic cardiomyopathy (HCM) experience an ongoing risk of SCD. RCM = restrictive cardiomyopathy.

STUDY LIMITATIONS. An important limitation in this study was the relatively small number of children with SCD, particularly within the less common CM phenotypes, which limits analysis of potential risk factors, including CM etiology, and precludes multivariable analysis.

One could argue that our study may underestimate the incidence of SCD, in large part due to our very stringent definition of SCD. Cardiac transplant may have improved outcomes for some study patients and thereby masked their risk of SCD. However, the majority of patients who underwent transplant had signs and symptoms of CHF and would therefore not have qualified for the definition of SCD we used in this study. In addition, despite our long follow-up duration, patients with HCM may not have entered their highest risk period, which is likely to be in early adult life (19).

This study was not designed to test the efficacy of heart failure therapy for SCD prevention. Medical therapy and indication for ICD insertion were at the discretion of individual physicians, leading to a wide heterogeneity in therapy and interventions across the cohort. Given this heterogeneity, we are unable to comment on the protective effect of individual medical therapies. Across the country, there was not uniformity in investigations performed at follow-up; in particular, exercise stress testing and ambulatory electrocardiogram monitoring were not available for all patients with HCM. Traditional risk factors for SCD in adult patients with HCM could therefore not be examined.

CONCLUSIONS

This national population-based study encompassing all Australian children with CM over a 10-year period, with a long duration of follow-up, provided unique insights into the comparative incidence of SCD in children with different CM phenotypes and identified predictors of this potentially preventable catastrophic outcome. Further corroboration in larger childhood studies of individual CM phenotypes will ultimately facilitate optimal management strategies by clarifying which patients are at greatest risk of SCD and might benefit from primary prevention ICD therapy. Continuing follow-up of this cohort into adulthood is likely to reveal an ongoing risk of SCD in this population.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: CM are at variable risk of sudden death related to CM phenotype. In those with dilated CM, a family history of dilated CM and more severe left ventricular dysfunction are risk factors for sudden death, whereas among those with hypertrophic CM, posterior wall thickness is a risk factor.

TRANSLATIONAL OUTLOOK: Further research involving larger cohorts is needed to enhance risk stratification and guide more effective targeting of strategies to prevent arrhythmic death.

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KEY WORDS cardiomyopathy, epidemiology, pediatrics, sudden death

APPENDIX For a list of variables used in the study, please see the online version of this article.