First paediatric cohort for the evaluation of inflammation in endomyocardial biopsies

Degener F. (1,2), Salameh A. (3), Pickardt T. (4), Manuylova T. (5), Kostelka M. (6), Daehnert (3), Berger F. (1,2,7), Messroghli D. (2,8,9), Schubert S. (1,2), Klingel K. (5) [- On behalf of the MYKKE consortium -]

German Heart Center Berlin, Department of Congenital Heart Disease - Pediatric Cardiology, Berlin, Germany (1); DZHK (German Centre for Cardiovascular Research), partner site Berlin, Germany (2); Heart Center, University of Leipzig, Clinic for Pediatric Cardiology, Leipzig, Germany (3); Competence Network for Congenital Heart Defects, Berlin, Germany (4); Cardiopathology, Institute for Pathology and Neuropathology, University Hospital Tübingen, Tübingen, Germany (5); Heart Center, University of Leipzig, Department of Cardiac Surgery, Leipzig, Germany (6); Charité - Universitätsmedizin Berlin, Department for Pediatric Cardiology, Berlin, Germany (7); German Heart Center, Internal Medicine - Cardiology, Berlin, Germany (8); Charité - Universitätsmedizin Berlin, Department for Cardiology, Berlin, Germany (9)

Objectives
Endomyocardial biopsy (EMB) remains the gold standard for the diagnosis of myocarditis in children and adults. The existing WHO/ISFC criteria for lymphocytic cell infiltrates by Richardson et al. are based on myocardium of adults. The aim of this study was to analyse histopathological signs of inflammatory myocardial disorder in a paediatric cohort.

Methods
The study prospectively enrolled patients <18 years with EMB, collected during a planned open heart surgery with routine resection of endomyocardial tissue from ventricular site. All patients had no history of infection or myocardial inflammation. The myocardium was formalin fixed and thereafter paraffin-embedded. For histopathological and immunohistological analyses 5-mm-thick tissue sections were stained with haematoxylin and eosin, Masson’s trichrome, and Giemsa and examined by light microscopy. For immunohistological staining, monoclonal antibodies for the detection of T cells (CD3), B cells (CD20), macrophages (CD68) and major histocompatibility complex (MHC) II (HLA-DR) were used.

Results
Sixty-five endomyocardial samples from 65 patients were included. The myocardium derived from: 93.8% (n=61) right ventricular outflow tract, 4.6% (n=3) from the left ventricle and in 1.6% (n=1) from the right ventricle. The median patient age (interquartile range) at time of sampling was 0.6 (0.3-1.0) years, 66.2% male. A median of 2.5/mm² (1.0-4.0) CD3+ T cells, 0.5/mm² (0.0-0.5) CD20+ B cells and 4.0/mm² (2.0-4.0) CD68+ macrophages were detected. The MHC II grade was 0/mm² in 16.9% (n=11), 0-1/mm² in 53.8% (n=35) and 1/mm² in 27.7% (n=18). All of these samples were below the current cut-off for myocarditis according to the WHO/ISFC criteria.

Conclusion
This is the first prospective study with analysing paediatric ventricular samples for the evidence of inflammatory myocardial disorder. The degree of lymphatic cell in children without myocardial inflammation lies far below the existing thresholds in adults. Therefore detection of an increased number of lymphatic cells in EMB might already define a pathological inflammation in patients with suspected myocarditis.