REVIEW

Long QT Syndrome in Athletes: Challenges in the Diagnosis and Management

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Abstract

The long QT syndrome (LQTS) is an inherited channelopathy characterized by a prolonged QT interval without structural heart disease posing a risk of sudden cardiac death. Especially in athletes, diagnosis is sometimes more difficult due to bradycardia and to the QT prolongation induced by the exercise. Based on limited clinical data which tend to demonstrate that exercise, especially swimming, is a trigger for cardiac events, participation in any competitive sports practice is not supported by 2020 European guidelines. However, based on retrospective studies and involving the patient-athlete in shared decision making, the 2015 US guidelines are more lenient. ***Rhythmos* 2021;16(4): 79-81.**

Key words: long QT syndrome; sudden cardiac death; torsade des pointes

Abbreviations: ECG = electrocardiogram; LQTS = long QT syndrome; SCD = sudden cardiac death; TdP = torsade des pointes

Introduction

The long-QT syndrome (LQTS) is an inherited heart rhythm disorder characterized by a prolonged QT interval on the ECG, in the absence of structural heart disease that predisposes to polymorphic ventricular tachycardia (torsades de pointes-TdP) and ventricular fibrillation (VF). LQTS affects ~1 in 2.500 people and its prevalence in elite athletes is estimated at 0.4%.[1,2] It is usually diagnosed in children and young adults, with a mean age at presentation of 14 years; the annual rate of sudden cardiac death (SCD) in untreated patients is estimated to be between 0.33%[3] and 0.9 %, and the rate of syncope is ~5%.[3,4]

The autosomal dominant forms of Romano-Ward syndrome (LQTS1-6 and 9-15) are characterized only by a prolongation of the QT interval. The three forms LQTS1-3 are responsible for the majority of the cases (~75%).[5]

Two other autosomal dominant forms of LQTS are associated with abnormalities beyond prolonged QT interval and arrhythmias. Andersen-Tawil syndrome (LQTS7) is characterized by episodes of muscle weakness and paralysis (periodic paralysis) and a variety of distinctive facial and skeletal features. Timothy syndrome (LQTS8) is a rare autosomal-dominant disorder characterized by physical malformations, as well as neurological and developmental defects, arrhythmias, structural heart defects, syndactyly (webbing of fingers and toes), and autism spectrum disorders. Moreover, two autosomal-recessive forms of LQTS (Jervell and Lange–Nielsen syndrome: JLN 1–2) are associated with profound sensorineural hearing loss.[5] To date, mutations in 17 distinct LQTS genes have been discovered. Patients with LQTS who participate in intense sports have an increased risk of SCD compared to the general population.

Clinical characteristics of LQTS

The main clinical manifestations of LQTS include syncope, tachycardia episodes and SCD. In subjects with prolonged QT interval under conditions of emotional or physical stress interval, nonsustained episodes of TdP can occur and may lead to VF.[6] Among symptomatic persons without treatment, the 10-year mortality is ~50%. Clinical events may be precipitated by specific triggers, including exercise and particularly swimming in LQT1, emotional stress or sudden loud noises in LQT2 and rest in LQT3.[7]

Pitfalls in QT measurement and diagnosis of LQTS in athletes

A variety of T-wave morphologies are associated with the most common long QT syndromes. LQT1 has been associated with smooth, broad-based T-waves, while LQT2 is associated with notched T-waves.[5] LQT3 is often associated with a prolonged isoelectric ST segment with a late onset, asymmetrical T-wave, or biphasic T-waves.[8]

Diagnosis of LQTS requires correct measurement of QT interval on ECG either using the ECG machine algorithm or manually. The ECG machines use always Bazett's formula (QTc = QT / √RR; QT in ms, RR in sec) for QTc calculation (from the beginning of the QRS to the end of the T wave) and the accuracy is ~90-95%.[9] Bazett's formula is sometimes inaccurate, especially in extreme heart rates, under-correcting for slower heart rates and overcorrecting for higher heart rates.[10] Specifically, athletes have frequently slow heart rates due to higher vagal tone at rest. In these cases, the ECG is recommended to be repeated when the heart rate is ~60 bpm. Also, Holter ECG monitoring is also useful to measure QT interval at a stable heart rate of 60 BPM, where no adjustment for heart rate is needed.

As regards the proper measurement of the QT interval, the difficulty is always to define the end of the T wave, especially if U waves co-exist. T wave is best assessed always in leads II or V5. If a U-wave is present, the end of T wave is estimated using the "Teach-the-Tangent" or "Avoid-the-Tail" method, drawing the tangent line to the steepest part of the descending portion of the T wave.[11]

It must be noted that the QT interval could be increased in athletes due to the enhanced vagal tone independently of the induced bradycardia. An isolated long QT interval in an athlete may be a result of the delayed repolarization due to increased left ventricular mass. According to the latest ECG recommendations for the athletes, QTc values of >470 ms in men and >480 ms in women are the thresholds of QT prolongation.[12]

Clinical suspicion of LQTS is based on abnormal ECG findings, symptoms, and family history. Schwartz score includes data from the ECG and from the clinical and family history to stratify the patients in low (≤1 point), intermediate (1-3 points), or high probability (≥3 points) categories (**Table 1**).[13]

Family screening in athletes, especially for first degree relatives, is recommended when the phenotype of the possible LQTS is not clear, in order to make the diagnosis more powerful.

Table 1. Criteria for Diagnosis of Long QT Syndrome

Electrocardiographic Findings	
QTcb ≥480 ms 460-479 ms 450-459 ms (in males)	 3 2 1
QTc 4th min of recovery from exercise stress test ≥480 ms	1
Torsades de pointes	2
T-wave alternans	1
Notched T-wave in 3 leads	1
Low heart rate for age	0.5
Clinical history	
Syncope With stress Without stress	 2 1
Congenital deafness	0.5
Family history	
Family members with definite LQTS	1
Unexplained SCD <30 y among immediate family members	0.5

As regards the genetic testing, although there are no specific guidelines for athletes, the EHRA and HRS recommend it when there is a strong clinical suspicion for LQTS based on clinical history, family history and expressed ECG phenotype (resting ECGs or provocative stress testing with exercise or catecholamine infusion) (class I).[14] Additionally, in patients with QT prolongation in the absence of clinical conditions that might prolong the QT interval (ie, electrolyte abnormalities, hypertrophy, bundle branch block) on serial 12-lead ECGs defined as QTc >480 ms (prepuberty) or >500 ms (adults) (class I). Genetic testing is also recommended in asymptomatic patients with idiopathic QTc values of >460 ms (prepuberty) or >480 ms (adults) on serial 12-lead ECGs (class IIB). Moreover, genetic testing is recommended for family members and other close relatives following the identification of a LQTS-causative mutation in an index case (first identified individual in a group of related cases among those with a possible heritable).[5] Silent mutation carriers accounted for 36% of LQT1 patients, 19% of LQT2 patients, and 10% of LQT3 patients in 1 cohort.[6]

Medical Treatment

It is well known that risk stratification for SCD in the general adult population is based on the most important predictors such as QT interval ≥500 ms, male sex in childhood and female sex in adulthood, and a history of syncope.[15] Persons with LQT1 are at higher risk of lethal cardiac events during exercise, especially swimming. In these patients, the incorrect shortening of QT interval during tachycardia due to dysfunction of IKs channels may lead to TdP. The protective effect of beta blockers in these patients relates to reduction of the transmural myocardial dispersion of repolarization which is enhanced with the surge of isoproterenol.[16] Beta-blockers are recommended in patients with a diagnosis of LQTS who are asymptomatic with QTc ≥470 ms and/or symptomatic with syncope or documented VT/VF (class I). LQTS patients who are asymptomatic with QTc ≤470 ms may also benefit from beta-blocker therapy (class IIa). Beta-blockers of choice in this situation are propranolol (at a dose of ≥2-4 mg/kg/d) and nadolol (1-1.5 mg/kg/d). Other β-blockers, such as atenolol and metoprolol, have lower response rates.[17] Although their widely usage, β-blockers are prohibited in certain sports, such as underwater sports, archery, automobile sports, billiards, darts, golf, shooting. In patients with LQT3 sodium channel blockers, like mexiletine, flecainide and ranolazine can be administered additionally to a β-blocker.[15]

Recommendations About Competitive Sport Participation in LQTS

There is a difference in the recommendations about the management of patients with LQTS as regards the participation in competitive sports between the two sides of the Atlantic. The latest US guidelines published in 2015 recommend athletes with symptomatic LQTS or abnormal ECG with prolonged QT should be evaluated by specialist cardiologists with expertise on this field. The participation in competitive sports (except swimming in LQTS1) for a symptomatic patient with LQTS may be considered after treatment titration and with all the precautionary measures taken and only if the athlete has been asymptomatic for at least 3 months on treatment.[18] In asymptomatic genotype-positive/phenotype-negative athletes (concealed channelopathy), experts recommend the participation in all

competitive sports with all the precautionary measures. These include the avoidance of QT-prolonging drugs, electrolyte/hydration replenishment and avoidance of dehydration and electrolyte disturbances, avoidance of hot weather training and the most important is the existence of a personal automatic external defibrillator (AED) with all the staff being well trained in its use. Although data are limited for athletes with ICDs, 2015 AHA/ACC guidelines suggest that an athlete with an ICD may be permitted to participate in sports if there have been no shocks for 3 months. The return of the athletes to their sport, including those with ICDs, depends on co-decision with their family.

The recently published 2020 ESC guidelines on sports cardiology are more restrictive for athletes with LQTS. Since the risk of cardiac events during sports activities is largely gene-specific, genetic testing and cascade screening of family members should be performed following a clinical diagnosis of LQTS. Participation in high-intensity recreational and competitive sports, even when on beta-blockers, is not recommended in individuals with a QTc>500 ms or a genetically confirmed LQTS with a QTc≥470 ms in men or ≥480 ms in women.[19]

Survivors of aborted SCD, irrespective of receiving beta-blocker, should be referred for an ICD implantation. According to ESC guidelines, the presence of an AED 'as part of the athlete's personal sports safety gear' seems to be impractical in some cases (e.g. winter sports, water sports), and it places an added responsibility on clubs or other bystanders, which cannot be justified by a medical recommendation for an individual athlete. Moreover, the AED efficacy has not been reported to reach 100% as it should be in such cases.[20]

Conclusion

There is a debate between the ESC and ACC/AHA guidelines regarding the participation of athletes with LQTS in competitive sports. The key point in the management of these patients and their families is the evaluation from LQTS expert cardiologists and information should be given on the potential risks. Until further studies are available on this highly controversial topic, an individualized approach after a well-informed and extensive discussion with the patient and caregivers is recommended.

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