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**Endothelin-1 plays an important role in the Fontan circulation.**

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**Objectives:** To evaluate whether endothelin-1 (ET-1) plays an important role in the Fontan circulation.

**Methods:** First, we measured the serum ET-1 levels taken from the pulmonary artery in 32 patients with single ventricle (SV) physiology and compared this group with 28 patients with biventricular physiology (BV). Second, 13 patients who underwent right heart bypass were evaluated using lung histopathological and immunohistochemical studies. For 10 of these patients, quantitative real-time PCR analyses of ET-1, endothelin receptor type A and type B were performed.

**Results:** First, The serum ET-1 levels in the patients in the Fontan, Glenn and BV groups were  $1.7 \pm 1.2$ ,  $1.1 \pm 0.6$ , and  $0.9 \pm 0.5$  pg/mL, respectively. The serum ET-1 level positively correlated with the mean pulmonary artery pressure in Fontan circulation ( $p < 0.01$ ). Second, in patients with failed Fontan circulation, the pulmonary arteries exhibited severe medial hypertrophy and the overexpression of ET-1 in the endothelium and media. Quantitative real-time PCR analyses also confirmed that the mRNA expression of ET-1 was increased in patients with failed Fontan circulation.  
**Conclusions:** Medial hypertrophy and the overexpression of ET-1 in the pulmonary arteries may induce failure of the Fontan circulation. There is an association between ET-1 and SV physiology in maintaining vasoconstriction of the pulmonary artery and promoting vascular remodeling.