00007 - Influence of hemodynamic overload with or without pressure overload on myocardial remodeling in children with congenital cardiac defect: implication of exosomes and intracellular fibrosis activation pathways

N. Farhat[1,*], R. Heying[2], A. Rüffer[3], J. Vazquez-Jimenez[3], M. Beghetti[4], M.C. Seghaye[1]

[1]CHU Liège - Liège (Belgium),
[2]KU Leuven - Leuven (Belgium),
[3]UK Aachen - Aachen (Germany),
[4]HUG Genève - Genève (Switzerland)

Introduction
Children with hemodynamically significant congenital heart defects (CHD) develop myocardial structural changes defined as myocardial remodeling. This results in myocardial cell death, fibrosis and dysfunction.

Objective
This project aims to study the complex mechanisms related to myocardial remodelling in children with CHD including the myocardial inflammatory, growth, apoptosis and fibrosis signaling pathways. We aim to highlight the role of micro-RNAs (miRNAs) and exosomes as important and easily measured biomarkers of myocardial remodeling.
Correlations between laboratory findings and clinical parameters will also be analyzed.

Methods
75 infants and children < 18 years undergoing primary surgical repair for CHD associated with hemodynamic overload of the right ventricle will be prospectively investigated.
A broad cardiologic preoperative assessment focused on the right ventricular morphology and function will be made. Myocardial and blood samples will be taken before cardiopulmonary bypass initiation.
Expression of different inflammation, growth, cell death and fibrosis mediators will be assessed at mRNA- and protein level as well as micro-RNA and exosomes in the myocardium and blood.

Expected results
We expect to clarify the activation pathways involved in cell death and fibrosis of the patient myocardium facing hemodynamic overload due to CHD and to identify circulating biomarkers allowing to detect early structural changes linked to myocardial remodeling.

Perspectives
Our results should help to better understand the complex mechanisms of myocardial remodeling in CHD and therefore to propose pharmacologic interventions that would avoid myocardial cell loss and fibrosis according to patient's mi-RNA- and exosomal profile.