

Sudden Arrhythmic Death during Exercise: a Post-mortem Genetic Analysis

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Background: Sudden cardiac death is a natural and unexpected death that occurs within one hour of the first symptom. Most sudden cardiac deaths occur during exercise, mostly due to myocardial infarction. After autopsy, some cases, especially in the young, are diagnosed as cardiomyopathies or remain without a conclusive cause of death. In both situations, genetic alterations may explain the arrhythmia.

Objective: Our aim was to identify a genetic predisposition to sudden cardiac death in a cohort of postmortem cases of individuals who died during exercise, structurally normal heart, and classified as arrhythmogenic death.

Methods: We analyzed a cohort of 52 post-mortem samples from individuals <50 years old who had a negative autopsy. Next generation sequencing technology was used to screen genes associated with sudden cardiac death.

Results: Our cohort showed a male prevalence (12:1). Half of deaths occurred in individuals 41–50 years of age. Running was the most common exercise activity during the fatal event, accounting for 46.15% of cases. Genetic analysis identified 83 rare variants in 37 samples (71.15% of all samples). Of all rare variants, 36.14% were classified as deleterious, being present in 53.84% of all cases.

Conclusions: A comprehensive analysis of sudden cardiac death-related genes in individuals who died suddenly while exercising enabled identification of potentially causative variants. However, many genetic variants remain of indeterminate significance, so further work is needed before clinical translation. Nonetheless, comprehensive genetic analysis of individuals who died during exercise enables detection of potentially causative variants and helps identify at-risk relatives.