Circulating Biomarker for Myocardial Angiogenesis in Children and Adolescents with Severe Hypertrophic Cardiomyopathy

Fernlund E. (1,6), Gyllenhammar T. (2), Larsson A. (3), Ärnlöv J. (4,5), Carlsson M. (2), Liuba P. (6)
(1) Dept. of Pediatrics, Linköping University Hospital, Linköping University, Sweden; (2) Dept. of Clinical Physiology, Skane University Hospital, Lund University, Sweden; (3) Dept. of Medical Sciences, Uppsala University, Sweden; (4) Dept. of Medical Sciences, Cardiovascular Epidemiology, Uppsala University, Sweden; (5) School of Health and Social Studies, Dalarna University, Falun, Sweden; (6) Pediatric Cardiology, Skane University Hospital and Lund University, Lund, Sweden

Introduction: Hypertrophic cardiomyopathy (HCM) is characterized by gradual thickening of the myocardium with disruption of coordinated cardiac hypertrophy and angiogenesis resulting in impaired coronary collateralization. Endostatin, an important angiogenesis inhibitor, is a 20-kDa carboxy-terminal proteolytic fragment from the first non-collagenous domain of collagen XVIII, which is a central component of the extracellular matrix in the cardiovascular system.

Objective: To assess in young patients with familial HCM whether plasma endostatin relates to the severity of HCM as defined by the presence of intracardiac cardioverter-defibrillator (ICD).

Methods: Children and adolescents with family history and echocardiographic signs of HCM (n=14; median age 15 years, range 7-27 years) as well as healthy controls (n=21) underwent echocardiography with tissue Doppler imaging, cardiac magnetic resonance (CMR) and peripheral venous blood sampling for endostatin analysis. Half of the HCM patients (n=7; “ICD-HCM”) had earlier received ICD either for primary or secondary prevention for sudden cardiac death (SCD). The remaining HCM patients (“HCM”) were age-matched with ICD-HCM patients.

Results: The left ventricular (LV) thickness and mass, and the mitral septal and lateral E/e´ were significantly higher in the ICD-HCM group than in the other 2 groups (p<0.01). Plasma endostatin was higher in the ICD-HCM group (p=0.09 vs. controls) and correlated with septal E/e´ (p=0.006, r=0.5) and with LV septal hypertrophy (p=0.04, r=0.4). In the subgroup of HCM patients who underwent CMR, there was an inverse correlation between endostatin and myocardial perfusion response to adenosine on CMR (r=-0.45, p=0.08).

Conclusion: In patients with HCM, the degree of septal hypertrophy, diastolic dysfunction and myocardial perfusion response to adenosine correlate with plasma levels of endostatin, which is elevated in the ICD-HCM group. The findings suggest endostatin as additional biomarker for more severe adverse changes in the myocardium of these patients.