

Genetic Test in Arrhythmia?; Sudden Death in Patients without Structural Heart Disease

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Inherited cardiac disorders without structural heart disease predisposing to lethal arrhythmia or sudden cardiac death includes channelopathies (long-QT syndrome (LQTS), Brugada syndrome (BrS), etc). As the genetic bases and molecular mechanisms of the inherited diseases have been identified and understood better, genetic testing for disease-causing mutation has made its transition from discovery through translation, and is clinically available. HRS/ERHA expert consensus (2011) provides the state of genetic testing for the channelopathies. A Class I recommendation was applied for genetic testing with a clinical suspicion when the positive predictive value is high. The diagnostic, prognostic, and therapeutic contribution of a genetic test result is disease dependent for the index case.

Comprehensive or LQT1-3 (*KCNQ1*, *KCNH2*, and *SCN5A*) targeted LQTS genetic testing is recommended in any patient with a strong clinical index for LQTS. Recent European Society of Cardiology guideline (2015) recommended that LQTS is diagnosed in the presence of a confirmed pathogenic LQTS mutation, irrespective of the QT duration (Class-I, Level-C). When the causative mutation is identified in clinically affected index cases, mutation-specific genetic testing of all first-degree relatives is indicated. BrS 1 (*SCN5A*) targeted genetic testing can be useful for a index of clinical suspicion. *SCN5A* accounts for the >75% of BrS genotype positive cases, however, the yield of *SCN5A* genetic testing for robust clinical cases of BrS is about 25%.

Genetic counseling is recommended for all patient and relatives with the familial heart disease. However, current genetic testing has potential limitations. Whole genetic abnormalities could not be covered by targeted genetic testing because novel variants have been identified more and more. In addition, bioinformatics is important to determine the clinical pathogenicity. The genetic/genomic advances will propel cardiologists into the era of personalized medicine.

References

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