Long QT Syndrome (LQTS) is a disorder that affects the electrical system of the heart, and may lead to sudden cardiac death. Diagnosis of LQTS is based on specific criteria, with a large focus on the duration of the corrected QT interval (≥470 ms in men and ≥480 ms in women). Current management therapies include β-blockers, implantable cardioverter-defibrillator, and left-cardiac sympathetic denervation. Prolongation of the QT interval typically occurs as a result of a delay between the onset of depolarization and completion of repolarization (increasing action potential). There are three major genotypes of congenital LQTS: LQTS1, LQTS2, and LQTS3 (constitute 80-90% of the 15 reported genotypes).

Torsades de pointes (TdP) is the trademark, adrenergic-mediated polymorphic ventricular tachycardia associated with LQTS. Onset of TdP is triggered through the propagation of action potential and propagation of repolarization that causes a load of Ca2+. The first line of therapy for LQTS is the use of β-blockers, as they inhibit sympathetic influences on cardiac cells and prolong the effective refractory period.

Implantable cardioverter-defibrillator (ICD) and left cardiac sympathetic denervation (LCSD) are treatment options for patients on full-dose β-blocker therapy who still experiencing syncopal episodes. β-blockers frequently prescribed are Propranolol and Nadolol. Atenolol and metoprolol have demonstrated more clinical failures, with metoprolol being associated with a 4-fold increase in event recurrences. β-blockers are effective in preventing stress-induced cardiac events (i.e. exercise), but appear to have no significant affect on sleep triggered events. Non-compliance and QT prolonging medications are responsible for most life threatening cardiac events caused by “β-blocker failures.” Each individual genotype of LQTS may respond differently to treatments.

The use of β-blockers is limited, due to their longer half-life, with propranolol a close second. Surgical interventions, such as an ICD and LCSD, may be suggested when β-blocker therapy is not sufficient. Physicians may benefit most from approaching treatment of LQTS based on the underlying genotype, as each genotype has differing triggers and may respond to treatments differently.

5. Yanfei Ruan, MD; Nian Liu, MD; Carlo Napolitano, MD, PhD; Silvia G. Priori, MD, PhD. Therapeutic Strategies for Long QT Syndrome: Does the Molecular Substrate Matter? Circ Arrhythmia Electrophysiol 1: 290-297, 2008.