

Concealed cardiomyopathy as a frequent cause of idiopathic ventricular fibrillation in a representative Czech cohort of survivors of sudden cardiac arrest (SCA)

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Introduction: The complex diagnostic work up in SCA survivors often does not yield a concrete cardiological diagnosis. Moreover, there is conflicting evidence whether genetic testing could support or guide clinical diagnostics.

Purpose: To assess the molecular architecture of idiopathic ventricular fibrillation in cases without apparent evidence of specific structural or arrhythmic cardiac disease at initial diagnostic work up in a representative Czech cohort.

Patients and Methods: Between 2013 - 2020 we have ascertained 100 SCA survivors (54 M / 46 F; age range at cardiac arrest 5-69 years). Genetic counselling was followed by massively parallel DNA sequencing using custom-made panels comprising 100 cardiac conditions-related genes. Subsequently, thorough cardiological screening examinations in first degree relatives were carried out. Presence of pathogenic variants was validated by Sanger DNA sequencing and through family segregation analyses.

Results: Highly likely or certain molecular aetiology (i.e. based on the presence of Class 4 or 5 variants) was disclosed in 20/100 (20%) in PKP2 (3x), SCN5A (4x), RYR2 (3x), TTN (2x), PLN, FLNC, PRKAG2, KCNH2, KCNQ1, SLC4A, TNNT2, and DSP. Interestingly, the KCNE1 p.Asp85Asn (LQT 5 lite) variant, was detected in further 3/100 cases, representing a recognized risk factor for ventricular arrhythmias.

Conclusions: Genetic testing facilitates stratification of the cause of arrhythmia in a substantial portion of SCA survivors. The utility of positive outcomes of genetic testing was substantiated in 10/20 gene positive patients, where the genetic stratification led to diagnosis of concealed arrhythmogenic cardiomyopathy, whose extent of morphological changes was under the diagnostic sensibility of imaging modalities or ECG. Our results enable individualized care in SCA survivors and assure targeted preventive approaches in their relatives.