

## **Thrombotic profile in Fontan patients assessed by whole-blood assays and endothelial biomarkers**

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### **Introduction**

After a Fontan procedure the patient face an increased risk for thromboembolic complications. The etiology for this increased risk is not well defined. This study aimed to evaluate whether global whole-blood assays of coagulation as well markers of endothelial activation/damage and glyocalyx degradation can detect hypercoagulability in Fontan patients.

### **Methods**

We performed kaolin-activated thrombelastography (TEG) and functional fibrinogen determined by TEG on citrated whole blood, and multiple electrode platelet aggregometry (MEA) on heparinized blood from Fontan patients. Furthermore, plasma was analyzed for biomarkers reflecting tissue/endothelial cell/glyocalyx damage (histone-complexed DNA fragments, Protein C, soluble CD40 ligand, soluble thrombomodulin, syndecan-1, tissue-type plasminogen activator). Variables from whole-blood assays and the endothelial biomarkers were compared in patient groups, stratified according to age, antithrombotic therapy, post-Fontan thromboembolic event, and degree of glyocalyx degradation (concentration of syndecan-1). Correlations between endothelial biomarkers and demographic-, anatomical-, clinical- and biochemical parameters were investigated.

### **Results**

Whole-blood assays were performed in 118 Fontan patients (median age: 14.0 years; IQR: 8.1-19.5) and analyses of endothelial biomarkers were performed in 79 Fontan patients (median age: 14.0; IQR: 8.2-19.5). Of the 118 patients, 79 (67%) received antiplatelet therapy, 27 patients (23%) vitamin K antagonist, three patients (3%) unfractionated heparin, and nine patients (8%) no antithrombotic therapy. Six patients (5%) had a known post-Fontan thromboembolic event. None of the patient groups demonstrated evidence of hypercoagulability in the whole-blood assays compared to reference data and no statistically significant differences were found between groups in the stratified analyses, except for those expected from type of antithrombotic therapy. A strong correlation between the endothelial biomarkers was found in all age- and antithrombotic therapy groups. Concentration of all the endothelial biomarkers was above the median in six patients (8%) (chi-square test,  $p=0.11$ ). No other general correlation was found.

### **Conclusions**

Eight percent of Fontan patients show evidence of considerable endothelial activation/damage including glyocalyx degradation assessed by endothelial biomarkers. This subset of patients is potentially more thrombogenic than other Fontan patients, however no characteristics of this group were discovered. Whole-blood assays did not show evidence of hypercoagulability in Fontan patients and thrombotic profile was identical between different Fontan groups.