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Editorial

The Outcome of Long QT Syndrome: What is the Optimal Therapy?

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Congenital long QT syndrome (LQTS) is an inherited primary arrhythmia characterized by a prolonged QT interval on surface electrocardiography and is associated with gene mutation encoding cardiac ion channels related to ventricular repolarization. It can lead to life-threatening cardiac arrhythmias-torsades de pointes ventricular tachycardia and ventricular fibrillation. The clinical symptoms in patients with LQTS are manifested with syncope, generalized seizures, and sudden cardiac arrest, depending on the duration and severity of ventricular arrhythmias. Until now, at least 17 pathologic gene mutations of LQTS subtypes were idenitified. However, patients with LQT1, LQT2, and LQT3 with gene mutations involving KCNQ1, KCNH2, and SCN5A constitute more than 75% of patients with genetically identified LQTS.[1-5]

Although the aggressive medical and interventional management improved clinical outcome of LQTS, therapeutic strategy should be indivisualized according to genotype and phenotype characteristics. Additionally, risk stratification of sudden cardiac death is essential to improve the prognosis.

In this issue of the *Korean Circulation Journal*, Ahn et al.[6] investigated the clinical and genetic characteristics, treatment strategies, and outcomes of 105 patients with congenital LQTS in Korean single center study between 2000 and 2016 retrospectively. A total of 90 (71%) out of 105 patients with LQTS were performed genetic testing. Among them, LQTS types 1, 2, 3 account for approximately 60% of all congenital LQTS cases. And aborted cardiac arrest was documented in 30% of the symptomatic 70 patients. As initial treatment, ß-blockers were administered in 86% of patients. Among them, 27% of patients experienced breakthrough cardiac events (BCEs) in this cohort. Additionally, implantable cardioverter defibrillators (n=27, 39%) and left cardiac sympathetic denervation (LCSD) surgery (n=7, 10%) were performed. Only 1 patient died. The 10-year BCEs-free survival rate was 73.2% in this cohort.

We already have data supporting that prolonged QTc interval ≥480 ms increased the risk of cardiac events.[3-5] There has been also good data supporting the role of β-blocker medication in preventing cardiac event in LQTS1 and LQTS2.[7]

According to the HRS/EHRA/APHRS guidelines for LQTS management, there is no evidence to favor cardioselective or non-cardioselective beta-blockers. Long acting beta-blockers such as nadolol and propranolol have been recommended as the effective medication in

patients who are symptomatic for syncope or documented ventricular tachycardia/ventricular fibrillation and/or asymptomatic with a QTc ≥470 ms.[3]

However, non-responders still had BCEs during β-blocker treatment. The patients with LQTS type 3 and multiple mutations are not responsive to β-blocker treatment.[6][8]

Because arrhythmic events are manifestated with gene-specific pattern, genetically tailored therapy is highlighted. In high-risk patients with a LQTS, LCSD and/or implantable cardioverter defibrillator (ICD) are recommended. LCSD surgery and ICD implantation are effective in primary and secondary preventing cardiac arrhythmic events.[3-5] Recently Niaz et al.[9] reported about LCSD monotherapy in LQTS between 2005 and 2020. Among the 1,400 patients with LQTS, a total of 204 patients (15%) underwent LCSD. Sixty-four (31%) of 204 patients were treated with LCSD alone and only 3 patients have experienced a post-LCSD nonlethal BCEs during mean follow-up of 2.7±2.4 years. They concluded LCSD was safe and effective in selective patients who do not tolerate β-blockers.

ICD implantation is recommended for patients with survivors of a cardiac arrest in LQTS and is considered in patients with refractory BCEs under medications.[3-5][8] However, potential complications associated with ICD still remain in pediatric patients. Gaba et al.[10] reported 170 patients (14%) with ICD implantation in LQTS (670 patients) and non-LQTS (557 patients). Among them, 12 of 1,227 (1%) had ICD removed because of inappropriate shocks, a device-related infection, and device malfunction. They emphasized unnecessary ICD placement due to overdiagnosis and overtreatment can be associated with high rate of complications in younger patients.

Gene-specific LQTS therapies including sodium channel blockers such as mexiletine, flecainide, and ranolazine have been reported in high-risk patients with LQTS type 3 or in patients with recurrent cardiac events despite ICD and LCSD therapies.[3]

In the era of genetic testing, approximately 20–25% of patients with LQTS are diagnosed by the presence of an LQTS gene mutations without QTc prolongation.[3]

Although outcomes have improved with various therapeutic modalities, the precise detection of concealed mutation of LQTS and further gene-specific treatment strategies are still needed.

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