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Children with atrial septal defect and significant left-to-right shunt show myocardial remodeling

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Background:
Myocardial remodelling characterises a state of cellular and organ adaptation that involves inflammation, cell growth and cell death. The balance between mechanisms inducing cell growth and those inducing cell death by apoptosis determines whether cardiac function remains compensate or deteriorates in cardiac failure.

Objectives:
To assess whether myocardial remodeling occurs in patients with atrial septal defect (ASD) with left-to-right shunt.

Methods:
15 children with ASD (10 females, age range 4-7 years, median 6.5 years) who were scheduled for surgical ASD closure were included. Myocardial specimens of the right atrium were obtained before connecting cardiopulmonary bypass. Gene expression of factors indicating mechanical stress (ANF), protective mechanisms (c-Fos, Hsp70, Hsp90), growth and angiogenesis (CT-1, HIF-1alpha, VEGF), fibrosis of the extracellular matrix (PIIIP), and regulating apoptosis (FasL, Bak, Bcl-xL) were determined by quantitative real time PCR.

Results:
In all patients, expression of ANF, c-Fos, Hsp70, Hsp90 confirmed myocardial stress whereas expression of CT-1, HIF-1alpha, VEGF and PIIIP confirmed remodelling with signals leading to cell growth, angiogenesis and fibrosis. All patients showed expression of FasL, Bak, Bcl-xL indicating apoptosis regulating mechanisms with a shift towards the expression of the apoptosis inhibitory factor Bcl-xL . Expression of factors inducing growth and angiogenesis correlated with the expression of factors responding to stress and also with the expression of apoptosis regulating proteins. Interestingly, expression of the apoptosis regulating proteins correlated with the marker of fibrosis PIIIP.

Conclusions:
Myocardial remodeling occurs in young children with ASD as a sign of compensatory adaptation and goes along with signals inducing hypertrophy, angiogenesis, fibrosis and apoptosis. In this stage of cardiac disease, antiapoptotic factors outbalance proapoptotic factors. A shift towards a net proapoptotic effect, which was not yet observed in this group, might mark the beginning of the transition from compensated to decompensated heart failure.