A retrospective study of cardiomyopathy in children and adolescents: aetiology and function of oxidative phosphorylation (OXPHOS)

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Introduction:
Cardiomyopathy (CMP), a heterogeneous group of myocardial disorders, is rare in children but carries a high mortality rate. The heart muscle is structurally and functionally abnormal, leading to muscle and electrical dysfunction. In most cases CMP presents itself with a ventricular hypertrophy (HCM) or dilatation (DCM) and leads to progressive heart failure and eventually cardiovascular death (Figure 1). The aetiology is divers and often hereditary. The main causes are isolated mutations, neuromuscular dysfunctions, malformation syndromes and metabolic disorders, including deficiency in OXPHOS-mechanism (Figure 2). The severity and familial recurrence of CMP mandates further genetic elaboration and consequently prenatal diagnostics.

Methods:
Between 2003 and 2011, 66 patients with CMP were in follow up (140/26). Diagnoses were made between 1984 and 2011, most of them presenting at neonatal age. ‘Mitochondrial Disease Criteria’ (MDC) indicating possible defects in oxidative phosphorylation (OXPHOS), were implemented to the patients with currently unknown aetiology or a suspicion of metabolic disorder (Table 2). A score of 1 to 7 was assigned, depending on muscle symptoms (max.2 points), central nervous system abnormalities (max.2 points) and multisystem involvement (max.3 points), with a maximal clinical score of 4 points. Subsequently metabolic results (elevated lactate, pyruvate, alanine) were added to the calculation (max.4 points).

- Score 1: mitochondrial disorder unlikely
- Score 2 to 4: mitochondrial disorder possible
- Score 5 to 7: mitochondrial disorder probable

Results: overview of the population
Aetiology was known in 53% of the patients and was divided into genetic (27/35) and non-genetic (8/35) causes (Figure 3). An overview of the study population is presented in Table 1.

Results: The function of ophos
In 11 patients, CMP was associated with a metabolic disease, with 64% (7/11) respiratory chain defects (Figure 4). In 31 (47%) patients, the aetiology was not yet established. After selection of the patients with unknown aetiology or a suspicion of metabolic disorder, the MDC-criteria were implemented on 21 patients. Suspicion of OXPHOS-deficiency was raised in 17 patients (≥2) (Table 2).

Conclusion:
Presentation and aetiology of CMP in children is heterogeneous. OXPHOS-deficiency is relatively frequent. In our study population these disorders are probably under diagnosed.