Boston Children's Hospital
Heart Center

Thromboelastography Testing Provides Effective Risk Stratification for Bleeding in Patients on Extracorporeal Membrane Oxygenation Support

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No Disclosures.

Background

- Extracorporeal Membrane Oxygenation (ECMO) is life-saving in children with cardiac failure refractory to conventional heart failure therapies

- However, anticoagulation therapy is required to prevent thrombosis on the ECMO circuit

- Bleeding occurs in 39% of all and 49% of children with cardiac disease supported with ECMO (surgical site 32%, cerebral 9%).

Werho et al. PCCMJ 2015.

Background

- Anticoagulation management practices from 2011 survey results from 121 ELSO centers indicate:
  - Use of activated clotting time is preferred by 97%;
  - ATIII by 82% (51% routinely)
  - Anti-factor Xa (UFH) by 65% (40% routinely)
  - 43% utilize thromboelastography (18% routinely)

- However, laboratory methods for assessment of the coagulation system such as activated partial thromboplastin time (aPTT) and UFH in children are not highly predictive of bleeding.

Bembea et al. PCCR 2013; Kitchens CS. J Thromb Haemost. 2005; 3(12):2607-11.

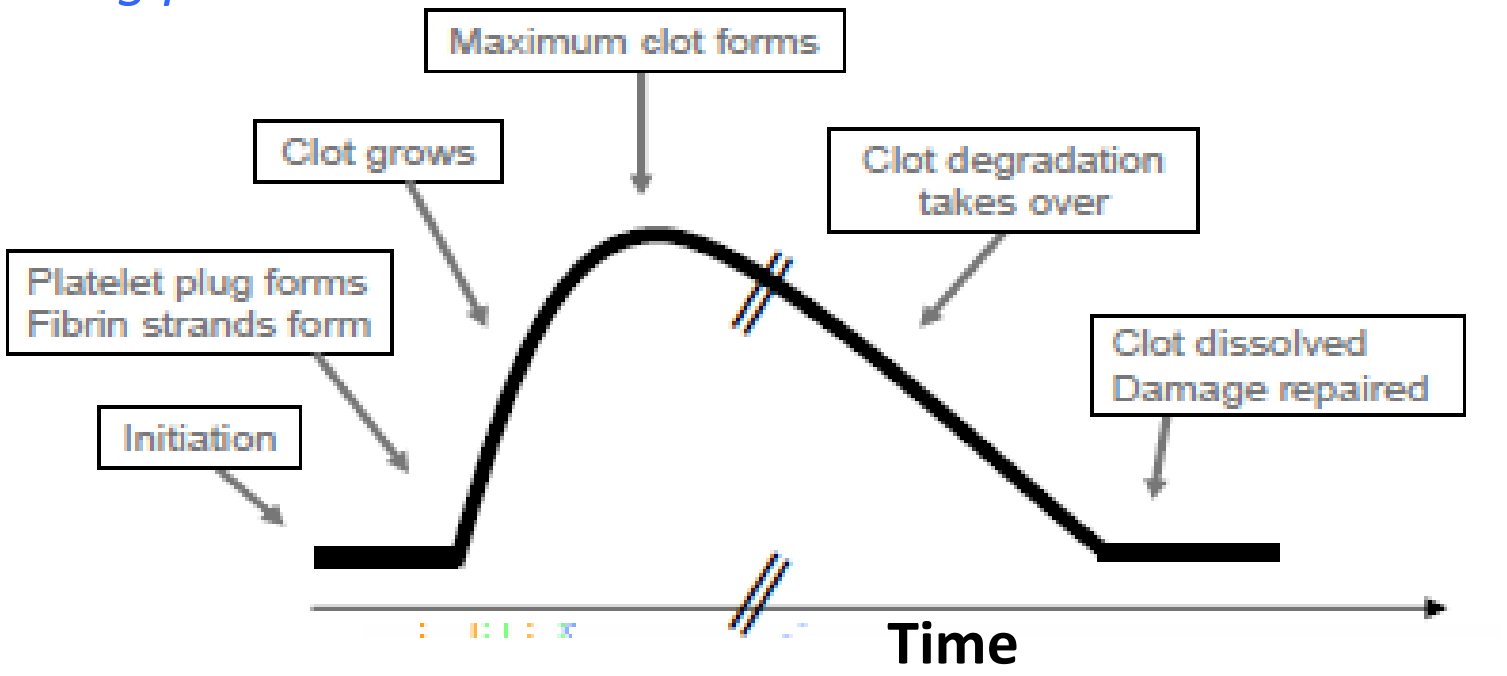
Background

- There is now increased interest in understanding the value of TEG in monitoring anticoagulation in children
- TEG is frequently used in adults undergoing cardiac surgery and VAD placement
- To date there are limited data on the association between TEG and clinical outcomes in children on ECMO.

The Clot Process

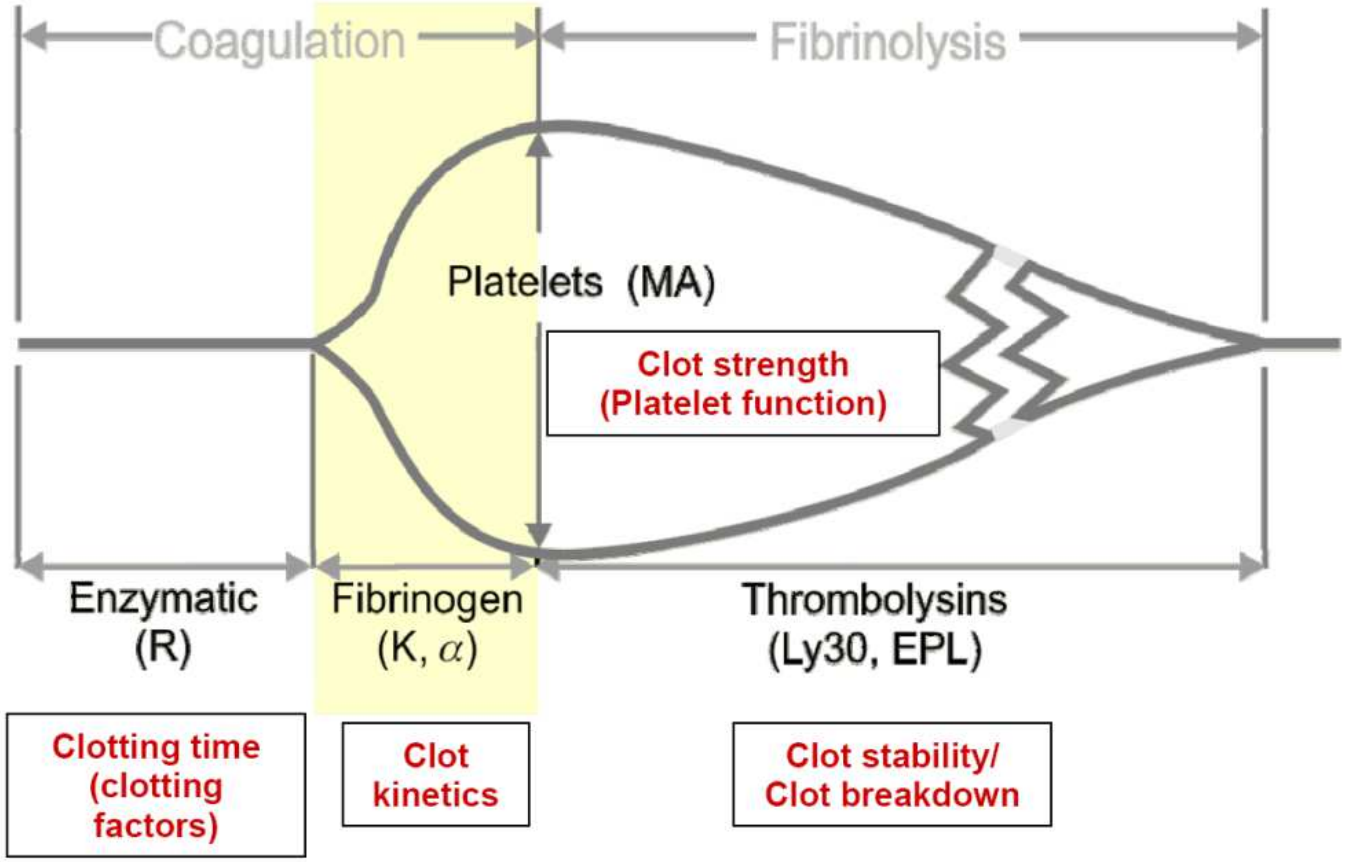
- Traditional hemostasis tests measure pieces of this process

- TEG generates parameters related to each phase of the clotting process



Ref: Omert L, TEG Overview, Haemonetics 2009.

What Does TEG® Report?



TEG Panel

	Parameter	Description
R	Reaction time, min	Time to initial clot formation
K	Clot time, min	Time to achieve a certain clot strength
Angle	Rate of clot formation, degrees	Speed at which fibrin build-up occurs
MA	Maximum amplitude, mm	Related to strength of the fibrin clot
G	Clot strength, dynes/sec	Strength of the fibrin clot
Lysis 30	Clot lysis in 30 min, %	%decrease in amplitude 30 min after MA

Tahkur and Ahmed, Int J of Perinatal Ultrasound & Appl Tech. 2013; 1:25-29.

Aims

- To describe TEG findings in pediatric patients on ECMO support
- To construct a risk stratification scheme for ECMO patients to identify those at lowest and highest risk of bleeding.

Hypothesis

We hypothesize that the physical properties of clot formation by TEG may provide improved risk stratification for bleeding in children on ECMO support.

Methods

- Single-center clinical data collection, May 2015 to Jan 2017; retrospective analysis.
- Heparinase TEG performed in 40 children on whom ECMO was initiated for severe heart failure
- Whole blood samples were collected 6-12 hrs post-ECMO initiation with daily collection on support up to 10 days. TEG was performed within 1 hour of collection.
- Traditional tests (non-TEG) such as aPTT, UFH and fibrinogen were performed concomitantly on plasma

Bleeding Definition

Bleeding was defined as meeting at least one of the following:

- Chest tube output 10 cc/kg/hr of blood associated with > 4.0 point decrease in hematocrit AND requirement for blood product transfusion of >20 ml/kg/day

- Bleeding requiring administration of Factor VIIa

- Any re-exploration for bleeding

Statistical Methods

- Generalized additive modeling to assess nonlinear relationships between continuous predictors and bleeding (bleed-day yes/no)

- Associations between predictors vs. bleeding were estimated using linear and logistic regression for correlated observations (random effects models)

- Classification and Regression Tree (CART) analysis was used to identify low vs. high risk subgroups.

Results

- The cohort (N=40) had median age 0.5 years, IQR 0.1 to 2.4, range 1 d to 15.4 years

- Average of 4 days per patient

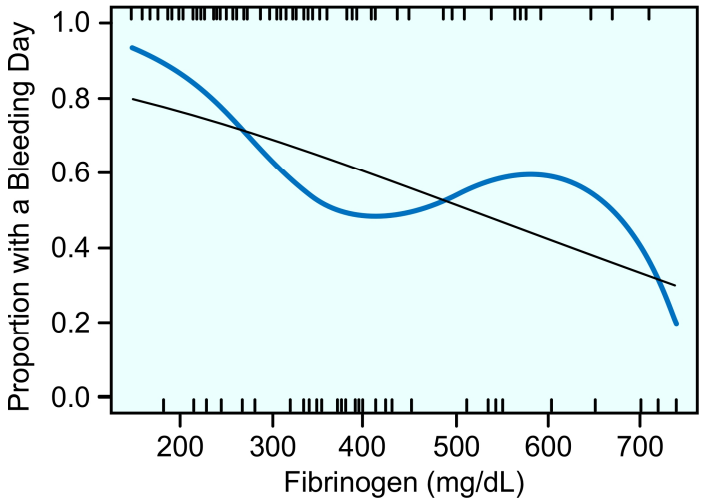
- Bleeding occurred:
  - on 72 of 159 days (45%)
  - in 25 patients (62%)

Traditional Parameters vs. Bleeding

	Median Value		
Parameter	**Bleeding**	**No Bleeding**	**P-value***
aPTT, sec	66	79	.55
UFH, IU/mL	0.3	0.3	.84
Fibrinogen, mg/dL	324	395	.01
Anti-thrombin III, %	87	70	.39

*p-value from mixed effects model

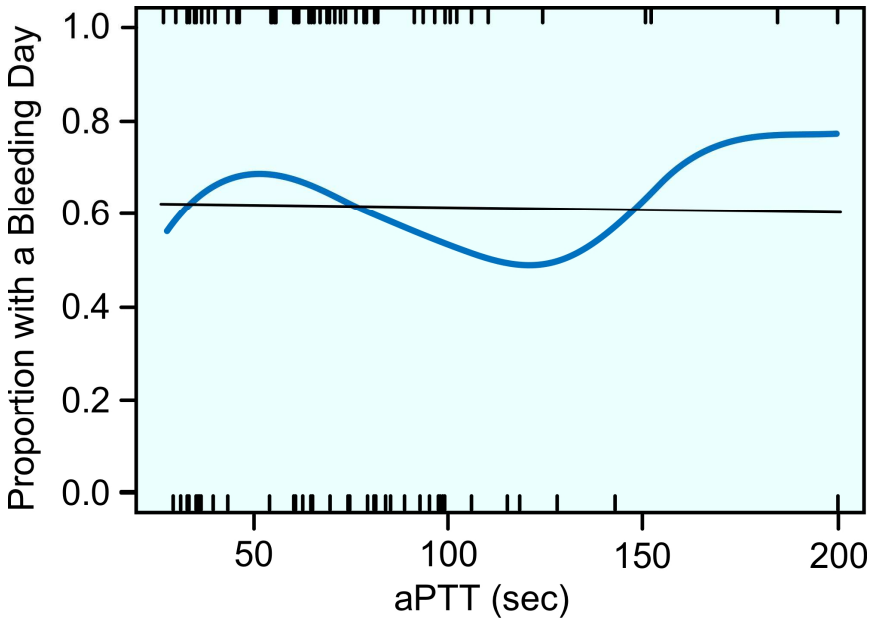
Odds ratio [OR] 0.68 per 100 mg/dL, 95% CI 0.45-1.05



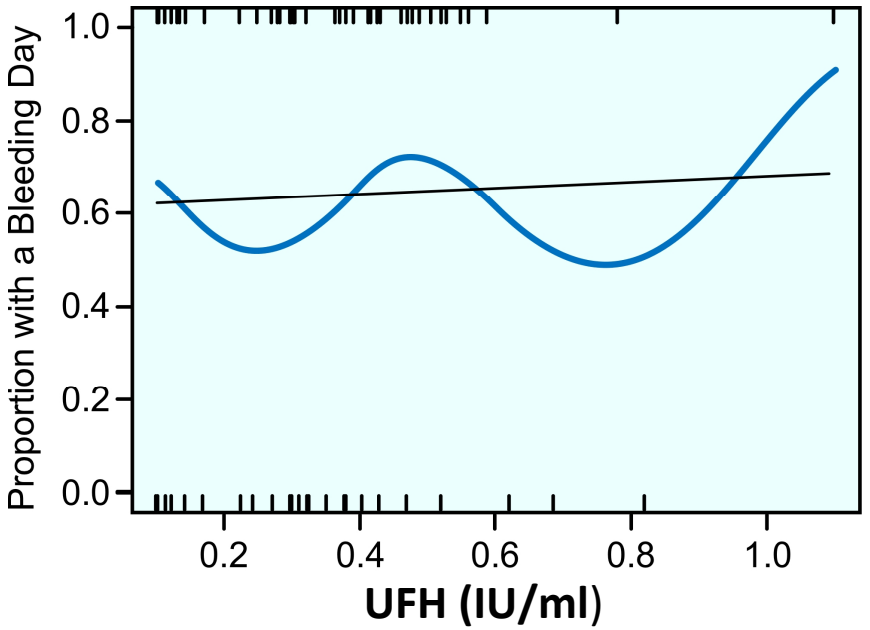
aPTT and UFH vs. Bleeding

No association was found between aPTT or UFH with bleeding

Bleeding vs. No Bleeding
77±44 78±36 sec



Bleeding vs. No Bleeding
0.31±0.20 0.30±0.19 IU/ml

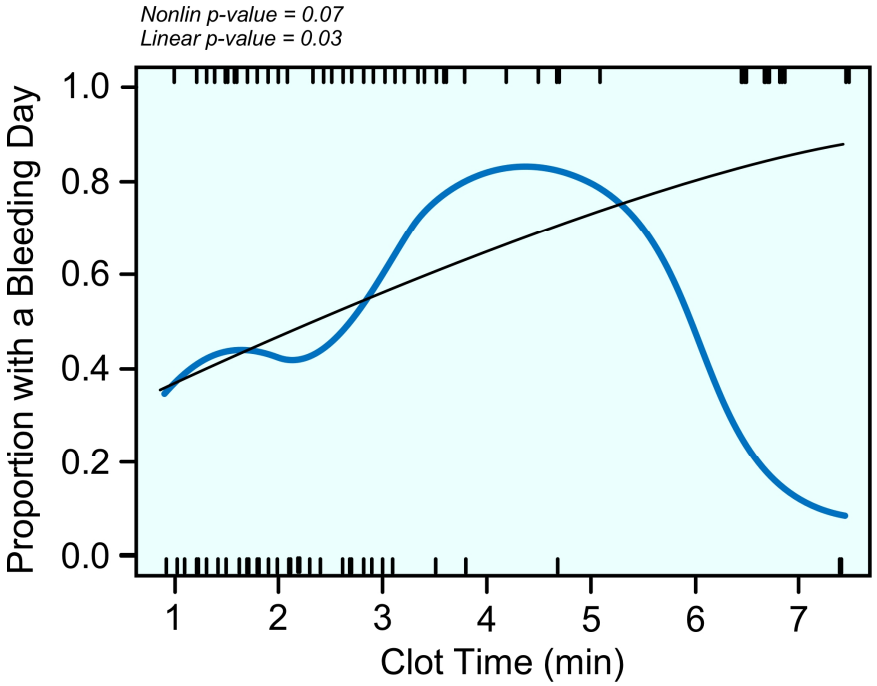


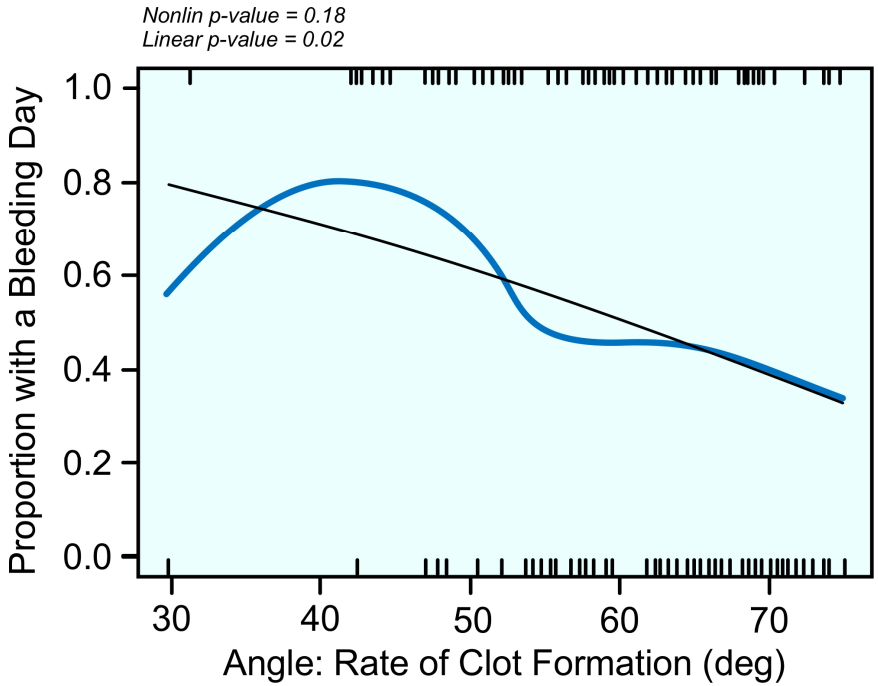
TEG vs. Bleeding

	Median Value		
TEG Parameter	**Bleeding**	**No Bleeding**	**P-value***
No. of days	72	87	
R, min	9.8	9.2	.73
K, min	2.1	1.8	.09
Angle, degrees	61.4	64.5	.10
Max amplitude, mm	57.5	61.3	.04
G, dynes/sec	6.8	7.9	.09
Clot lysis 30 min, %	0.0	0.4	.09

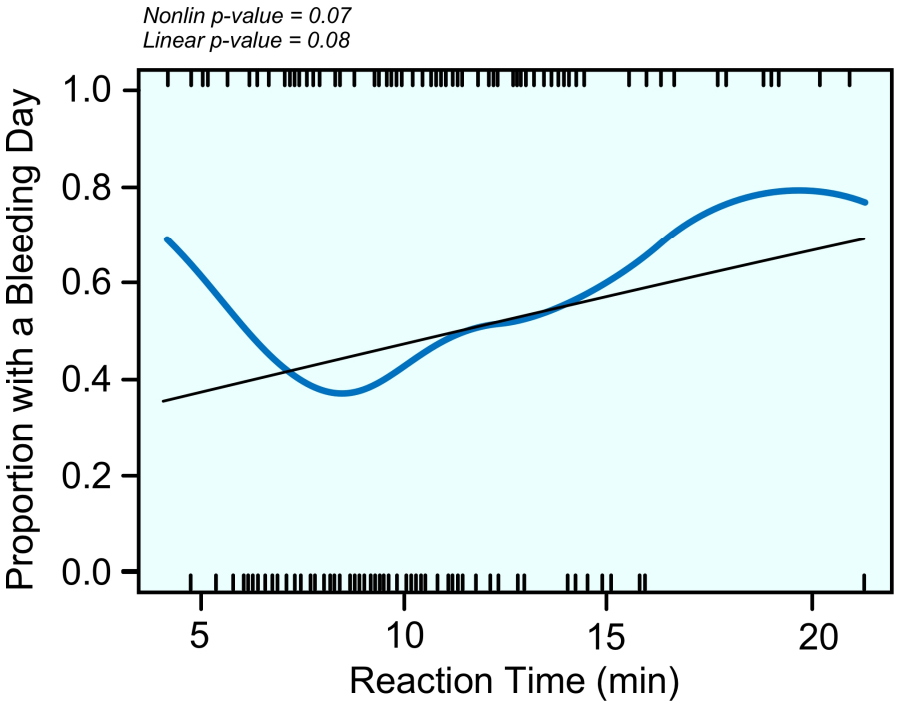
*p-value from mixed effects model

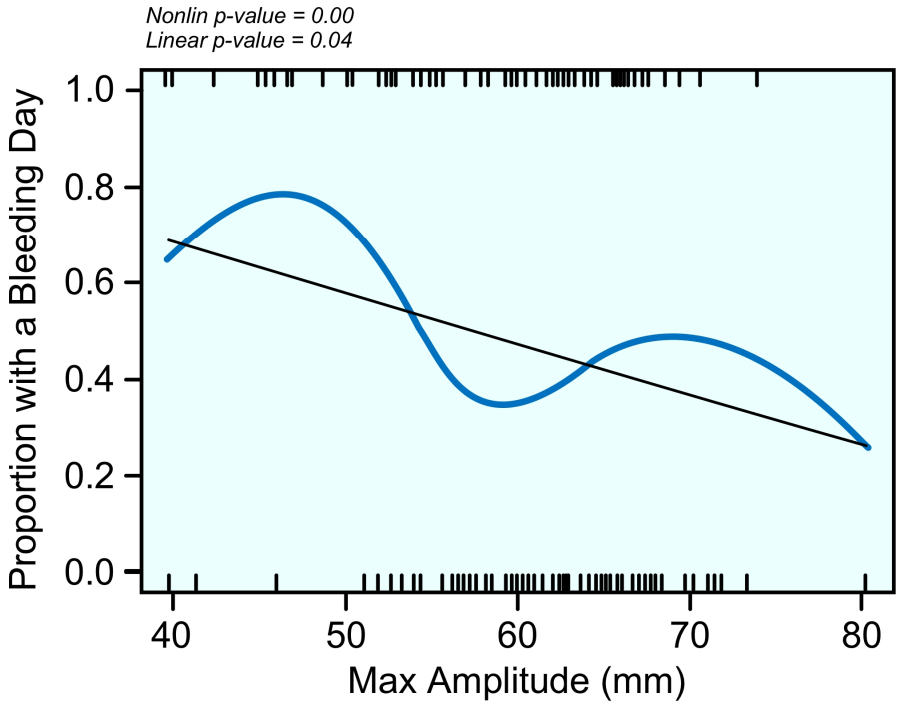
TEG vs. Bleeding





TEG vs. Bleeding





Maximum Amplitude

- The single strongest predictor of bleeding was a maximum amplitude (MA) of <55.4 mm:

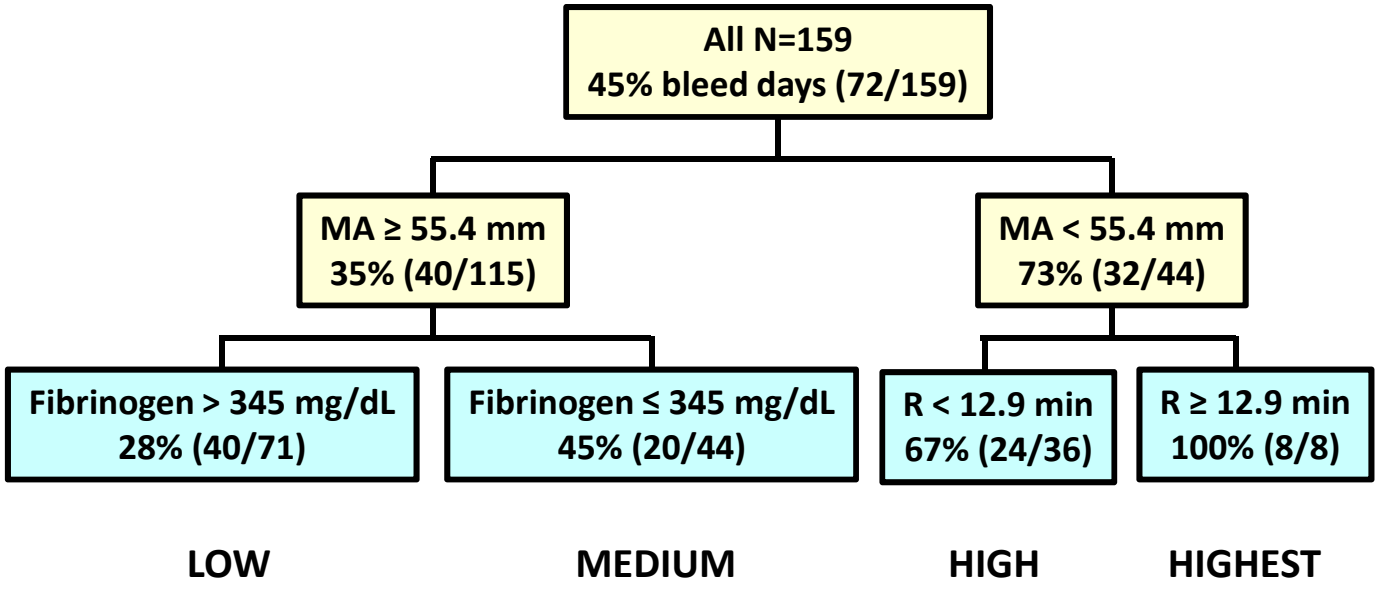
  Odds ratio 3.28, 95% CI 1.63-6.60, p<.001

- Bleeding occurred on **73% vs. 35%** of ECMO days for MA<55.4 vs. ≥55.4 mm

- MA was < 55.4 mm on **44% of bleed days vs.14% of non-bleed days**

CART

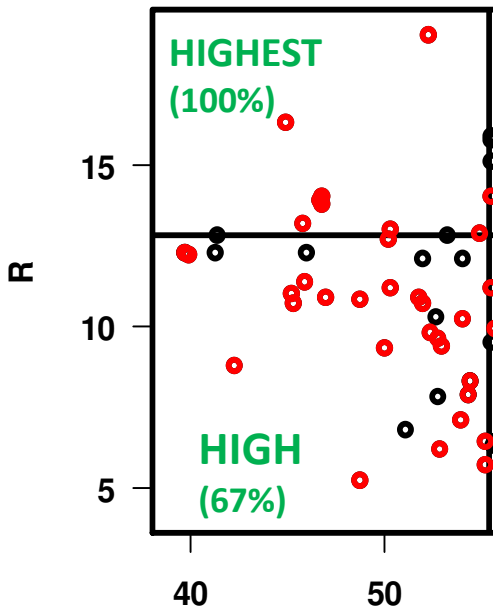
159 days on support in 40 children



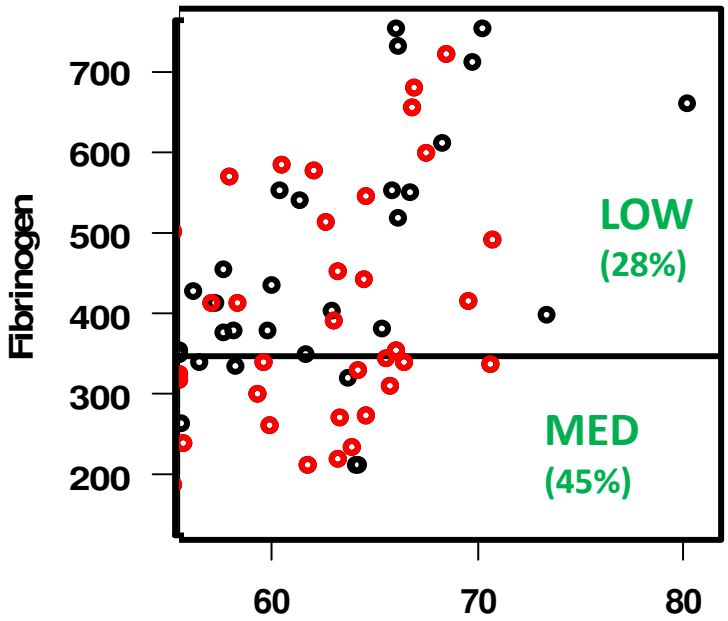
c-statistic 0.67, model p=0.002

MA=maximum amplitude

Bleeding Risk Subgroups



LOW MA
(mm)



HIGH MA
(mm)

Limitations

- The relatively small sample size of this cohort limits our ability to precisely identify the specific cut points that define high risk

- The goal of this study was to identify the predictive power of anticoagulation parameters; however, an additional portion of the variation in bleeding may be explained by accounting for other clinical factors, such as degree of organ failure at time of ECMO initiation and whether ECMO was initiated directly from CPB.

Conclusions

- TEG MA and reaction time combined with fibrinogen concentration can jointly identify subgroups of children who are at low vs. high risk of bleeding while on ECMO support.

- Further research with larger samples is necessary to confirm the specific thresholds identified for risk stratification using TEG.

Thank you