Clinical Impact of an Anticoagulation Protocol Revision for Extracorporeal Membrane Oxygenation (ECMO) Patients

Adele Venable, PharmD*, Alice Beane, PharmD, BCPS, BCCCP
Norton Healthcare Department of Pharmacy; Louisville, KY

BACKGROUND

- ECMO is used for managing respiratory and/or cardiac failure
- Anticoagulation is vital to maintain a clot-free oxygenator circuit
- The Extracorporeal Life Support Organization (ELSO) anticoagulation guidelines suggest heparin with the following recommendations:
  - Bolus: 50-100 units/kg at time of cannulation
  - Continuous infusion: 7.5-20 units/kg/hr
  - Monitoring: institution-specific approach
- Many anticoagulation laboratory assessments for monitoring heparin exist to help reduce the incidence of hemorrhagic and thrombotic complications
- Activated clotting time (ACT) and anti-Xa assays are the two most commonly utilized tests for ECMO anticoagulation protocols across institutions

Anti-Xa assays have shown less variability and better correlation with heparin concentration compared to ACT, leading Norton Healthcare to undergo the following protocol revision on 11/17/2020

	Protocol	Initial dose	Monitor	Goal range
	ACT Heparin	7 units/kg/hr	ACT	180-220 seconds, or per MD order
NEW	Anti-Xa Heparin Standard	15 units/kg/hr	Anti-Xa	0.3-0.7 IU/mL
NEW	Anti-Xa Heparin Low-dose	10 units/kg/hr	Anti-Xa	0.3-0.5 IU/mL

CLINICAL QUESTION

Does a higher initial heparin infusion dose and utilizing anti-Xa level monitoring affect bleeding complications or thrombotic complications, as compared to a lower initial heparin infusion dose and ACT monitoring?

OUTCOMES

Primary Outcomes

Efficacy	Thrombotic complications	• Clot requiring circuit change • DVT confirmed by doppler • PE confirmed by CT
Safety	Hemorrhagic complications	• Composite of major and minor bleeding, identified by use of refractory major, major, or minor hemorrhagic protocol

Secondary Outcomes

Efficacy	Time to target goal range	• Minutes from initiation of infusion to first lab result in goal range
Efficacy	Time in target goal range	• Minutes spent in goal range for first seven days
Operational	Median heparin dose in goal range	• Median dose in units/kg while in goal range
Operational	Protocol adherence	• Number of times protocol appropriately followed within 2 hours of resulting lab
Safety	Mortality	• Death during hospitalization

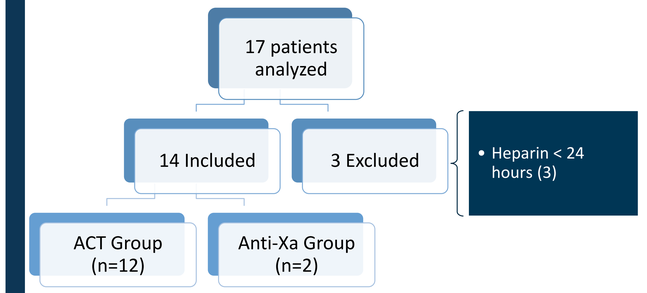
METHODS

Retrospective, quasi-experimental study

ACT group	Anti-Xa group
Jan. 1, 2018 – Nov. 16, 2020	Nov. 17, 2020 – Feb. 12, 2021

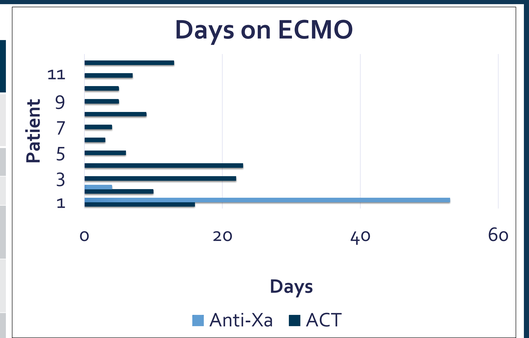
Inclusion	Exclusion
▪ Adults ≥18 years ▪ ECMO initiation & anticoagulation with heparin	▪ Prisoners ▪ On heparin < 24 hours

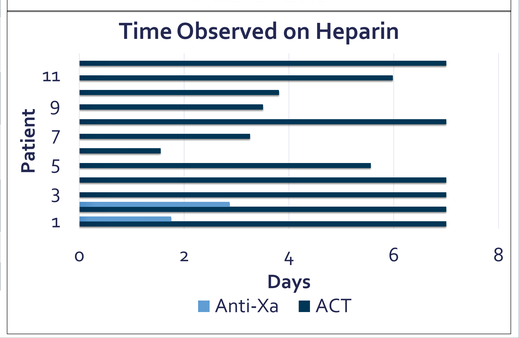
STUDY ALLOCATION



STUDY CHARACTERISTICS

Baseline Characteristics	ACT (n=12)	Anti-Xa (n=2)
Duration of ECMO, days median (IQR)	8 (5-13.8)	28.5 (16.3-40.8)
Age, yrs median (IQR)	39 (27-49.5)	59 (59-59)
Male gender, no. (%)	10 (83)	2 (100)
Weight, kg median (IQR)	122.1 (98.5-148.2)	95.85 (87.5-104.2)
Type of ECMO, VV no. (%)	8 (66.7)	1 (50)
Baseline labs		
Hemoglobin, g/dL median (IQR)	11 (9.7-12.5)	12.6 (11.9-13.4)
Hematocrit, % median (IQR)	35.5 (31.8-39.9)	40.85 (38.9-42.8)
Platelet, 10*3/uL median (IQR)	229.5 (108.5-299)	171.5 (143.3-199.8)
Fibrinogen, mg/dL median (IQR)	336 (228.8-706)	367 (292-442)
INR median (IQR)	1.25 (1.1-1.5)	1.1 (1.1-1.2)
PTT, sec median (IQR)	39.75 (39.3-98.7)	88.65 (85.2-92.1)





RESULTS

Primary Outcomes	ACT (n=12)	Anti-Xa (n=2)
Thrombotic Complications		
Circuit Change, DVT, PE	0	0
Hemorrhagic Complications		
Minor, Major, Refractory Hemorrhagic Protocol	0	0

Secondary Outcome	ACT (n=12)	Anti-Xa (n=2)
Time to Target Goal Range, minutes, median (IQR)	256.5 (57-973.5)	511.5 (349.3-673.8)
Time in Goal Range, percent, median (IQR)	51.8 (40.5-66.4)	27.2 (24.3-30.1)
Median Heparin Dose in Goal Range, units/kg/hr, median (IQR)	12.8 (9.8-16.5)	5.5 (4.9-5.9)
Adherence, percent, median (IQR)	84.6 (78.6-86.8)	71.7 (62.8-80.6)
Mortality, no. (%)	5 (41.6)	2 (100)

STUDY CRITIQUE

Strengths

- Evaluation of most widely used anticoagulant
- Collection of bolus dose to account for confounding
- Standardized collection of thrombotic complications

Limitations

- Time period of Anti-Xa group
- Small sample size
- Study definition for hemorrhagic and thrombotic complications

DISCUSSION

Primary Outcomes	• Given the low incidence for thrombotic complications, it was not unexpected this small study size did not experience any • Study definitions for primary outcomes were not all encompassing
Secondary Outcomes	• Median heparin dose while in goal range for ACT group supports increased initial heparin dose seen in the new protocol • Unable to draw conclusions regarding time to and time in target goal range due to sample size of the Anti-Xa group

NEXT STEPS

COLLABORATE with ECMO team to share data → IDENTIFY barriers for lack of hemorrhagic order set use → CONTINUE ongoing data collection in the anti-Xa group

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DISCLOSURES

Dr. Venable and the other investigators have no actual or potential conflicts of interest in relation to this presentation.