AEPC-YIA Session

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AEPC-YIA Session（I-AEPCYIA）

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[I-AEPCYIA-5] Genetic Background of Patients with Childhood-Onset Cardiomyopathy: Results from a Retrospective Cohort Study

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INTRODUCTION:Childhood-onset cardiomyopathy (CMP) has a rare incidence of approximately 1/100 000 children. 40-50% of children have a positive familial history of cardiomyopathy or sudden cardiac death and the general yielding across the different types of CMP is 50-60%, with dilated CMP (DCM) having the lowest genetic yield (20-30%). A high proportion of rare disease phenocopies such as metabolic disorders and RASopathies is generally found in early childhood (<10yrs).
AIM: To investigate genotype-phenotype correlations and cardiac outcomes.
METHODS:Children under 18yrs who presented at our institution between 1990-2024 with any type of CMP, were included in the study. Demographic, genetic, and cardiac outcome data were collected and analyzed.
RESULTS:A total of 157 children (63.1% male, mean age: 5.3±5.8yrs) were diagnosed with CMP. The most frequent subtypes were DCM (49%) and hypertrophic CMP (HCM, 47.1%) with fewer cases of restrictive CMP (RCM, 5 patients) and arrhythmogenic CMP (ACM, 1 patient). Nearly half of the patients (46.5%) were diagnosed during infancy. Genetic screening was performed in 68.8% of patients, most frequently in HCM (74.3%). Overall, a causative variant was identified in 56.5%. Genetic yield was higher in children with HCM in comparison to those with DCM (65.4% vs 46.9%, p=0.067). Additionally, in 15.7% variants of unknown significance (VUS) were found. A trend of higher genetic yield was seen in older age groups. In infants (0-1yrs), a variant in a metabolic or RASopathy gene was found in 57.1%. Notably, sarcomere gene variants, traditionally associated with adult-onset CMP, contributed to 28.6% of infant cases. Major cardiac events occurred in 43.3%. Of all patients 25.5% died, 12.1% underwent a heart transplant and 7% received an implantable cardioverter-defibrillator. No significant differences in outcomes were observed across CMP subtypes.
CONCLUSIONS:Genetic testing identified the underlying etiology in over 50% of patients with childhood-onset CMP. While rare disease phenocopies are highly prevalent in infants, sarcomere gene variants –once thought to be limited to adult-onset CMP– can also manifest in a very young age. These findings underscore the importance of early genetic testing to guide diagnosis and management.

Figure 1. a) Distribution of cardiomyopathy subtypes. DCM= Dilated CMP, HCM = Hypertrophic CMP, RCM = Restrictive CMP, ACM = Arrhythmogenic CMP b) Causative variants (likely pathogenic and pathogenic) per gene category, displayed according to age group. In the "structural" group genes encoding the Z-disc (ACTN2, NEXN2), nuclear envelope (LMNA), cytoskeletal (FLNC, DES) and junctional membrane (JPH2) are included.