Clinical usefulness of genetic testing in Asian patients with inherited arrhythmia syndrome

Introduction: Genetic testing is used to diagnose inherited arrhythmias, without structural heart disease, that predispose to sudden cardiac death. We aimed to investigate the genetic features of patients with inherited arrhythmia syndrome using genetic testing in real-world clinical practice.

Methods: This was a prospective, single-center study in South Korea. Total consecutive 66 patients who experienced sudden cardiac death who encountered with ventricular fibrillation or ventricular tachycardia without overt heart disease were enrolled, and tested Next Generation Sequencing (NGS) panel. If clinically significant genetic variants were found, familial screening with targeted genetic testing was encouraged to identify familial genetic inheritance and its clinical relevance.

Result: Among the patients, 11 (16.7%) were diagnosed with Brugada syndrome, 11 (16.7%) were long QT syndrome, and 10 patients were idiopathic VF (15.1%). Other 34 patients had sudden cardiac death events and were suspected to have primary genetic arrhythmia syndrome, but did not fulfill the diagnostic criteria. Of 11 Brugada syndrome patients, 8 patients had genetic variants and 4 of them showed SCN5A variant (36.4%), which was higher compared to Caucasian data for diagnostic yield (20-25%). Other than SCN5A, variants were found in CACNB2, PKP2, SCN3B, TMEM. Seven of 11 patients (63.6%) with long QT syndrome were detected to have genetic variant (2 patients with KCNQ1, 1 patients with KCNH2 , 1 patient with SCN5A). Of 10 idiopathic VF patients, 8 patients were found to have variant, (KCNQ1, SCN5A, RYR2, etc). Of all patients, 39 patients (59.1%) were detected with gene mutation. Among the 39 patients with documented gene mutation, Brugada syndrome patients showed higher prevalence of SCN5A mutation than other disease entity (p:0.012), corresponding with fact that SCN5A is a key gene mutation in Brugada syndrome. Cascade screening in 13 families were done. Familial screening did not show distinct gene mutation (p:0.724). Of 13 cases, 5 cases were found to have same variant (38.5%). Only 1 case was diagnosed with Brugada syndrome, showing type 1 Brugada EKG. None of the family experienced sudden cardiac death.

Conclusion: This study showed that NGS-based genetic testing improved the diagnostic yield of inherited cardiac arrhythmias in Asian, suggesting it may be helpful to lead therapeutic implication as
well as clinically useful to confirm the diagnosis.