

Short QT syndrome

A newly defined and easily missed cause of sudden cardiac death

BY ABDULWAHAB ARRAZAGHI, MB

The majority of sudden cardiac deaths are related to structural heart disease. Approximately 20%, though, occur in individuals with normal hearts, and short QT may be responsible for some of these cases. A newly recognized, silent genetic disease, it consists of a constellation of signs and symptoms, including a short QT interval on the electrocardiogram (ECG), a tall and peaked T wave and a structurally normal heart. There may be episodes of syncope, paroxysmal atrial fibrillation or life-threatening arrhythmias. Short QT may be inherited as an autosomal dominant mutation and can kill in age groups varying from infancy to adulthood. In 2003, Gaita and colleagues confirmed its familial nature, in a study of two families — six patients — with syncope, palpitations, resuscitated cardiac arrest and sudden death. The genetics were identified in 2004.

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Signs and symptoms

- highly variable, ranging from no symptoms to atrial fibrillation, from recurrent syncope to sudden death
- short QT interval < 330 msec
- tall and peaked T wave
- inducible ventricular fibrillation in electrophysiologic studies
- no related, correctable cause
- family history of sudden death
- high familial incidence of palpitations and paroxysmal atrial fibrillation
- age of onset
 - often young, otherwise healthy individuals
 - in neonates, sudden death may be falsely attributed to SIDS

Diagnosis

- no set guidelines
- based on characteristic history, ECG findings and electrophysiologic testing
- ECG — short QT interval (< 330 msec), followed by tall and peaked T wave
- measure QT interval at close to 60 beats/min
 - do not correct for heart rate
 - particularly important in children, whose normal heart rate > 100 beats/min at rest
 - in presence of tachycardia, QT interval may be normal, but as the heart rate slows, QT may show no or minimal prolongation
- differential diagnosis — rule out other factors that abbreviate the QT interval
 - hypercalcemia
 - digoxin
 - thyrotoxicosis
 - hypermagnesemia
 - increased sympathetic tone
- echocardiogram — structurally normal
- electrophysiologic study
 - short refractory periods, in atria and ventricles
 - ventricular fibrillation on programmed stimulation

Causes

- heterogeneous — three forms of disease
- short QT interval due to
 - reduced inward currents of sodium or calcium in the action potential of cardiac cells, or
 - increased flow of potassium outward
- three genes identified so far
 - KCNH₂, or *HERG*, the human ether-a-go-go-related gene
 - KCNQ₁
 - KCNJ₂
- each encodes a different potassium ion channel involved in repolarization
- KCNH₂ gene responsible for the channel with rapidly activating rectifier outward current (*I_{Kr}*)
- two different missense mutations in KCNH₂ gene result in substitution of asparagine for lysine at codon 588, an area at the outer mouth of the channel pore
- mutated channel increases activity of outward potassium currents in phases 2, 3 of the cardiac action potential, leading to shortening of the plateau phase (phase 2), refractory periods and overall QT interval
- KCNQ₁ gene responsible for the slowly activating delayed outward potassium current (*I_{Ks}*); mutation leads to gain of function and shortening of interval
- KCNJ₂ gene encodes the inward rectifier current (*I_{K1}*) proteins that form the channel pore; mutated channels showed selective speeding of late repolarization

Red flags

Rule out short QT syndrome in the following clinical scenarios:

- lone atrial fibrillation at young age
- idiopathic atrial or ventricular arrhythmias
- next of kin with short QT interval
- family member with sudden cardiac death
- QT interval < 330 msec at 60 beats
- in rapid heartbeat, lack of QT prolongation with slowing heart rate
- individuals with ECG demonstrating tall and peaked T waves

References:

- Gussak I et al. *Cardiology* 2000;94(2):99-102.
- Gaita F et al. *Circulation* 2003;108(8):965-70.
- Schimpf R et al. *J Cardiovasc Electrophysiol* 2003;14(12):1273-7.
- Brugada R et al. *CMAJ* 2005;173(11):1349-54.

Treatment

- implantable cardioverter defibrillator (ICD)
 - first choice in symptomatic patients
 - particularly useful in individuals with aborted sudden death
 - not suitable for young children
- pharmacologic — for those refusing ICD implants or who have unacceptable, inappropriate shocks
- Class Ic and III antiarrhythmic drugs — don't produce significant QT prolongation, not recommended for treatment
- quinidine
 - potentially effective therapy
 - prolongs QT interval/effective ventricular refractory period to more than 200 msec
 - prevents occurrence of induced ventricular fibrillation
 - important for infants and children where ICD isn't feasible
- therapy varies with mutation type
 - important to identify responsible gene
- refer possible cases to a cardiologist/arrhythmia expert for subsequent management and treatment stratifications

Prevention

- ECG screening
- identify family members at risk — clinical interview, baseline ECG, echocardiography and in some cases, electrophysiologic and genetic studies
- genetic screening — may prevent sudden deaths reported in infants and newborns