

Atrioventricular regurgitation and biomarkers in Fontan Circulation

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Introduction: The detrimental role of the Fontan circulation in the hepato-intestinal system has been well documented. Fontan patients are at risk of complications such as hepatic fibrosis and protein losing enteropathy (PLE). Our goal was to understand the relationship of possible disease biomarkers to other aspects of this circulation, detected by echocardiography.

Methods: Forty-four Fontan patients followed in outpatient clinic were prospectively studied with laboratory evaluation and transthoracic echocardiogram (TTE). Regarding atrioventricular (AV) dominant valve regurgitation on TTE, patients were classified by two experienced operators in 2 groups: those without significant regurgitation (none or mild) and those with significant regurgitation (moderate or severe). Selected biomarkers were related to hepatic disease (aspartate transaminase (AST), alanine aminotransferase (ALT), total bilirubin (TB), gamma-glutamyl transferase (GGT) and alkaline phosphatase (ALP)), PLE (total protein and albumin), intestinal inflammation (fecal calprotectin (FC)) and cardiac function (NT-proBNP). Statistical inference was performed using R CRAN version 3.5.0. Linear regression and ANOVA were used for continuous variable correlation.

Results: Median age at Fontan completion was 6 years (SD 3) and median age at current evaluation was 19 years (SD 7). No patient had previous diagnosis of hepatic disease and 4 patients (9%) had PLE. Mean values and standard deviation (SD) of selected biomarkers were: total protein 7g/dl (SD 1), albumin 4.5g/dl (SD 0.7), AST 30U/L (SD 10), ALT 28U/L (SD 11), TB 0.9mg/dl (SD 0.5), GGT 78U/L (SD 62), ALP 148U/L (SD 101), FC 92mg/kg (SD 62), NT-proBNP 388pg/ml (SD 1031). The most common abnormality on TTE was significant AV regurgitation in 20 patients (45.5%). Statistical analysis showed a strong correlation between this and levels of TB ($p=0.016$), GGT ($p=0.013$), FC ($p=0.003$) and NT-proBNP ($p=0.045$). Higher FC was also related to higher NT-proBNP ($p=0.004$).

Conclusion: Fontan patients with significant AV valve regurgitation have abnormal values of several biomarkers related to cardiac, hepatic and intestinal disease. Presence of more than mild AV valve regurgitation in Fontan patients defines a high-risk group requiring tight follow-up.