

**Inflammation, growth, fibrosis and apoptosis in right atrial myocardium of infants with atrial septal defect**

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**Introduction**

Atrial septal defect (ASD) is a relatively common congenital heart disease with an estimated prevalence 2 per 100 live births. Changes in atrial tissue properties, including interstitial fibrosis, increased myocyte size and alterations in ultracellular structure have been described in these patients. The exact mechanisms underlying this remodeling are not yet understood.

The aim of this study was to explore mRNA expression of genes coding for inflammation (IL1 $\beta$ , IL6, TNF $\alpha$ ), angiogenesis (HIF1 $\alpha$ , VEGF), hypertrophy (CT-1, IGF1,), and apoptosis (Fas, BAK, Bcl-xL) in right atrial myocardium of children with ASD.

**Patients and methods**

12 infants with ASD were investigated with a mean age of 64,5 months. Myocardial Samples taken before institution of cardiopulmonary bypass were analyzed by Real time PCR to study the expression of genes involved in myocardial growth, inflammation, hypertrophy and apoptosis.

**Results**

All patients showed preoperative myocardial inflammation with expression of mRNA coding for IL 1 $\beta$ , IL 6, and TNF $\alpha$ . Myocardial remodeling led to hypertrophy, angiogenesis, and myocardial fibrosis with expression of mRNA coding for CT-1, HIF-1  $\alpha$ , TGF  $\beta$  and VEGF. Gene expression of extracellular pro-apoptotic factor FasL, intracellular apoptosis regulating factors Bak and Bcl-xL were also detected. There was a strong positive correlation between expression of IL1 $\beta$  and TGF $\beta$ , respectively (rs: 0,91, p<0,05). There was also an association between myocardial hypertrophy (CT-1) and the expression of the vascular stimulating factor HIF-1  $\alpha$  and the angiogenesis growth factor VEGF, respectively: Expression of CT-1 correlated with that of VEGF (rs = 0.964; p <0.001), and expression of HIF-1 $\alpha$  correlated with that of VEGF (rs = 1.0, p = 0.003)

**Conclusion**

Myocardial remodeling is a multi-factorial process involving inflammatory- and intracellular signaling pathways, which may have synergistic or antagonistic effects. At a stage of the disease, volume overload activates pro-apoptotic factors that will initiate transition from compensated hypertrophy to decompensated heart failure. This processes, which is highly regulated, has a primordial role in the pathophysiology of heart failure. Our results suggest that IL1 $\beta$  may regulate TGF $\beta$  expression as a feedback mechanism to limit extra cellular matrix degradation in response to injury.