Clinical Presentation of Pediatric Patients at Risk for Sudden Cardiac Arrest

Aarti Dalal, DO[1,2], Richard J. Czosek, MD[3], Joshua Kovach, MD[4], Johannes C. von Alvensleben, MD[5,6], Santiago Valdes, MD[7], Susan P. Etheridge, MD[8], Michael J. Ackerman, MD, PhD[9], Debbie Auld, RN[1], Jeryl Huckaby, RRT, MS[1], Courtney McCracken, PhD[1], and Robert Campbell, MD, FAAP[1]

Objectives To identify the clinical presentation of children and adolescents affected by 1 of 4 cardiac conditions predisposing to sudden cardiac arrest: hypertrophic cardiomyopathy, long QT syndrome (LQTS), catecholaminergic polymorphic ventricular tachycardia (CPVT), and anomalous origin of the left coronary artery from the right sinus of Valsalva (ALCA-R).

Study design This was a retrospective review of newly diagnosed pediatric patients with hypertrophic cardiomyopathy, LQTS, CPVT, and ALCA-R referred for cardiac evaluation at 6 US centers from 2008 to 2014.

Results A total of 450 patients (257 male/193 female; median age 10.1 years [3.6-13.8 years, 25th-75th percentiles]) were enrolled. Patient age was ≤13 years for 70.4% of the cohort (n = 317). Sudden cardiac arrest was the initial presentation in 7%; others were referred on the basis of abnormal or suspicious family history, personal symptoms, or physical findings. Patients with LQTS and hypertrophic cardiomyopathy were referred most commonly because of family history concerns. ALCA-R was most likely to have abnormal signs or symptoms (eg, exercise chest pain, syncope, or sudden cardiac arrest). Patients with CPVT had a high incidence of syncope and the greatest incidence of sudden cardiac arrest (45%); 77% exhibited exercise syncope or sudden cardiac arrest. This study demonstrated that suspicious or known family history plays a role in identification of many patients ultimately affected by 1 of the 3 genetic disorders (hypertrophic cardiomyopathy, LQTS, CPVT).

Conclusion Important patient and family history and physical examination findings may allow medical providers to identify many pediatric patients affected by 4 cardiac disorders predisposing to sudden cardiac arrest. *(J Pediatr 2016;177:191-6).*

Pediatric sudden death is a devastating problem worsened by the fact that the death may have been preventable. Pediatric sudden cardiac arrest can result from a variety of cardiac conditions (some genetic/heritable), trauma, or use of medications/drugs (over-the-counter, prescription, "recreational").[1]

Fortunately, not all pediatric patients affected by these cardiac conditions present with a sentinel event of either sudden cardiac arrest or sudden cardiac death. Instead, children and adolescents may be referred for pediatric cardiac evaluation from primary care offices or emergency departments as a result of symptoms, suspicious or known family history, or the findings of a physical examination. Understanding the features that result in an appropriate referral for a condition in which there is a risk of sudden cardiac arrest may improve recognition of and referrals for these conditions. The goal of this multicenter study was to understand the clinical features that prompt pediatric cardiology referral and evaluation in patients ultimately diagnosed with 1 of 4 of the more common cardiac conditions that may predispose to pediatric sudden cardiac arrest: hypertrophic cardiomyopathy, long QT syndrome (LQTS), catecholaminergic polymorphic ventricular tachycardia (CPVT), and anomalous origin of the left coronary artery from the right sinus of Valsalva (ALCA-R).

Methods

This was a multicenter, retrospective chart review of all newly diagnosed pediatric patients (aged ≤21 years) with hypertrophic cardiomyopathy, LQTS, CPVT, and

AAP	American Academy of Pediatrics
ALCA-R	Anomalous origin of the left coronary artery from the right sinus of Valsalva
CPVT	Catecholaminergic polymorphic ventricular tachycardia
ECG	Electrocardiogram
LQTS	Long QT syndrome

From the [1]Children's Healthcare of Atlanta, Department of Pediatrics, Emory University School of Medicine, Atlanta, GA; [2]Monroe Carell Jr. Children's Hospital at Vanderbilt, Department of Pediatrics, Vanderbilt University School of Medicine, Nashville, TN; [3]The Heart Institute, Cincinnati Children's Hospital Medical Center, Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH; [4]Children's Hospital of Wisconsin, Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI; [5]C.S. Mott Children's Hospital, Department of Pediatrics, University of Michigan Medical School, Ann Arbor, MI; [6]Children's Hospital Colorado, Department of Pediatrics, University of Colorado School of Medicine, Aurora, CO; [7]Texas Children's Hospital, Department of Pediatrics, Baylor College of Medicine, Houston, TX; [8]Primary Children's Hospital, Department of Pediatrics, University of Utah School of Medicine, Salt Lake City, UT; and [9]Mayo Clinic, Department of Pediatric and Adolescent Medicine, Mayo Clinic College of Medicine, Rochester, MN

M.A. serves as a consultant for Boston Scientific, Gilead Sciences, Medtronic, and St. Jude Medical and receives royalties from Transgenomic for Familion-Long QT syndrome and Familion-Catecholaminergic polymorphic ventricular tachycardia genetic tests. The other authors declare no conflicts of interest.

http://dx.doi.org10.1016/j.jpeds.2016.06.088

ALCA-R presenting for their first pediatric cardiac evaluation between January 2008 and December 2014.

Data were collected from 6 different high-volume pediatric centers in the US with large primary and secondary care outpatient networks, including (1) Children's Healthcare of Atlanta, Atlanta, Georgia; (2) Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; (3) Children's Hospital of Wisconsin, Milwaukee, Wisconsin; (4) C.S. Mott Children's Hospital, Ann Arbor, Michigan; (5) Texas Children's Hospital, Houston, Texas; and (6) Primary Children's Hospital, Salt Lake City, Utah. Each center's institutional review board independently approved this study. Data use agreements between each site and the primary data collection site (Atlanta) also were obtained.

Study data were collected from pediatric referrals, emergency department reports, and parent interviews and were managed with REDCap (Research Electronic Data Capture) hosted at Children's Healthcare of Atlanta.[2] REDCap is a secure, Web-based application designed to support data capture for research studies, providing (1) an intuitive interface for validated data entry; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for importing data from external sources.

Centers entered demographic, diagnostic, and testing data on patients with first-time cardiology referrals from January 2008 to December 2014. Detailed information, including demographics, diagnosis, and testing questions about the survey can be found at https://redcap.choa.org/redcap/surveys/?s=YLEKM8YJMF.[3]

Patient referrals were classified according to one or more of the following reasons: (1) concerning personal history or family history of sudden cardiac arrest; (2) previous syncope or seizures; (3) previous chest pain, shortness of breath, or palpitations as assessed by an emergency department or primary care provider; (4) abnormal cardiac physical examination findings; and (5) abnormal or suspicious cardiac diagnostic studies. Disease diagnosis was determined by the managing institution and was based on clinical characteristics with genetic testing data provided when available and appropriate. Patients with positive genetic testing but negative phenotypic expression were included in the database. Patients with LQTS were diagnosed on the basis of the Schwartz criteria[4] with additional diagnostic testing (exercise testing, epinephrine challenge, and genetic testing) when available. Patients with hypertrophic cardiomyopathy were diagnosed according to published guidelines[5] using echocardiogram as well as cardiac magnetic resonance imaging and genetic testing when available. Patients with CPVT were diagnosed[6] on the basis of positive exercise testing, epinephrine/isoproterenol challenge, and/or genetic testing. Patients with ALCA-R were diagnosed on the basis of echocardiography. Data were reported as level 1, representing any and all intake data from the referring practitioner, and level 2, additional data derived during the pediatric cardiac evaluation.

Data were tabulated and summarized with means and SDs, medians and ranges, or counts and percentages, as appropriate. Analyses were performed using SAS 9.4 (SAS Institute, Cary, North Carolina).

Results

A total of 450 patients (257 male, 193 female), median age 10.1 years (3.6-13.8 years, 25th-75th percentiles) were enrolled from the participating centers with a fairly even distribution: Children's Healthcare of Atlanta (96/21.3%), Cincinnati Children's Hospital Medical Center (86/19.1%), C.S. Mott Children's Hospital (71/15.8%), Texas Children's Hospital (70/15.6%), Primary Children's Hospital (66/14.7%), and Children's Hospital of Wisconsin (61/13.6%). The final diagnoses were LQTS (n = 239), hypertrophic cardiomyopathy (n = 168), CPVT (n = 31), or ALCA-R (n = 12). Of 450 patients, 317 were aged ≤13 years (70.4%). Thirty-three patients presented with sudden cardiac arrest (7.3%; n = 12, 5, 14, and 2 for LQTS, hypertrophic cardiomyopathy, CPVT, and ALCA-R, respectively).

LQTS

LQTS was diagnosed in 239 patients, median age 9.1 years (3.2-12.7 years, 25th-75th percentiles). Seventy-seven percent (n = 184) of the patients were aged ≤13 years. Only 12 patients (5%) with LQTS presented with a sentinel event of sudden cardiac arrest, with 5 at rest, 4 during activity, and 3 in an unknown setting. Instead, 52% (n = 125) of the 239 patients with LQTS were referred secondary to a worrisome family history. There were 91 patients who presented because of possible LQTS-associated symptoms, including 48 (20%) with syncope (exertional in 17) and 7 with seizures. There were 48 patients (20%) referred in level 1 evaluation because of an abnormal electrocardiogram (ECG) finding, typically a borderline or prolonged QT interval.

At the end of level 2 evaluations, 210 of 239 patients (88%) were diagnosed with phenotype-positive LQTS with ECG evidence of LQTS. There were 29 patients (12%) with concealed LQTS (genotype positive/phenotype negative). All were asymptomatic and were referred because of a family history of LQTS (**Table I**).

Hypertrophic Cardiomyopathy

The diagnosis of hypertrophic cardiomyopathy was made for 168 patients, median age 11.1 years (2.6-14.1 years; 25th-75th percentiles); 65% (n = 109) were aged ≤13 years. Like the patients with LQTS, those with hypertrophic cardiomyopathy (n = 168) were referred most often because of a family history of known hypertrophic cardiomyopathy (39%, n = 65). Additional family history was obtained after cardiology evaluation in 18% of patients (n = 30), resulting in a total of 95 patients (57%) with a known or suspicious family history. Another reason for referral was the presence of a cardiac murmur (n = 64, 38%). There was a prevalence of sudden cardiac arrest (13%) in this population.

There were 40 patients (24%) who were referred specifically as the result of abnormal outpatient testing (ECG or