

### Myocardial collagen turnover and myocardial fibrosis are associated with systemic right ventricle dysfunction and wall stress in transposition of the great arteries palliated by atrial switch

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**Background:** Heart failure is a serious event in patients with transposition of the great arteries (D-TGA) after atrial redirection surgery (Mustard-Senning operation). Mechanisms of the late failure of the systemic right ventricle (sRV) are poorly characterized. We aimed to determine the role of myocardial fibrosis in systolic and diastolic sRV dysfunctions.

**Methods:** Determinants of systolic and diastolic functions of sRV were prospectively studied in 49 patients (median age 32 years, male: female ratio = 3:4) with atrially switch D-TGA compared to 26 healthy subjects similar for age and sex. Diastolic and systolic functions of sRV were assessed using echocardiography and cardiac magnetic resonance imaging (CMR). Fibrosis extent within sRV myocardium was evaluated using gadolinium-enhanced magnetic resonance and serum turnover collagen biomarkers.

**Results:** Late gadolinium enhancement (LGE) was diagnosed in 35% of patients with D-TGA, and collagen degradation biomarkers measured by MMP1/TIMP1 ratio were significantly increased in D-TGA compared to healthy subjects ( $1.0 \times 10^{-2}$  vs.  $2.5 \times 10^{-2}$ ,  $p=0.04$ ). MMP1/TIMP1 as well as LGE lesions were significantly associated with sRV wall stress ( $r=0.77$ ,  $p<0.01$ . Figure 1A) and early sRV filling velocity/ early myocardial velocity ( $r=0.53$ ,  $p=0.02$ . Figure 1B). sRVEF was strongly correlated with sRV wall stress ( $r=-0.74$ ,  $p<0.01$ ) and fibrosis markers (pro-MMP1/TIMP1,  $r=-0.81$ ,  $p<0.01$  Figure 1C, and LGE,  $p<0.01$ ).

**Conclusions:** Impairment of diastolic and systolic functions of sRV is related to myocardial matrix remodeling, which is the consequence of longstanding RV pressure overload. Research in medical therapies that reduce fibrosis is warranted in this setting.

