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QRS prolongation is strongly associated with life-threatening ventricular arrhythmias in children with dilated cardiomyopathy

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dilated cardiomyopathy;
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BACKGROUND: The incidence of sudden death in children with dilated cardiomyopathy has been estimated at $< 1\%$ annually. This number, however, may underestimate the incidence of life-threatening arrhythmias. The objective of this study was to assess the incidence of and identify risk factors for life-threatening arrhythmias in children with dilated cardiomyopathy.

METHODS: We conducted a retrospective record review of 183 children with dilated cardiomyopathy treated at a single center between 2000 and 2011. Life-threatening arrhythmia was defined as any ventricular arrhythmia that resulted in syncope or hypotension and required medical intervention. Risk factors for life-threatening arrhythmias were identified with univariate analyses. A prediction model was constructed with multivariate logistic regression and receiver operating characteristic curves.

RESULTS: Nineteen patients experienced life-threatening arrhythmias, representing an annualized rate of 4.9%. Outpatient life-threatening arrhythmias occurred at a rate of 2.2% per year. Predictors of outpatient life-threatening arrhythmias were longer QRS duration ($p = 0.003$) and increased left ventricular posterior wall (LVPWd) thickness ($p = 0.03$). Only QRS duration remained significant in multivariate logistic regression (odds ratio, 1.8 for every unit increase in z-score; 95% CI, 1.01–1.9; $p = 0.04$). For all life-threatening arrhythmias, prolonged QRS duration was the only significant risk factor in multivariate logistic regression (odds ratio, 1.5; 95% CI, 1.1–2.2; $p = 0.02$).

CONCLUSION: In children with dilated cardiomyopathy, as QRS duration increases, so too does the risk of life-threatening arrhythmias. Life-threatening arrhythmias occurred at an annual rate of 5%, which was much higher than the previously reported rate of sudden cardiac death in this population.
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Dilated cardiomyopathy is the most common cause of heart failure in children, with an annual incidence of 0.57 to 1.13 per 100,000.[1,2] Despite numerous advances in the treatment of adults with dilated cardiomyopathy, outcomes remain poor in children with this diagnosis, with an incidence of death or transplantation of 31% at 1 year and 46% at 5 years.[1,3] However, sudden cardiac death has been reported as rare in children with dilated cardiomyopathy, with an estimated incidence ranging from 1% annually to 3% over 5 years.[4,5] These reports omit missed sudden death episodes and some exclude patients with an implantable cardioverter-defibrillator (ICD), which may influence the reported results.

To date, no study has accurately characterized the frequency of life-threatening arrhythmia in children with dilated cardiomyopathy. We hypothesized that life-threatening arrhythmias were more common than suspected in children with dilated cardiomyopathy. In this study, we aimed to determine the incidence of and risk factors for

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life-threatening arrhythmias in pediatric patients with dilated cardiomyopathy and to create a predictive model for life-threatening arrhythmia in these patients.

Materials and methods

The Institutional Review Board at Stanford University approved this study.

Study cohort and data source

A retrospective record review was performed of 183 children with dilated cardiomyopathy at Lucile Packard Children's Hospital at Stanford between January 1, 2000, and December 31, 2011. Standard definitions of dilated cardiomyopathy were used: a left ventricular diameter at end diastole (LVDd) z-score > 2 and ejection fraction (EF) $< 55\%$.[2,6] Etiologies of dilated cardiomyopathy included primary idiopathic, familial, or cardiomyopathy secondary to myocarditis, anthracycline toxicity, metabolic dysfunction, autoimmune processes, or neuromuscular disease. The study excluded patients with hypertrophic or restrictive cardiomyopathy.

Data collection

Data were collected using RedCAP 3.4.1 (Vanderbilt University, Nashville, TN), a Web-based application designed to support data capture for research studies.[7] Demographic and clinical data, including sex, race, age at presentation, and length of follow-up, were recorded. All hospitalizations and outpatient visits were reviewed for presentation symptoms and medications. Presenting symptoms for heart failure included syncope/near syncope, palpitation, dyspnea, chest pain, dizziness, or orthopnea. Electrocardiograms, Holter, and other ambulatory event monitors were reviewed to identify arrhythmia events for all patients.

Baseline measurements, including heart rate, rhythm, and measurements of key intervals (PR, QRS, and QTc) were obtained from all available electrocardiograms. Echocardiograms were reviewed for ejection fraction, left ventricular diameter at end diastole (LVDd), and end systole (LVDs), left ventricular posterior wall thickness at end diastole (LVPWd), ratio of left ventricular posterior wall thickness-to-end diastolic diameter (LVPW/LVDd), and interventricular septum thickness at end diastole (IVSd). Because heart rate and QRS duration vary by age, and LVDd, LVDs, LVPWd, LVPW/LVDd, and IVSd vary by body size, these values were normalized by z-scores.[8,9] In patients who developed life-threatening arrhythmia, ventricular function from the most recent echocardiogram before the event was recorded. Cardiac function in the remaining patients was assessed at the first outpatient visit for dilated cardiomyopathy.

For patients who experienced life-threatening arrhythmia, all cardiac medications prescribed to that patient at the time of the event were recorded. For all other patients, we recorded all cardiac medications prescribed according to the most recent follow-up date. Heart failure medications included digoxin, angiotensin-converting enzyme inhibitors, and diuretics. Anti-arrhythmic medications included amiodarone. β-Blockers were classified as both a heart failure and anti-arrhythmic medication.

ICD data, including indication for implantation and appropriate and inappropriate discharges, were documented as well as the indication for each discharge.

Definitions

Data collection started on the first date that patients were diagnosed with dilated cardiomyopathy. For those diagnosed before establishing care in the Pediatric Heart Failure program at Lucile Packard Children's Hospital, data collection began on the first date they were seen by the Heart Failure program. If patients experienced organ death, defined as death or cardiac transplantation, the date of organ death was taken as their last date of follow-up.

For the purposes of this study, life-threatening arrhythmia was defined as an episode of ventricular fibrillation (VF) or ventricular tachycardia (VT) that led to hypotension or syncope and required interventions (ie, medical or electrical cardioversion), with or without cardiopulmonary resuscitation. Each life-threatening arrhythmia event was further classified as inpatient or outpatient, depending on

Table 1 Baseline Characteristics and Treatment of Patients in the Study

Demographics	Mean ± SD or No. (%) ($N = 183$)
Age, years	7.9 ± 6.6
Sex	
Male	103 (56)
Female	80 (44)
New diagnosis of dilated cardiomyopathy	125 (68)
Follow-up, years	2.1 ± 2.5
Hospitalized for cardiac reason	135 (74)
Cardiac hospitalizations, No.	1.4 ± 1.5
Organ death	66 (36)
Death	19 (10)
Cardiac transplantation	47 (26)
Baseline electrocardiography	
Heart rate, beats/min	105 ± 27
QRS duration, msec	88 ± 23
Baseline echocardiography	
Ejection fraction, %	34 ± 16
z-Score	
LVDd	4.2 ± 4.0
LVDs	6.0 ± 5.0
LVPWd	1.2 ± 2.2
IVSd	1.1 ± 2.0
Medications	
Digoxin	49 (27)
Diuretics	91 (50)
Amiodarone	10 (5)
β-Blockers	66 (36)
ACE inhibitors	109 (59)
Inotropes	79 (43)
Implantable cardioverter-defibrillator	
Total implanted, No.	14
Primary prevention	7
Secondary prevention	7
Appropriate discharges, No.	5
Inappropriate discharges, No.	0
ICDs removed, No.	5

ACE, angiotensin-converting enzyme; HR, heart rate; IVSd, interventricular septum at end diastole; LVDd, left ventricular diameter at end diastole; LVDs, left ventricular diameter at end systole; LVPW/LVDd, ratio of left ventricular posterior wall thickness over left ventricular diameter at end diastole; LVPWd, left ventricular posterior wall thickness at end diastole; SD, standard deviation.