

Staged Fontan procedure ameliorates Ventricular hyper-fibrogenesis in the patients with single ventricular circulation

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Background: Preserving ventricular function before and after Fontan procedure is a key element in establishing successful Fontan circulation. We tested the hypotheses that 1) volume overload and/or cyanosis generally observed in the single ventricle (SV) circulation before Fontan surgery is associated with ventricular hyper-fibrogenesis and 2) Fontan procedure effectively ameliorates ventricular fibrogenesis, but sustained hyper-fibrogenesis in the Fontan ventricle is associated with ventricular diastolic dysfunction.

Methods: Serum levels of amino-terminal propeptide of type III procollagen (PIIIP), a marker of fibrogenesis, were measured in 63 patients with a single ventricle (SV) and in 111 healthy children (control). The children with SV were divided into three groups according to clinically relevant stage: (1) Unoperated children or children who underwent first-stage repair (Blalock-Taussig shunt or pulmonary artery banding: BTS/PAB group, n=63). (2) Children who underwent second-stage palliation (Glenn group, n=59). (3) Children who underwent Fontan surgery (Fontan group, n=36). For the children with SV, serum levels of Renin, Angiotensin, and Aldosterone were also evaluated.

Results: The PIIIP levels decreased significantly after the Glenn procedure, and further decreased after the Fontan procedure, although the level was still significantly higher than that of the control (BTS/PAB group: 5.3 ± 2.1 , Glenn group: 1.8 ± 1.0 , Fontan group: 1.5 ± 0.5 , Control: 1.1 ± 0.3 U/ml). Increased ventricular volume load assessed by pulmonary to systemic flow ratio (Q_p/Q_s) was significantly associated with increased PIIIP levels in children with BTS/PAB ($r=0.674$, $p<0.01$), while PIIIP levels in the Glenn group correlated significantly with the severity of cyanosis ($r=0.459$, $p<0.01$). In the Fontan group, high PIIIP levels correlated significantly with increased ventricular diastolic stiffness assessed by end-diastolic pressure-area relationship ($r=0.44$, $p<0.05$). The serum levels of Aldosterone remarkably decrease in parallel with the surgical stage, same as the trends of PIIIP. After the Fontan completion, serum levels of Renin, angiotensin and aldosterone were significantly correlated with that of PIIIP.

Conclusions: Our results suggest ventricular hyper-fibrogenesis in patients with SV circulation. Staged-Fontan procedure can ameliorate this process, and additional therapies aiming at anti-fibrogenesis, such as inhibition of Renin-Angiotensin-Aldosterone system, may be additively effective in improving the patient's prognosis after the Fontan procedure.