Evaluation of the coagulation system in children with two-ventricle congenital heart disease

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Introduction: Coagulation factor abnormalities as a cause of a hypercoagulable state observed in some children with single ventricle physiology have been evaluated, and multiple coagulation factor abnormalities involving both pro-and anticoagulant proteins have been described. These studies have suggested that the abnormalities reflect aspect of single ventricle and Fontan physiology (1,2). There is minimal or no data available on plasma concentrations of coagulation factors in infants and children with congenital heart disease (CHD) in general. The aim of this study was to evaluate coagulation factor values in children with two ventricle congenital heart defects, including both cyanotic and noncyanotic lesions.

Methods: With informed consent, coagulation factors were assayed in a total of 38 infants and children with two ventricle CHD; divided into 3 groups. Group I (3-12 months): 13 infants mean age 5.4 ± 1.8 months, group II (12-48 months): 14 children mean age 2.2 ± 1.1years and group III (>48 months): 11 children mean age 5.8 ± 1.9 years. Healthy children without CHD were assayed as controls (3-12 months: 30 infants mean age 8.0 ± 2.6 months, 12-48 months: 42 children mean age 2.5 ± 1.3years and >48 months: 18 children mean age 9.5 ± 2.7 years). Specific clotting assays included: Factors II, V, VII, VIII, IX, X, Protein C and S, plasminogen and antithrombin III were measured by standard assays.
Data represent mean ± SD, a Bonferroni adjustment was used for multiple comparisons.

Result: Result is as shown in the table, with significant differences between group I and the controls for all variables except factor VIII, for group II there were significant differences for all variables except factor VIII, Antithrombin III and Protein S and for Group III the only difference was for factor IX.

	Ages 3-12 months			Ages 12-48 months			Ages > 48 months		
Variable (%)	**Controls (n = 30)**	**Patients (n = 13)**	**p value**	**Controls (n = 42)**	**Patients (n = 14)**	**p value**	**Controls (n = 18)**	**Patients (n = 11)**	**p value**
Factor II	90 ± 12	71 ± 13	<0.001	94 ± 11	81 ± 10	<0.001	94 ± 17	85 ± 11	0.14
Factor V	117 ± 17	101 ± 32	<0.05	111 ± 18	93 ± 11	<0.001	99 ± 20	84 ± 17	0.05
Factor VII	88 ± 20	71 ± 21	<0.05	90 ± 18	71 ± 14	<0.001	93 ± 30	69 ± 19	0.03
Factor VIII	78 ± 20	68 ± 18	0.16	88 ± 23	79 ± 19	0.21	96 ± 28	73 ± 30	0.05
Factor IX	66 ± 15	41 ± 14	<0.001	71 ± 12	53 ± 13	<0.001	82 ± 22	54 ± 22	0.003
Factor X	95 ± 14	63 ± 20	<0.001	94 ± 11	73 ± 13	<0.001	92 ± 20	78 ± 15	0.05
Antithrombin III	106 ± 13	89 ± 18	<0.001	105 ± 16	98 ± 11	0.18	111 ± 11	104 ± 12	0.18
Plasminogen	88 ± 15	70 ± 15	<0.001	100 ± 13	85 ± 10	<0.001	98 ± 16	91 ± 12	0.25
Protein C	81 ± 17	44 ± 9	<0.001	101 ± 21	67 ± 15	<0.001	90 ± 21	83 ± 14	0.36
Protein S	89 ± 20	66 ± 16	<0.001	86 ± 15	75 ± 16	0.02	89 ± 21	91 ± 39	0.87

Discussion: Coagulation factor concentrations and activities mature at varying rates after birth, with some not approaching adult values until late childhood (3). This study found that, when compared to healthy infants of similar age, there was a high incidence of both pro- and anticoagulant factor abnormalities in patients < 48months with two ventricular CHD, approaching normal levels in children > 48 months. These coagulation factor abnormalities are similar to the abnormalities seen in patients with single ventricular physiology in patients <48 months. Whether these abnormalities are part of a genetic predisposition, result from hemodynamic or pathophysiologic abnormalities in patients with CHD in general such as altered cardiac out put, congestive heart failure or failure to thrive is unknown.

1). Odegard et al. Annals of Thoracic Surg 2002;73:1770-7
2). Odegard et al. J Thorac Cardiovasc Surg 2002;123:459-465.
3). Andrew et al. Blood 1992;80:1998-2005.