

The Short QT Syndrome

A note from the SADS Foundation

We provide this information with the hope that informing physicians and other health care providers, as well as the public, will encourage early and correct diagnosis and proper therapy for congenital short QT syndrome (SQTS), resulting in the reduction and ultimately elimination of sudden cardiac arrest (SCA) and sudden cardiac death (SCD).

What do Patients and Parents Need to Know about SQTS?

- The warning signs and symptoms of SQTS.
- Who to see for proper testing.
- How to protect their children and themselves.
- How to expand their family pedigree and contact other family members who may be at risk

What do Physicians need to know?

- When to consider SQTS as a possible diagnosis.
- When to refer patients for diagnosis & treatment.
- Information about genetic testing for SQTS and other SADS conditions.
- How to develop a family pedigree and to perform family cascade testing for SQTS.

What is SQTS?

SQTS is an inherited channelopathy described only recently (in 2000) (1) that may cause arrhythmias that could lead to syncope or sudden cardiac death in individuals with otherwise structurally normal hearts.

SQTS is a disturbance of the heart's electrical system. It is caused by inherited abnormalities of proteins in the cardiac cell membranes called ion channels. When ions, such as potassium, sodium, calcium, and chloride, pass through the cell membrane, they generate the electrical activity (depolarization and repolarization) that controls the heart's mechanical contraction. Our window to the heart's electrical activity is through the electrocardiogram (EKG or ECG). In patients with SQTS, abnormal potassium and sodium ion channels shorten the repolarization (recharging) process and the QT interval, thus predisposing patients to certain cardiac arrhythmias and possibly SCA/SCD. Thus, SQTS is an abnormality in the electrical recharging (repolarization) phase of the heart's electrical cycle.

References

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The Sudden Arrhythmia Death Syndromes (SADS) Foundation is a leader in education, research and advocacy. Our Mission is to save the lives and support the families of children & young adults who are genetically predisposed to sudden death due to heart rhythm abnormalities.

A Guide for Patients and Health Care Providers



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What is the QT interval?

The QT interval is a time interval on the ECG. It represents the time from the initiation of electrical depolarization of the heart's pumping chambers (ventricles) to the end of the recharging (repolarization) phase for each cardiac cycle (heartbeat). It is measured in milliseconds and closely approximates the time from the beginning of the ventricles' electrical contraction to the end of repolarization.

The QT interval is an absolute measure of time. The QT is affected by the heart rate (the QT shortens during heart rate acceleration and lengthens during heart rate slowing). The corrected QT interval (the QTc) is a calculated number that attempts to correct for variations in heart rate. While the corrected QT interval is not a perfect measure, it is easy to use, providing a practical day-to-day ECG assessment. Unfortunately, there is no single QTc cutoff value that will distinguish all patients with short QT syndrome from healthy controls. Instead, the shorter the QTc the higher the odds that the diagnosis is present, always taking into consideration that short QT syndrome is a very rare disease. Based on limited published data obtained from large general populations as well as the few SQTS patient series, a QTc interval less than 350 milliseconds on a resting ECG should raise the possibility of short QT syndrome. QTc intervals ranging from 220-360 milliseconds (1,2,3) have been reported in some SQTS patients. Additionally, ECG changes including tall, peaked, and abnormal T-waves in the precordial leads, as well as a short or even absent ST segment on the resting ECG may be seen as features of short QT syndrome.



What are the Clinical Symptoms of SQTS?

SQTS diagnosis should not be made solely on the basis of a QTc less than 350 milliseconds. Comprehensive patient and family history are additional key components of this syndrome.

The clinical presentation of SQTS can be quite varied among patients. This diagnosis may be associated with sudden infant death syndrome in patients less than 6 months of age, and alternatively, initially diagnosed in geriatric patients. In a 2006 report², cardiac arrest occurred in 34% of SQTS patients and for 28% of this group it was the first clinical presentation. Palpitations occurred in 31%, syncope in 24%, atrial fibrillation in 17%, and many patients experienced frequent early beats from the lower pumping chambers (premature ventricular contractions-PVCs). 38% of patients were asymptomatic and diagnosed only after comprehensive family cascade testing.

When should the diagnosis be suspected?

SQTS should be suspected in any patient presenting with sudden unexpected/unexplained SCA or SCD, or in patients with symptoms of palpitations, syncope or unexplained seizure, early age onset atrial fibrillation, or in any patient with a known family history of SQTS.

How is the diagnosis made?

As above, the diagnosis is often made by ECG findings characteristic for SQTS (defined above) and associated known or suspicious patient and family history for SQTS. SQTS is a difficult diagnosis because great overlap exists between the QTc of the affected and the healthy population.

What about genetic testing?

SQTS is now recognized as being an inherited primary electrical disorder of the heart, inherited in an autosomal dominant pattern (50-50 chance of inheritance from an affected parent). Clinical genetic testing for disease causing mutations known to be associated with clinical SQTS can now be performed. The clinical genetic test (genotype) would generally be ordered on the family member felt most likely to be clinically affected (index case or proband). If a disease causing SQTS gene mutation is identified, other first-degree family relatives will be tested for that specific mutation and if positive they would then be labeled as genotype-positive for SQTS themselves, even if the clinical findings are non-diagnostic. Any genotype positive SQTS identified individual should still be regarded as having a risk for SQTS symptoms and



complications. The diagnostic evaluation should be made by specialists dedicated to the field of short QT because the potential for over-diagnosis and under-diagnosis of SQTS is significant. The risk of over-diagnosis of SQTS in healthy athletes is particularly high⁴.

What is the treatment and who should be treated?

Implantation of a permanent cardiac defibrillator (ICD) may be the single most definitive treatment option for patients with SQTS, symptomatic or pre-symptomatic. However, ICD therapy is not perfect, and is frequently associated with technical and/or psychological complications. The decision to implant an ICD should be made only after careful discussion of the benefits, risks, and alternatives with patients and parents.

Treatment with medications known to prolong the ECG QT interval may be considered. Some anti-arrhythmic agents (e.g. quinidine) have QT prolonging side effects, and thus may be beneficial in patients with SQTS. Likewise, attempts to treat SQTS patients with medications alone should be carefully guided by clinicians who are experts in the diagnosis and management of SQTS. Drug non-compliance and drug failure may leave patients at risk for SQTS symptoms and complications.