Novel serumbiomarkers in early stages of hypertrophic cardiomyopathy in the young

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Introduction:
Hypertrophic cardiomyopathy (HCM) is the most common monogenic cardiac disorder and the leading cause of sudden cardiac death in the young. Although in a majority of HCM cases there are gene mutations coding for sarcomere proteins, the clinical course is difficult to predict, as these mutations do not show any clear relationship to the degree of myocardial hypertrophy. Hence identification of early markers for this disease is important. The aim of this study was to investigate novel serum biomarkers reflecting myocardial remodeling, microfibrosis and coronary endotheliopathy and cardiac magnetic resonance (CMR) in young presymtomatic HCM patients and HCM-risk individuals.

Methods:
A cohort of 102 participants (mean age 15,9 years) consisting of HCM patients (n=21), HCM-risk individuals (n=16), healthy controls (n=52) and young athletes (n=13) were included in this study. All subjects underwent cardiac ultrasound (conventional and tissue Doppler imaging) and serum analysis for Myostatin, Cathepsin S, Endostatin, type I collagen degradation marker (ICTP), Matrix Metalloproteinase (MMP) 9, vascular (VCAM) and intercellular adhesion molecules (ICAM). In a subset of the study population (18 HCM, 9 HCM-risk, 9 controls including 4 athletes), myocardial perfusion was measured at rest and after adenosine vasodilation on cardiac magnetic resonance.

Results:
The mitral annulus E/e’ by tissue Doppler was decreased in both the HCM-risk and HCM group (p<0.05), whereas global perfusion during adenosine was decreased only in the HCM group (p<0.05) compared to other groups. MMP-9 (p=0.01), VCAM (p=0.04), Cathepsin S (p=0.008) and Endostatin (p <0.0001) were all increased in the HCM group compared to other groups. Both Cathepsin S and Endostatin showed weak correlation to left ventricular mass and E/e´ (p<0.05, r>0.3 for both).
Myostatin was decreased and ICAM was increased in the HCM-risk group (p<0.01). ICAM correlated with myocardial perfusion during adenosine stress(p=0.04, r=0.4).

Conclusion:
To the best of our knowledge, this is the first study to suggest early onset changes in biomarkers of myoblast regulation, endothelial function and matrix remodeling in young presymptomatic HCM patients and in HCM-risk individuals.