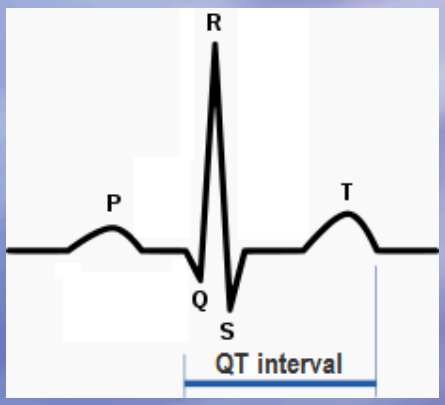

Understanding the genetics of Long QT syndrome

Long QT syndrome (LQTS) is a condition that affects the way the heart beats. At the end of one heartbeat, the heart muscles re-set (repolarize) to get ready for the next heartbeat. The time it takes the heart muscles to re-set is called the "QT interval". In long QT syndrome the heart muscles take longer than usual to re-set. Individuals with LQTS have a much higher chance for abnormal heartbeats (cardiac arrhythmia).

Symptoms of long QT syndrome include:

- Palpitations (rapid heartbeat)
- Fainting
- Seizure
- Cardiac arrest (sudden stopping of the heart)

These symptoms can happen during exercise, at rest, or as a result of being startled or stressed. In rare cases, arrhythmia can lead to sudden death. Most deaths related to LQTS can be prevented with early diagnosis and treatment.

How is long QT syndrome diagnosed?

LQTS is diagnosed by a doctor based on your medical history, your family history, a physical exam, and an electrocardiogram (also called ECG or EKG). The ECG measures the rhythm of your heartbeat. There are specific findings that lead to a diagnosis of long QT syndrome. Most people with LQTS have hearts that look and sound normal, but their ECG shows abnormal electrical activity. Some people with LQTS have a normal ECG at rest, and only show abnormal heartbeats when they exercise or take certain medications.

What causes long QT syndrome?

LQTS is caused by pathogenic variants (harmful changes) in genes that help control the heart's electrical system. When one of these gene is not working right, it can cause irregular heartbeats.

How is long QT syndrome inherited?

The genes that cause LQTS can run in the family. In most families this condition is inherited in an autosomal dominant manner. This means that both men and women can have LQTS. It also means a parent with a pathogenic variant in a LQTS gene has a 50% (1 in 2) chance to pass the variant to any child.

SCREENING FOR LONG QT SYNDROME

The main screening recommendation for those at risk for long QT syndrome is regular electrocardiogram exams. How often screening is needed depends on your age and medical history.

Electrocardiogram (ECG) is a heartbeat rhythm tracing. It records the electrical activity of your heart as it beats. An ECG can detect abnormal electrical signals, including differences in the QT interval. Normally an ECG is only done for a few minutes at a time.

Special ECGs may be done to test for irregular heartbeats that may not show up on a regular ECG:

- A stress test is an ECG done while you exercise on a treadmill or stationary bike.
- A chemical or pharmacological stress test is an ECG done after taking a medication that makes the heart work harder.
- A Holter monitor or ZIO patch is a portable form of ECG that records your heartbeat for a much longer period of time. These monitors may be worn on the body for 24 to 48 hours or as long as 14-30 days.

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GATHERING YOUR FAMILY HISTORY: WHAT TO ASK

When you gather family history, it is helpful to ask about medical problems that might be related to LQTS:

Ask about:

- Fainting spells or blackouts
- Dizziness with work, exercise, or even at rest
- Heart arrhythmias/palpitations (irregular heartbeats)
- Seizures
- Sudden cardiac death

How is genetic testing done?

A blood or saliva test can be done to look for pathogenic variants in LQTS genes. Genetic testing works best when there is a clear diagnosis of LQTS in the family and testing starts with a person who has the condition. Current genetic testing finds a pathogenic variant in about 70% of people thought to have LQTS. You can learn more about genetic testing by talking with a genetic counselor.

What are the benefits of genetic testing?

Genetic testing for LQTS can be helpful in two ways: **better medical care** and **family testing**. Cardiologists use results from genetic testing to guide a person's medical care and management. Plus, genetic testing can be offered to family members once a pathogenic variant is known. Testing can show which family members are at high risk even when there are no heart symptoms. Healthy people with a pathogenic variant can lower the chance for serious heart problems by having regular cardiac screening. They can also avoid medications and exposures that raise the risk for symptoms. A family member who did not inherit the variant can be reassured.

What if genetic testing doesn't find a pathogenic variant?

Genetic testing is not always able to find a pathogenic variant. Some variants cannot be found by the current tests. There are also many different genes known to cause LQTS, but some LQTS genes have not been discovered yet. So, there could be a genetic cause for LQTS even when test results are negative (no harmful variants found). Cardiac screening may still be recommended for family members.

What happens if I inherit a pathogenic variant in an LQTS gene?

If you inherit a pathogenic variant in a LQTS gene, you are more likely have symptoms of long QT syndrome during your lifetime. However, some people who inherit a variant have normal heartbeats and never develop symptoms. Regular cardiac screening is recommended for anyone with a genetic change that can cause LQTS. You should also avoid drugs that can prolong the QT interval.

What happens if I develop Long QT syndrome?

Even when an ECG shows a long QT interval, many people never have severe heart problems and are able to live a normal life. However, some people develop symptoms, such as fainting, dizziness, fatigue, and heart palpitations. Less often, an irregular heartbeat can lead to cardiac arrest or sudden death. Treatment can minimize or prevent symptoms and lower the chance of serious problems. Treatment may include regular follow-up, lifestyle changes, medication, and implantable automatic defibrillators, as needed.

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