Abstract: P1247

FLNC pathogenic variants in patients with various cardiomyopathies: prevalence and genotype-phenotype correlations

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Background/Introduction: Pathogenic variants FLNC encoding filamin C have been firstly reported to cause myopathies, and were recently linked to isolated cardiac phenotypes. However, few data on phenotype-genotype correlation are available.

Purpose: Our aim was to estimate the prevalence of FLNC pathogenic variants in cardiomyopathies and to study the relations between phenotype and genotype.

Methods: DNAs from a cohort of 1150 unrelated index-patients with an isolated cardiomyopathy (700 hypertrophic, 300 dilated, 50 restrictive cardiomyopathies, and 100 left ventricle non-compactions) have been sequenced on a custom panel of 52 cardiomyopathy disease-causing genes.

Results: A FLNC pathogenic variant was identified in 28 patients corresponding to a prevalence ranging from 1 to 8% depending on the cardiomyopathy subtypes. Truncating variants were always identified in patients with dilated cardiomyopathy, while missense or in-frame variants were found in other phenotypes. This work reported for the first time a left ventricular non-compaction associated with FLNC pathogenic variant.

In the cohort, nine patients (32%) were implanted with an automatic defibrillator. In 7 families (25%), history of sudden cardiac death (SCD) before 50 years was reported. A personal or family history of sudden cardiac death (SCD) was significantly higher in patients with truncating variants than in patients carrying missense variants (p=0.01). Four patients died of cardiac cause including 3 from SCD and 1 from heart failure.

Conclusion. This work highlights the role of FLNC in cardiomyopathies. A correlation between the type of the variant and the cardiomyopathy subtype was observed as well as with SCD risk. These new data should be taken into consideration for patient’s management and primary prevention of sudden cardiac death.