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Sports Participation in Genotype Positive Children With Long QT Syndrome

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ABSTRACT

OBJECTIVES The study sought to examine the prevalence and outcomes of sports participation (both competitive and recreational) in our single-center LQTS genotype positive pediatric population.

BACKGROUND The risks of sports participation in patients with long QT syndrome (LQTS) are not clearly elucidated.

METHODS A retrospective review was performed on genotype positive patients referred for the evaluation and management of LQTS between 1998 and 2013 at the Children's Hospital of Philadelphia. Pediatric patients participating in competitive or recreational sports were included in the analysis and their charts were reviewed for documented LQTS events during follow-up.

RESULTS The cohort of genotype-positive LQTS patients included 212 patients, and 103 patients (49%, female n = 53, average follow-up 7.1 ± 4.0 years, average QTc 468 ± 42 ms) participated in sports. A total of 105 LQTS disease-causing mutations were identified: *KCNQ1* n = 60 (58%), *KCNH2* n = 36 (35%), *SCN5A* n = 6 (6%), *KCNE1* n = 1 (1%), and *KCNE2* n = 2 (2%). All patients were treated with beta-blockade, with noncompliance in 1 patient and intolerance in 1 patient. Twenty-six patients participated in competitive sports (26%, female n = 15, average follow-up 6.9 ± 4.1 years, average QTc 461 ± 35 ms). Seventy-seven patients (75%, female n = 35, average follow-up 7.3 ± 3.9 years, average QTc 470 ± 43 ms) participated in recreational sports. No patients had LQTS symptoms during sports participation. Five appropriate implantable cardioverter-defibrillator shocks occurred in 2 patients, though none were related to sports participation.

CONCLUSIONS In this series no cardiac events and no deaths were observed in treatment-compliant LQTS children while participating in sports in 755 patient-years of follow-up. (J Am Coll Cardiol EP 2015;1-2:62–70) © 2015 by the American College of Cardiology Foundation.

Congenital long QT syndrome (LQTS) is a cardiac ion channelopathy characterized by syncope, ventricular arrhythmias (torsade de pointes) and sudden death (1). Children and adolescents are particularly at risk for life-threatening arrhythmias as this patient population is more often exposed to known triggers. As our understanding of the genotype-phenotype relationship has evolved, we now know that LQT triggers are genotype specific and risk assessment hinges on age, gender, mutation location, and QTc duration (2–5). Though several LQT subtypes exist, the majority (75%) involve the 3 most common forms, which are LQT1 (*KCNQ1* gene), LQT2 (*KCNH2* gene), and LQT3 (*SCN5A* gene).

Arrhythmia triggers, which are LQTS subtype specific, are often the result of the catecholaminergic surge seen with competitive exercise (6). For this reason, expert consensus statements have limited if not eliminated most competitive sports participation in children and young adults with LQTS. Specifically, the 36th Bethesda Conference guidelines restrict competition to billiards, bowling, cricket, curling, golf, and riflery, the well-known Class IA sports (low static/low dynamic intensity) (7). Asymptomatic long

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QT patients with baseline QT prolongation (QTc duration of 470 ms or more in males, 480 ms or more in females) are also disqualified from commonly played competitive sports (Bethesda recommendation #2). Complicating these recommendations is the ill-defined distinction between LQTS cardiac events associated with competitive, recreational and school based physical education programs. Additionally, expert consensus statements do not allow for sports participation in asymptomatic LQTS patients who are adequately treated with beta-blockers despite accumulating evidence that beta-blockers are protective and confer great benefit among patients with LQT1, the most common form of LQTS. Contending with these complex issues, many parents of LQTS children have engaged in extensive dialogue with their pediatric electrophysiologist and have chosen sports participation for their children, despite published guidelines.

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Recent data by Johnson and Ackerman (8,9) suggest that sports participation in LQTS may be safer than previously thought. Outside of this single study, no other data examining the prevalence of arrhythmic events in treated, genotype-positive, LQTS patients participating in sports exists in the literature. Similar to the tenets of self-determination and patient/family autonomy embraced by Johnson and Ackerman (8,9), our institution's clinical practice has evolved over the years to allow sports liberalization in some LQTS patients. The aim of our series was to examine retrospectively the prevalence and outcomes of sports participation (both competitive and recreational) in our LQTS genotype positive pediatric population.

METHODS

STUDY DESIGN. After obtaining Institutional Review Board approval, a retrospective review was performed on patients referred to the Pediatric Arrhythmia Clinic at the Children's Hospital of Philadelphia for the evaluation and management of LQTS between January 1, 1998 and May 15, 2013. Inclusion criteria for this series were: 1) LQTS patients (male or female) >4 and <21 years of age at the time of sports participation; 2) genotype-positive LQTS patients; and 3) patients actively participating in recreational or competitive sports. Patients excluded from the analysis were: 1) patients treated for LQTS without genotype confirmation; 2) patients found to have LQTS single-nucleotide polymorphisms not thought to be disease causing; 3) patients with incomplete medical records or inconsistent follow-up at the Children's Hospital of Philadelphia; and 4) LQTS patients ≤4 years of age as they were deemed too young to engage in consistent athletic activity. The primary predetermined endpoint was a serious adverse event during or up to 2 h after sports defined as: 1) tachyarrhythmic death or externally resuscitated cardiac event; 2) syncope; or 3) severe injury, defined as requiring hospitalization, resulting from syncope or arrhythmia. The secondary endpoints included: 1) appropriate implantable cardioverter-defibrillator (ICD) shock; 2) inappropriate ICD shock; 3) automatic external defibrillator (AED) shock; and 4) ICD system damage. Genetic analysis of the susceptibility genes described previously was performed through 2 commercial laboratories (Familion, PGxHealth, New Haven, Connecticut; and Gene DX, Gaithersburg, Maryland). Medical records were reviewed for demographics, clinical history, symptoms, treatment regimen, documentation of sports participation, type of sports played, level of participation (competitive or recreational), and LQTS-related events at initial and each subsequent visit. A patient's symptomatic status was defined as follows: 1) asymptomatic, if there were no symptoms referable to the cardiovascular system; 2) LQTS-related symptoms, in the presence of aborted cardiac arrest, exertional or atypical syncope; and 3) non-LQTS-related symptoms (e.g., vasodepressor syncope, chest pain, dizziness), if patients had complaints that were determined to be non-LQTS related by the evaluating electrophysiologist. Patients were considered genotype positive, phenotype negative if the QTc intervals were <470 males, <480 females and in the absence of rhythm-related syncope or sudden cardiac arrest. All patients in this series were evaluated and followed by a pediatric electrophysiologist and QT duration measurements on electrocardiogram (ECG), ambulatory Holter monitoring data, exercise stress test data, and medication compliance at each visit (initial and subsequent) were rereviewed from the medical records documentation.

SPORTS PARTICIPATION. All patients underwent an initial and subsequent LQTS evaluation by a pediatric electrophysiologist. Follow-up evaluations were generally performed on an annual basis and included an ECG, ambulatory Holter monitor, and exercise stress test. During evaluations, as part of routine clinical care, the patient's inclination to participate in sports was extensively discussed, including potential risks, data from published literature, our clinical experience, the Bethesda Conference Guidelines, and risk assessment as it related to

ABBREVIATIONS AND ACRONYMS

AED = automatic external defibrillator

ECG = electrocardiogram

ICD = implantable cardioverter-defibrillator

LQTS = long QT syndrome