EXPLORING THE ROLE OF NGS IN GENETIC PROFILING FOR UNDERSTANDING NON-VIOLENT SUDDEN CARDIAC DEATH IN ASTANA

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Sudden cardiac death is an unexpected and often unpredictable event that can have serious consequences for the health and lives of individuals not only in middle age but also in young individuals. Mutations, particularly in genes associated with cardiovascular disease, may play a main role in the development of such events, but their exact role and impact require detailed study and prevention of the development of new mutations by using the Next-generation sequencing (NGS).

To evaluate the diagnostic importance of next-generation sequencing (NGS) by using our developed cardiogenetic panel in molecular autopsy in sudden non-violent deaths.

A prospective study was conducted from 2018 to 2023 focusing of young individuals aged 18 to 45 years resigning in Astana who died of non-violent CVD. The data were analyzed from RSCE «Forensic Expertise Centre of the Ministry of Justice of the Republic of Kazakhstan» «Research Institute of Forensic Expertise» in Astana, blood samples were obtained from SCD victims for further DNA extraction. We implemented a next-generation sequencing (NGS) using the customized panel to target enrichment of coding sequences of 96 candidate genes in molecular autopsies of young adults who died of SCD. All identified genetic variants were classified according to ACMG guidelines in cases with non-diagnostic and diagnostic cardiac abnormalities (ischemic heart disease postmortem).

Targeted sequencing and stepwise filtering of annotated variants identified 251 unique variants in 86 genes out of 96 in the entire group of cases studied. In patients with SCD with ischemic changes in the heart postmortem, the most frequent mutations were identified in the TTN, MYBPC3, LAMA2, MYH6 and GAA genes. Pathogenic variants in the genes of ion channels KCNQ1, KCNJ2, SCN5A, RYR2 were detected in individuals with non-diagnostic structural anomalies of the heart. Genetic screening of individuals who died of SCD identified variants with likely pathogenic functional effects with high frequency in 63% and 35% of SCD cases with non-diagnostic and diagnostic cardiac abnormalities, respectively, showing the high diagnostic value of genetic screening using a panel of genes for targeted NGS.

Data from our prospective study have shown that genetic testing using NGS in young Astana victims with SCD results in a significant number of mutations, consequently, may allow genetic counselling of relatives to prevent SCD due to coronary heart disease and arrhythmias and may support differential diagnosis postmortem.

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