

Hypertrophic Cardiomyopathy in children: Genotypic-phenotypic correlation in a large Dutch cohort

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Introduction: Hypertrophic cardiomyopathy (HCM) is a genetically determined myocardial disease characterized by left ventricular hypertrophy of various morphologies, with a wide array of clinical manifestations ranging from no complaints to sudden cardiac death(SCD). Although risk factors for cardiac events such as myocardial thickness have been described earlier, the consequences and/or benefits of genetic testing are still unclear.

Aim: To investigate the genotype-phenotype correlation in a Dutch cohort of unrelated children with HCM.

Methods: Multicenter retrospective study in 7 centers in the Netherlands on children (0-18 years) presenting between June 1978 and October 2016 with left ventricular wall thickness of ≥ 2 SD above the population mean on echocardiography. Data were gathered till the latest visit before the patient turned. The genetic testing has changed over the years from DNA analysis by direct sequencing of all coding intron-exon boundaries of known HCM causing genes to next-generation-sequencing of a larger panel of HCM genes in the cases after 2012. Statistical analyses were performed by Kaplan-Meier curves and Poisson regression.

Results: Until now 78 patients (69% male) were included with a mean follow time of 11,5 years. In 45 patients results from genetic tests were available, of which 31 patients (65%) had one or more mutations and 14 (30%) had no mutations. Mutations were located in the *MYBPC3* (35%), *MYH7* (19%), *DSP* (2%), *PRKAG2* (2%), *POPDC2* (2%), *MYPN* (2%) and *TNNI3* (2%) gene. VT/VF-events occurred earlier ($p=0.034$) and more often ($p=0.0042$) in genotype-positive patients. SCD occurred in four patients in the genotype-positive group in the absence of any echocardiographic differences with the genotype-negative group.

Conclusions: We showed that the cardiac event rate is higher in genotype-positive children with hypertrophic cardiomyopathy

