Dizertační práce:

Diagnostika hypertrofické kardiomyopatie se zaměřením na genetické vyšetření

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Abstract

Introduction: Hypertrophic cardiomyopathy (HCM) is the most common monogenic cardiac disease with vast genetic and clinical heterogeneity. Genetic testing of HCM patients is important in determining the etiopathogenesis of the disease and is becoming an integral part of patient care.

Aim: The aims of our work included the following implementation of genetic testing in HCM in both basic and clinical research:

1. To identify genetic variants in a novel candidate gene *NEBL* coding Z-disc protein nebulette in HCM patients.
2. To determine clinical and echocardiographic variables associated with the presence of mutations in the most common sarcomeric genes in the Czech population.
3. To find echocardiographic parameters useful in determining the genotype of relatives before the development of phenotype.

Results: In a cohort of 95 patients with HCM we identified a novel genetic variant in a conserved spot of *NEBL* gene (p.H171R) in one patient. The variant was not found in a control population and was predicted to have a damaging effect on the protein's structure. In a cohort of 48 HCM patients tested for mutations in the most common sarcomeric genes, we found a significant association between a younger age at diagnosis and reverse morphology of interventricular septum and the presence of mutation. In a group of 20 genetically tested relatives, we confirmed the role of a combined echocardiographic index to identify genotype positive individuals.

Conclusion: Genetic testing is a useful tool in diagnostics of HCM. It allowed us to identify a mutation in a novel candidate gene for HCM, define factors associated with the presence of mutations in sarcomeric genes and factors capable of determining the genotype status of relatives.