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Anticoagulation Management during First Five Days of Infant-Pediatric Extracorporeal Life Support

Kirk R. Bingham, MS, CCP;* Jeffrey B. Riley, MHPE, CCP;† Gregory J. Schears, MD*

**Center for Cardiovascular Sciences and Department of Anesthesia, Mayo Clinic, Rochester, Minnesota; †SUNY Upstate Medical University, Syracuse, New York*

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Abstract: Anticoagulation during infant-pediatric extracorporeal life support (ECLS) has been a topic of study for many years, but management of anticoagulation is still only partially understood. Adequate anticoagulation during ECLS is imperative for successful outcomes and understanding the individual variables that play part is crucial for properly implementing anticoagulation management strategies. The purpose of our study was to compare the relationships between the variables of activated partial thromboplastin time (aPTT), activated clotting time, international normalized ratio, bleeding, thrombus formation, kaolin + heparinase thromboelastograph alpha angle, kaolin thromboelastograph reaction time (KTEG R-time), heparin dose rates (HDR), antithrombin (AT), anti-Xa, bivalirudin dose rate, argatroban dose rate, interventions, and transfusions. We hypothesized that the relationship between measures of anticoagulation would be influenced by the AT levels, and a therapeutic aPTT (60–80 seconds) could be achieved by increasing, or maintaining, the overall AT above a specific threshold for infant-pediatric patients on ECLS. Thirty-five infant-pediatric patients underwent ECLS between January 2013 and January 2016. The median age was 39 days with an average weight of 3.9 ± 4.3 kg. ECLS parameters collected at least every 24 hours for the first five ECLS days. Parameters recorded by retrospective chart review were analyzed using linear regression and receiver operator characteristic (ROC) analysis. We were unable to report a significant correlation between optimal aPTT and HDR at various AT levels. However, ROC analysis suggested that to maintain an aPTT above 60 seconds, an AT threshold of 42% or higher was observed when the HDR was >12 U/kg/h ROC analysis also determined that no thrombus was associated with an aPTT >64 seconds and decreased bleeding was associated with a KTEG R-time below 30 minutes. Based on these findings, we report multiple correlations that may help develop future standardized infant-pediatric ECLS anticoagulation protocols. **Keywords:** extracorporeal life support (ECLS), anticoagulation, pediatric, infant, extracorporeal membrane oxygenation (ECMO), antithrombin, heparin, bivalirudin, argatroban. *J Extra Corpor Technol. 2018;50:30–37*

Anticoagulation during infant-pediatric extracorporeal life support (ECLS) has been a topic of study for many years. Unfortunately, since the beginning of ECLS, management of anticoagulation is only partially understood (1,2). The ECLS Organization has written guidelines, but not standards for anticoagulation during ECLS (3). Adequate anticoagulation during ECLS is imperative for successful outcomes, which is accomplished by preventing potentially life-threatening thrombotic and hemorrhagic complications (4).

Unfractionated heparin has become the gold standard for ECLS anticoagulation. Activated clotting time (ACT) and activated partial thromboplastin time (aPTT) have become the most common anticoagulation monitoring tests (2,5,6). Heparin works by increasing the ability of antithrombin (AT) to prevent thrombotic events and ACT and aPTT reflect the coagulation status during ECLS (1). However, studies have shown varying outcomes when using ACT as the overall measure of anticoagulation (7,8). Other tests that are growing in popularity are the use of thromboelastograph (TEG) and the anti-Xa assay. TEG is used to evaluate the influence of heparin on bleeding/thrombotic events and the anti-Xa assay has been shown to be a better predictor of heparins availability for anticoagulation (9).

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Address correspondence to: Kirk R. Bingham, MS, CCP, 63 Citation Dr., Farmington, UT 84025. E-mail: u0450281@utah.edu
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Recently, direct thrombin inhibitors have been used during infant and pediatric ECLS (10–12). Argatroban (Triveni Interchem PVT, Gujarat, India) and bivalirudin (The Medicines Company, Parsippany, NJ) are used in our clinical practice when abnormal anticoagulation is observed with heparin utilization. Ranucci et al. (11) described the use of direct thrombin inhibitors in pediatric ECLS and found that their use as the sole anticoagulant can be performed safely. They also found that the use of direct thrombin inhibitors showed a better coagulation profile, less bleeding, and fewer allogeneic transfusions which reduced the overall cost of each patient. To support that claim, Nagle et al. (10) also studied the use of a direct thrombin inhibitor and found that it is a potential option for pediatric ECLS patients.

The purpose of our study was to compare the relationships between the anticoagulation variables of aPTT, ACT, INR, blood loss, thrombus formation in the circuit, alpha angle (AA), and kaolin thromboelastograph reaction time (KTEG R-time), vs. the variables of heparin dose rates (HDR), AT, anti-Xa, bivalirudin dose rate (BDR), argatroban dose rate (ADR), circuit interventions, and transfusions. We hypothesized that the relationship between measures of anticoagulation would be influenced by the AT and that a therapeutic aPTT (between 60 and 80 seconds) could be achieved by increasing, or maintaining, the overall AT above a specific threshold for infant-pediatric patients on ECLS.

MATERIALS AND METHODS

Patients and Data Collection

This retrospective chart review project qualified for exemption as a quality improvement project by the Mayo Clinic Institutional Review Board. After approval by the Center for Cardiovascular Sciences, we set out to collect descriptive statistics and relationships between anticoagulation parameters measured during infant-pediatric ECLS. Between January 2013 and February 2016, 45 patients were supported with ECLS. Five patients were supported <3 days and were excluded from this first 5-day observation and five patient families requested that data from their family members not be used for research. Therefore, we analyzed data from 35 infant-pediatric patients who were supported more than 3 days on ECLS. ECLS-specific data was gathered from each patient's medical records. Over the time period that we reviewed, small changes did occur within our ECLS practice, but nothing significant enough to alter the overall data we collected and analyzed. The data included all available patient anticoagulation variables which are summarized in Table 1.

Table 1. List of measured variables.

Anticoagulation Variables
HDR (U/kg/h)
BDR (mg/kg/h)
ADR (mcg/kg/min)
AT (%)
Anti-Xa (U/mL)
INR
Bleeding (mL/kg/24 h)
Circuit thrombus formation
KTEG R-Time (minute)
Kaolin + heparinase TEG AA (°)
Blood product transfusions (mL/kg/24 h)
Circuit Interventions for thrombus
Optimal relationship between APTT vs. HDR

The variables collected in the retrospective chart review.

ECLS

The extracorporeal circuit equipment included the Quadrox iD (Maquet, Wayne, NJ) with Bioline Surface Coating and the PediMag (for blood flows <1.5 L/min) or CentriMag (Thoratec, Pleasanton, CA). The size of the circuit was determined with the following algorithm: Maximum Blood Flow (MBF) .2–.6 L/min: Quadrox iD, PediMag, 3/16″ × 1/4″ A-V loop; MBF 1.3–1.5 L/min: Quadrox iD, PediMag, 1/4″ A-V loop; MBF 2.0–2.2 L/min: Quadrox iD, Centrimag, 1/4″ A-V loop; MBF 2.6–2.8 L/min: Quadrox iD, Centrimag, 1/4″ A × 3/8″ V. A heparin loading dose of 20–50 units/kg was used to raise the ACT above 250 seconds with a maintenance dose of 5.0–20.0 units/kg/h after bleeding stabilized to <1–2 mL/kg/h Heparin loading, and maintenance doses were selected based on our facilitie's current protocols and the clinicians judgment to obtain the desired ACT. During the ECLS run, we sought to maintain the patients' ACTs between 150 and 200 seconds and the aPTT between 60 and 80 seconds. The circuit contained a recirculation line with a stopcock manifold. Flow through the manifold was monitored and varied from patient to patient (between 150 and 250 mL/min). Anticoagulant drips were infused directly into the oxygenator. The Spectrum M4 Monitor (Spectrum Medical, Fort Mill, SC) was used to monitor blood flow, hemoglobin oxygen saturation, and to detect air emboli.

Bleeding and Thrombus Assessments

Bleeding from chest tubes and cannulation sites were assessed daily while on ECLS. These bleeding assessments occurred every hour and excessive bleeding was constituted as any blood loss >24 mL/kg/day. Blood transfusions were implemented on a case-by-case basis using a transfusion algorithm. When needed, red blood cells and non-red cell products were administered at 10–15 mL/kg for patients weighing <35 kg.

Thrombus assessments were done every shift, and any thrombus formation in the circuit was documented on a picture diagram of the circuit. A description of the size, location, mobility, and color of the thrombus was documented. All thrombi throughout the circuit, large enough

to see, were constituted as a positive response. Only thrombi located on the arterial side from the outlet of the oxygenator to the arterial cannula was documented as significant. The attending consultant and perfusionist completed a risk assessment of the thrombi, and it was determined whether a circuit intervention should be completed. Circuit interventions included oxygenator change out, arterial line clean/change out, connector clean/change out, and cannula clean/change out.

Laboratory Tests

According to our standard practice protocol for ECLS patient laboratory testing, AT was drawn daily (Tables 2 and 3) along with an aPTT and KTEG (KTEG, TEG 5000 Thromboelastograph Hemostasis Analyzer System, Haemonetics, Braintree, MA). KTEG monitoring included targeting the KTEG R-time above 10–12 minutes with an AA <30 degrees. Fresh frozen plasma and cryoprecipitate were used to maintain the KTEG R-time and a platelet transfusion was used to maintain an adequate AA. Anti-Xa levels were also analyzed for further anticoagulation analysis (13). ACT monitoring was performed using the i-STAT system with i-STAT cartridges (Abbott Point of Care, Abbott Laboratories, Abbott Park, IL).

Statistical Analysis

Selected recorded data during the first 5 days of ECLS were compared using linear regression and receiver operating characteristic (ROC) analysis. ROC, as described by Fawcett (14), is a program to visualize, organize, and select classifiers based on performance. Probability values of <.10 were considered statistically significant. Statistical analyses were performed using JMP statistical discovery software from SAS (Statistical Analysis Software, Cary, NC).

RESULTS

Patients

Of the 35 patients reviewed, 29 patients were supported for cardiac issues, five patients were supported for respiratory failure, and one was supported for extracorporeal cardiopulmonary resuscitation. Median age for all patients was 39 days (1st quartile = 7.5 days; 3rd quartile = 392.5 days); median weight was 3.95 ± 4.28 kg. Overall, 49% of the patients were discharged and alive at the time of analysis.

Tables 2 and 3 list the frequency distributions of the variables studied for infant-pediatric ECLS patients during their first 5 days on ECLS.

Linear Regression Analysis

When comparing BDR, the strongest correlations occurred when comparing it to AT, KTEG R-time, and AA. As the BDR increased, we observed a significant decrease in the AA. When comparing our BDR and ADR results, we found that BDR had more significant correlations with other variables than ADR. The HDR showed an inverse relationship with ACT and INR (as when one variable was increased, the other variable subsequently decreased). Also, as the AT increased, we did not observe subsequent increase in the ACT.

Table 2. Distribution of anticoagulation variables.

Parameter	ECMO Hour	Pt Days	25%tile	Median	75%tile	Mean
HDR U/kg/h	24	40	2	9	15	9
	48	40	8	13	19	14
	72	38	10	16	22	17
	96	35	11	15	20	17
	120	31	8	17	24	17
ADR mcg/kg/min	24	6	.25	.40	.63	.45
	48	8	.13	.30	.49	.29
	72	11	.10	.20	.45	.31
	96	13	.20	.30	.45	.45
	120	10	.20	.35	.70	.50
BDR mg/kg/h	24	2	.13	.17	.20	.17
	48	2	.05	.13	.20	.13
	72	4	.09	.16	.35	.20
	96	5	.09	.12	.30	.18
	120	6	.10	.18	.35	.23
AT supplement units	24	9	37	50	76	58
	48	10	33	44	57	44
	72	4	28	66	76	56
	96	8	37	54	84	57
	120	5	39	61	138	83

The frequency distribution of the anticoagulation variables collected. ADR, argatroban drip rate; AT, antithrombin; BDR, bivalirudin drip rate; ECLS Hour, sampling time during the first 5 days of ECLS support; HDR, heparin drip rate; Pt Days, number of patient days that were available for analysis; 25%tile and 75%tile are the 25th and 75th percentiles, respectively.

Table 3. Distribution of anticoagulation variables.

Parameter	ECMO Hour	Pt Days	25%tile	Median	75%tile	Mean	SD
AT(%)	24	30	26	39	53	40	16
	45	37	34	48	61	49	20
	72	36	37	53	71	56	22
	96	32	40	56	69	61	30
	120	28	50	62	76	62	17
ACT (seconds)	24	39	159	172	204	184	34
	48	37	173	184	200	186	26
	72	35	170	194	218	193	31
	96	29	172	194	220	198	33
	120	30	178	192	230	202	31
aPTT (seconds)	24	28	43	58	88	66	29
	48	40	51	72	78	71	29
	72	39	57	74	99	75	23
	96	34	59	71	94	76	25
	120	30	51	74	123	83	37
Anti-Xa (U/mL)	24	33	.05	.06	.17	.15	.23
	48	32	.05	.07	.19	.15	.21
	72	29	.05	.11	.19	.14	.12
	96	28	.05	.11	.17	.12	.07
	120	26	.05	.10	.16	.12	.09
KTEGR-time (minutes)	24	40	9.9	29.6	75.0	47.0	43.3
	48	40	10.0	27.6	57.1	38.0	34.0
	72	38	15.9	26.1	60.9	38.9	30.5
	96	34	15.1	27.9	47.8	37.0	28.8
	120	29	15.8	31.3	48.7	37.4	24.5
INR	24	40	1.2	1.5	1.8	1.5	.3
	48	39	1.2	1.3	1.6	1.5	.6
	72	39	1.1	1.3	1.7	1.5	.5
	96	33	1.1	1.3	1.6	1.4	.5
	120	28	1.2	1.3	1.6	1.4	.4
AA	24	38	45.8	56.5	64.3	52.2	15.0
	48	35	42.8	51.6	57.9	48.7	11.0
	72	36	40.0	48.2	58.7	61.7	82.1
	96	29	40.3	51.0	56.5	48.2	13.2
	120	27	33.9	49.6	57.8	45.8	17.1
Bleeding (mL/Ag/24 h)	24	39	19	27	59	60	113
	41	37	10	15	36	27	30
	72	38	8	15	34	28	43
	96	33	6	13	36	23	23
	120	28	5	13	35	23	28
Transfuse (mL/kg/24 h)	24	38	38	60	244	152	207
	48	40	10	20	25	5	24
	72	39	5	24	36	27	35
	96	34	9	27	40	28	24
	120	30	12	30	82	25	37
% ECC with thrombus	24	39				37%	
	48	40				88%	
	72	40				93%	
	96	35				88%	
	120	30				75%	
% ECC intervensions	24	39				5%	
	48	40				20%	
	72	40				13%	
	96	35				6%	
	120	30				7%	

The frequency distribution of anticoagulation variables collected. AT, antithrombin; ACT, activated clotting time; aPTT, activated partial thromboplastin time; ECC, extracorporeal circuit; ECLS Hour, sampling time during the first 5 days of ECLS support; KTEG R-time, kaolin thromboelastograph reaction time; AA, kaolin + heparinase thromboelastograph alpha angle; INR, international normalization ratio; Pt Days, number of patient days that were available for analysis.

After comparing HDR, we found multiple significant inverse correlations with ACT, INR, bleeding, and transfusions. This indicated that as the HDR increased, we noted a significant decrease in the aforementioned variables. These results are contrary to what we previously believed in that as the HDR was increased, there was a subsequent decrease in ACT.

When comparing INR, we found significant correlations with ACT, aPTT, AT, and KTEG R-time. As our INR

increased, ACT had a subsequent increase, aPTT increased, and KTEG R-time also increased.

Table 4 lists the regression matrix for all parameter pairs.

ROC Analysis

Using ROC analysis, patient laboratory values were further evaluated. All laboratory values were compared with observations with an optimal range of aPTT and HDR defined as aPTT >60 seconds and HDR >15 U/kg/h. All patients' daily laboratory values that corresponded with the optimal combination of aPTT and HDR values were deemed adequate for ECLS. The best relationship between the optimal value of aPTT/HDR and AT, KTEG R-time, and aPTT was when AT was at a threshold >42% (Figure 1). The strongest correlation was observed comparing the optimal aPTT-HDR combination to aPTT. As determined by the protocol, the threshold aPTT ($p < .001$) is obtained at 61 seconds. The ROC area under curve (AUC) was 75%.

After comparing multiple variables to the probability of forming no observed thrombus in the circuit (Table 5), the strongest ROC values came with aPTT ($p < .001$) threshold of 64 seconds. The ROC curve showed an AUC of 71% (Figure 1).

Table 5 shows the relationships between aPTT and AT and whether these measures could help predict the prevention of ECC intervention. Among those compared variables, there were no significant results. The number of ECC interventions was not significantly related to aPTT or AT using ROC analysis (Table 5). Bleeding <24 mL/kg/day was significantly related to a threshold ADR equal to .10 mcg/kg/min. The AUC for this comparison was 66%.

A KTEG R-time >30 minutes was significantly associated with excessive bleeding (AUC = 75.5%) (Figure 1). Also significant was the acceptable bleeding vs. HDR, anti-Xa, AT, and ADR. ADR showed a statistically significant ROC analysis with the threshold for ADR equal to .1 mcg/kg/min.

DISCUSSION

In our study of infant-pediatric patients supported with ECLS, we compared multiple anticoagulation variables. Through this analysis, results were obtained that may help to influence future ECLS anticoagulation protocols. The results are supported by many other studies that point toward the need for further anticoagulation monitoring assays other than the "gold standard" assays that have been used for many years (4,15–17).

We obtained similar regression results as other studies. In studies done by Bembea et al.(1) and Sulkowski et al. (18) comparing ACT and anti-Xa levels, they found that the ACT was not directly correlated with Anti-Xa levels. They also cautioned the clinician to beware of this anticoagulation comparison while managing pediatric ECLS. Within our study we also found no significant relationship between these two variables (Table 4). This insignificant relationship further demonstrates the inconsistency of using ACT and anti-Xa levels. Caution should be taken assuming ACT and anti-Xa levels correlate during monitoring in the infant-pediatric ECLS patient population.

When comparing HDR with ACT and INR, an inverse relationship between these variables was observed. It is difficult to quantify the relationship between these variables and thus be able to use ACT as a measure to understand patients' anticoagulation on ECLS. Other studies have shown similar results when ACT is compared with variables such as the AT level. Baird et al. (5) reported that

Table 4. Regression matrix for all parameters.

Parameter	BDR	ADR	HDR	Transfusion	Bleeding	AA	IVR	KTEGR	Anti-Xa	AT	APTT
Day pairs	19	47	157	147	161	165	168	161	148	151	170
ACT	NS	NS	–.148**	NS	NS	–.288*	.402*	.179*	NS	NS	.451*
APTT	NS	NS	NS	–.178*	NS	–.148**	.240*	.226*	NS	NS	
AT	.479*	NS	NS	NS	–.207*	NS	–.248**	NS	.191*		
Anti-Xa	NS	NS	.440*	NS	–.163**	NS	–.159**	.325*			
KTEGR	–.392**	NS	NS	NS	–.173*	–.121**	.148*				
IVR	NS	NS	–.287*	NS	NS	–.230*					
AA	–.602**	NS	NS	NS	NS						
Bleeding	NS	NS	–.141*	.730*							
Transfusion	NS	NS	–.223*								
HDR	NS	NS									
ADR	NS										

The regression analysis matrix for all parameters daily sample pairings. Day pairs are the number of × 24 ECMO hour pairs collected; AA, kaolin + heparinase TEG alpha angle (degrees); ACT, activated clotting time (sec); ADR, Argatroban drip rate (mcg/kg/min); Anti-Xa, heparin activity (U/mL); aPTT, activated partial thromboplastin time (seconds); AT, antithrombin; BDR, Bivalirudin drip rate (mg/kg/h); Bleeding, blood loss (mL/kg/24 h); HDR, heparin drip rate (U/kg/h); KTEGR, kaolin TEG reaction time (minutes); INR, international normalization ratio for PT (partial thomboplastin time (seconds)); Negative R value denotes an inverse relationship; NS, not statistically significant; *Denotes $p < .05$; **Denotes $p < .10$.

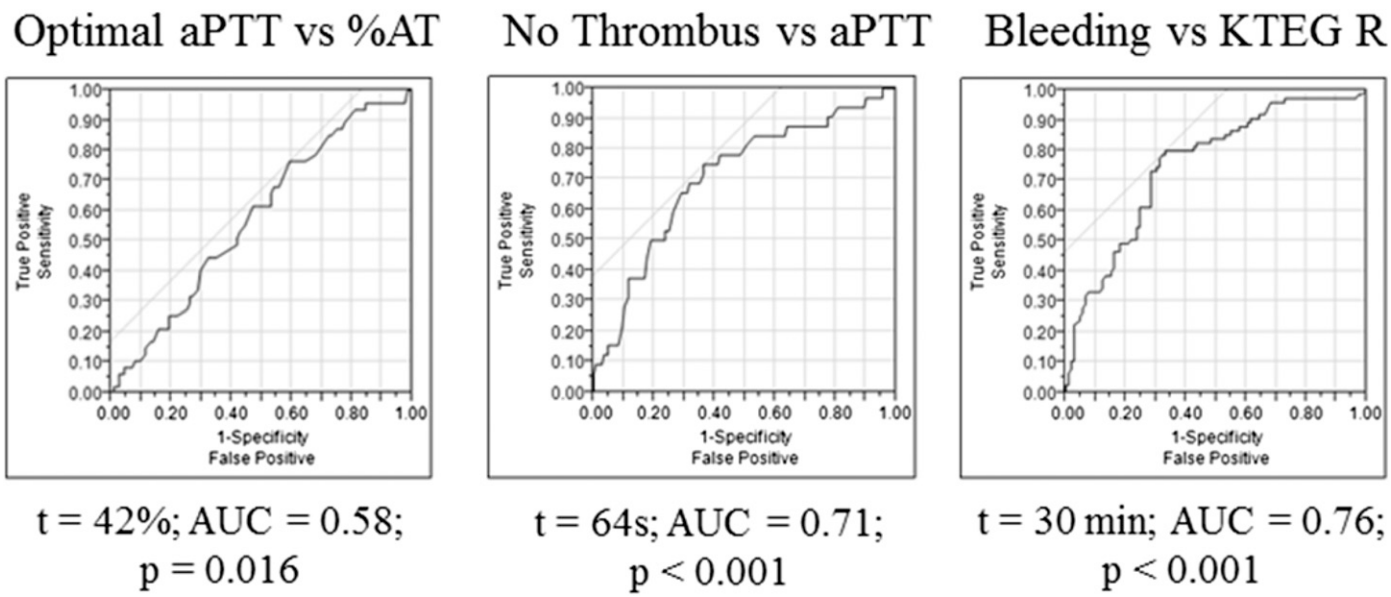

Figure 1. Receiver operating curves for optimal relationships between aPTT and HDR vs. AT, no thrombus observed in the circuit vs. aPTT, and acceptable bleeding vs. the KTEG R-time. aPTT, activated partial thromboplastin time; AT, antithrombin; AUC, area under curve; KTEG R, kaolin thromboelastograph reaction time. See Table 5 for % true and false, and positives and negatives.

using ACT to manage anticoagulation among pediatric ECLS patients may result in inadequate anticoagulation. These results and the results of other studies (15) illuminate the need for alternative anticoagulation monitoring for infant-pediatric ECLS patients.

Significant differences were found between BDR and ADR among our patients using linear regression. As reviewed, bivalirudin and argatroban are increasing in popularity for ECLS (10–12). Our results showed that ADR is not as significantly correlated as BDR in its association with AT, KTEG R-time, and AA (Table 4). BDR use has been reported for pediatric patients (10), and it also has been shown to yield a better coagulation profile, less bleeding, and less allogeneic transfusions (11) than HDR. Last, our results suggest that BDR was associated with higher AT while on ECLS. Other studies

Table 5. Receiver operating characteristics analysis.

Outcome	Parameter	Threshold	AUC	%True Pos	%True Xeg	%False Pos	%False Neg	Days (Y/N)	Chi-Sq *p*
Optimal aPTT and HDR	HDR (U/kg/h)	>15	.88	96%	80%	20%	0%	55/129	<.001
(*n* = 184 days)	aPTT (seconds)	>61	.75	98%	54%	45%	0%		<.001
	AT (%)	>42	.58	65%	36%	53%	20%		.016
	Anti-Xa (U/mL)	>.11	.64	55%	68%	26%	33%		.061
	AA (degrees)	<54	.61	71%	43%	46%	22%		.096
	KTEG R-time (minutes)	>12.8	.61	93%	29%	70%	4%		.147
No ECC thrombus	aPTT (seconds)	>64	.71	75%	63%	36%	25%	32/152	<.001
(*n* = 184 days)	HDR (U/kg/h)	>12	.68	66%	61%	38%	34%		<.001
	ACT (seconds)	>166	.64	44%	78%	15%	44%		.419
	AT (%)	>52	.61	47%	45%	46%	22%		.119
	KTEG R-time (minutes)	>60	.51	34%	78%	25%	66%		.245
No ECC intervention	aPTT (seconds)	>72	.63	55%	74%	26%	44%	165/19	.087
(*n* = 184 days)	AT (%)	>43	.59	55%	58%	42%	31%		.223
Acceptable bleeding	KTEG R-time (minutes)	<30	.76	65%	55%	27%	42%	109/56	<.001
(*n* = 185 days)	HDR (U/kg/h)	>7	.67	87%	39%	50%	21%		.023
	Anti-Xa (U/mL)	>.07	.67	53%	71%	45%	23%		.039
	AT (%)	>38	.66	74%	46%	39%	50%		<.001
	ADR (mcg/kg/min)	<.10	.61	30%	61%	14%	65%		<.001
	AA (degrees)	>42	.43	34%	91%	9%	61%		.112

Parameters are ranked based on the decreasing ROC analysis AUC for each outcome; Optimal is simultaneous aPTT >60 seconds and HDR >15 U/kg/h on q24 hours observation; Acceptable bleeding is <24 mL/kg/24 h; ACT, activated clotting time; ADR, Argatroban dose rate; Anti-Xa, heparin level; aPTT, activated Partial Thromboplastin Time; HDR, heparin dose rate; AA, kaolin + heparinase TEG angle; KTEG R-time, kaolin TEG reaction time; AUC, area under the curve.

have also shown less supplement of AT with BDR compared with HDR.

Many medicine-based studies have used ROC analysis to compare and contrast multiple classifiers (19). In our study, we used ROC analysis as a tool to compare our patients' anticoagulation variables. From our ROC analysis, we obtained multiple significant relationships among infant-pediatric ECLS anticoagulation variables (Table 5).

Our goals for this study were to determine the optimal combination of aPTT (>60 seconds) and HDR (>15 U/kg/h) and discover the AT needed to obtain the optimal aPTT and HDR combination. Through ROC analysis, it was determined that an AT threshold >42% is recommended to obtain the optimal relationship between aPTT and HDR. The AT threshold came with an AUC of .58 and a chi-square *p*-value of .016. From these results, it is recommended that the HDR be kept above 15 U/kg/h and AT be maintained above 42% to obtain an aPTT >60 seconds. Niebler et al. (20) discussed a significant outcome from maintaining the aPTT in a therapeutic range by maintaining the HDR and AT. They found that the patient showed no signs of excessive bleeding, blood product administration, or clots in the circuit with AT supplement. This suggested to them that maintaining the optimal aPTT, HDR, and AT is a proper anticoagulation strategy for ECLS.

After comparison of multiple variables to the incidence of no observed thrombus in the circuit, it was found that the most significant results occurred with aPTT (threshold (t) >64 seconds; AUC = .71; $p < .001$) and HDR (t >12 U/kg/h; AUC = .68; $p < .001$). By maintaining the aPTT above 64 seconds and the HDR above 12 U/kg/h, a significantly lower rate of circuit thrombi on the arterial side (post-oxygenator to arterial cannula) may be expected. Controlling the combination of aPTT, HDR, and AT values may reduce the number of thrombi in the circuit.

Use of other anticoagulation tests, such as KTEG, for ECLS patients has been growing (16,21,22). This is likely driven by the inconsistencies found with the traditional ACT test. When comparing acceptable bleeding (<24 mL/kg/day) to KTEG R-time, we observed that maintaining the KTEG R-time below 30 minutes related to a significant decrease in the amount of bleeding. This analysis came with an AUC of .76 ($p < .001$). We strive to use the KTEG R-time to indicate proper anticoagulation without significantly increasing the amount of bleeding in infant-pediatric ECLS patients.

Limitations

This retrospective chart review had multiple limitations. This review was a nonrandomized observational study limited by a small patient sample size, available patient parameters, and number of observed days on ECLS. Future studies will be beneficial to further our understanding of anticoagulation during infant-pediatric ECLS.

CONCLUSION

Based on our infant-pediatric ECLS patients' data, we were unable to find a definitive correlation between the combination of aPTT >60 seconds, HDR >15 U/kg/h, and AT. However, ROC analysis did suggest that to maintain an aPTT above 60 seconds, you must maintain an AT level of >42%. Our study also found multiple other correlations that may help develop future standardized anticoagulation protocols. These correlations include use of different anticoagulation tests (using high correlates) to predict anticoagulation, keeping the ADR below .10 mcg/kg/min may help reduce bleeding, maintaining aPTT above 64 seconds to prevent thrombus, sustaining HDR (when bleeding is controlled) above 12 U/kg/h to prevent thrombus, and keeping KTEG R-time below 30 minutes to decrease bleeding. Further controlled studies are needed to determine optimal anticoagulation management parameters and be able to write standardized anticoagulation protocols for infant-pediatric ECLS patients.

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