Thromboelastography (TEG) Based Reversal of Coagulopathy and the TXA Controversy

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What We Know...

- Trauma is the leading cause of death and morbidity for children in US
- Trauma Induced Coagulopathy (TIC)
  - Dysfunction of hemostatic and inflammatory systems in response to injury
  - Defined as INR > 1.3
  - Induced by hemorrhage
  - Associated with increased morbidity and mortality

Pediatric Massive Transfusion

- Ratio of blood products that simulates the components of whole blood
- Designed to deliver blood product to the bedside as rapidly as possible with minimal product waste

Cryoprecipitate
Consider every other round of blood product or fibrinogen < 150-200.
- dose 5ml/kg

Massive resuscitation protocols are great...but what about this concern for coagulopathy?

Coagulation Studies

- Bleeding time
- Activated Partial Thromboplastin Time (aPTT)
- Prothrombin Time (PT)
- Thrombin Time

Coagulation Cascade

Thromboelastography (TEG)

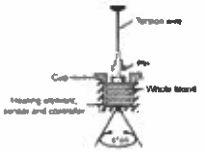
Trauma Induced Coagulopathy

- Traditionally defined as elevated INR but inadequate as treatment target
- Viscoelastic hemostatic assays (TEG and ROTEM)
  - Monitors all phases of coagulation
  - Depicts real-time component activity rather than static values
  - Also provides information if hypercoagulability
  - Elevated INR DOES NOT NECESSARILY INDICATE a true bleeding coagulopathy

TEG-Directed Resuscitation[1]

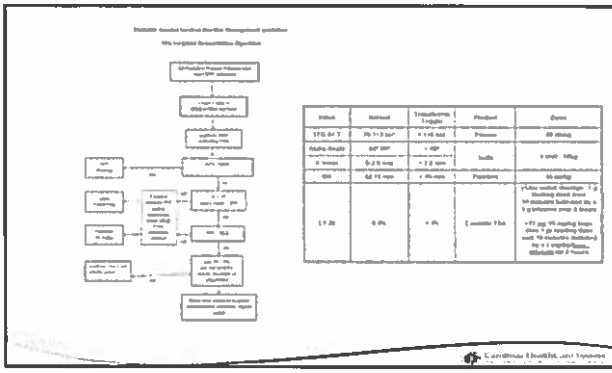
- Improved survival compared to MTP guided by conventional tests of coagulation cascade
- Better than traditional ratio-driven algorithms
- Utilize less plasma and platelet transfusions during resuscitation process
- When is TEG most useful?
  - Admission, OR, or ICU

What is a TEG?

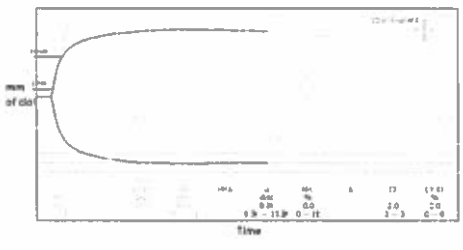


Whole picture of coagulation cascade

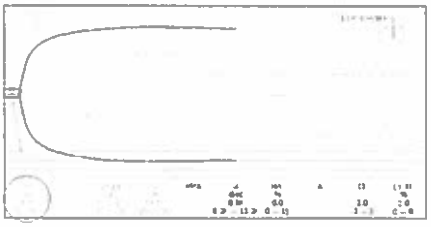
- Clot Initiation
- Clot Kinetics
- Clot Strength
- Clot lysis



Normal TEG Tracing



Clot time (R)



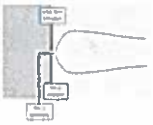
Clot Time Irregularities

Long Clot Time (R) > 8min

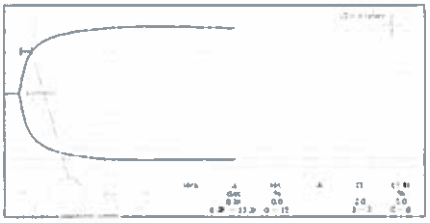
- Possible etiologies
  - Factor deficiency/dysfunction
  - Residual heparin
- Common treatments
  - FFP
  - Prothrombin

Short Clot Time (R) < 4min

- Possible etiologies
  - Enzymatic hypercoagulability
- Common treatments
  - Anticoagulant



Clot Kinetics



Clot formation time (K)

- Time from 2mm to 20mm clot to form

Alpha Angle (α) Value used most often

- Angle of line tangent to curve from 2mm to 20mm

Surrogate to assess rate and efficacy of clotting system to generate thrombin and conversion of fibrinogen to fibrin

Clot Kinetic Irregularities

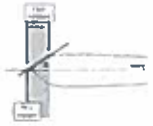
Prolonged Kinetics
K>4min; α<47°

Possible etiologies

- Low fibrinogen levels or function
- Insufficient retainment of thrombin generation
- Platelet dysfunction

Common treatments

- FFP
- Cryoprecipitate



Shortened Kinetics
K<1min; α>74°

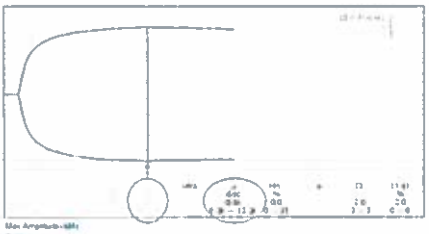
Possible etiologies

- Platelet hypercoagulability
- Fast rate of thrombin generation

Common treatments

- None

Clot Strength



Max Amplitude (MA)

- Max amplitude of clot excursion
- Clot strength = 80% platelets + 20% fibrinogen

Clot Elasticity (EQ)

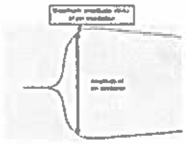
- Calculated from MA: $G = \frac{5000 \times A}{100 - A}$

Clot Strength Irregularities

High MA

Possible etiologies
- Platelet hypercoagulability

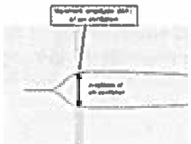
Common treatments
- Antiplatelet agents



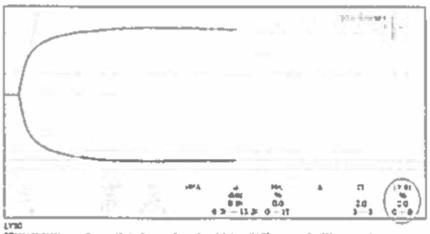
Low MA

Possible etiologies
- Poor platelet function
- Low platelet count
- Low fibrinogen levels or function

Common treatments
- Platelet transfusion



Clot Lysis



LY30

Estimated percent lysis value (EPL)

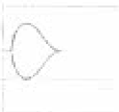
Coagulation Index (CI)

Fibrinolysis

Primary Fibrinolysis

LY30 >7.5% (or EPL >15%) with CI ≤1.0.

- Possible etiologies
  - High levels of tPA
- Common treatments
  - Antifibrinolytic agent



Secondary Fibrinolysis

LY30 >7.5% (or EPL >15%) with CI >3.0.

- Possible etiologies
  - Microvascular hypercoagulability (i.e. DIC)
- Common treatments
  - Anticoagulant

HERE COMES THE CONTROVERSY!

Tranexamic Acid (TXA)

- Lysine analog thought to bind plasmin and inhibit fibrinolysis but mechanism not fully known
- Administration within 3 hours of injury as bolus followed by drip infusion

DOSING

≥ 12 Years of Age
- Loading Dose: 1g in NS over 10 minutes
- Infusion: 1g in NS infused over 8 hours

Birth - 11Years of Age
- Loading Dose: 15 mg/kg (Max 1g) in NS over 10 minutes
- Infusion: 2 mg/kg/hour (Max total over 8 hours of 1g) in NS for 8 hours

Tranexamic Acid (TXA)

- Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage 2 Study (CRASH II) – Adult Patients
  - Small survival benefit in patients who received TXA within 3 hours of injury
- Pediatric Trauma and Tranexamic Acid (PED-TRAX)
  - Survival benefit for empiric TXA in children
  - Large percentage of penetrating and blast injuries
  - Does not necessarily mirror injuries in civilian population

Hyperfibrinolysis vs. Shutdown

- Fibrinolysis – physiologic process of clot breakdown required for wound healing and remodeling
- Excessive fibrinolysis yields increased clot breakdown and can promote bleeding
  - Treated with TXA administration
- But deficiency of fibrinolysis (shutdown) may promote thrombotic complications of DVT
- Patients in hemorrhagic shock requiring massive transfusion most often in fibrinolysis shutdown at time of admission

Why So Much Controversy?

- Mortality risk increased by odds ratio of 1.6 for shutdown and 3.3 for hyperfibrinolysis in adults[2]
  - Odds ratio of 6.2 in pediatric patients![3]
- Recent findings of increased mortality if TXA initiated > 3 hours after injury or no benefit from TXA[4,5]
- Hyperfibrinolysis is rare in children, especially with TBI and blunt injury, and appears to correct with hemostatic resuscitation[6]

So...What's the Verdict?

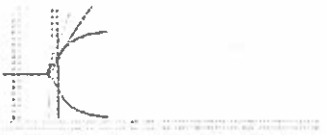
- **In general, empiric administration of TXA in children remains controversial with no clear consensus**
- **However, many support TEG-directed TXA administration according to hemorrhage and hyperfibrinolysis as indicated by LY30 value**

Quick Review

Parameter	Symbol	Definition
Clotting Time	R	Time from start to 2mm of clot amplitude (initial fibrin formation)
Clot Kinetics	K	Speed to reach 20mm clot amplitude (clot kinetics)
	α Angle	Measure of rapidity of fibrin build up and cross linking (fibrinogen level)
Clot Strength	MA	Direct function of max dynamic properties of fibrin and platelet bonding (Max platelet function)
	G	Conversion of MA to dynes/cm²
Coagulation Index	CI	Global hemostatic index
Clot Stability	LY30	Rate of amplitude reduction 30 min after MA
	EPL	Estimates % lysis on amplitude reduction after MA

Example 1

Value	Normal Range
R	4 – 8 min
K	1 – 4 min
α angle	47° – 74°
MA	55 – 73 mm
G	6 GH – 13 GH
EPL	0 – 15
LY30	0 – 8%



R413 Delayed clot formation, suspect heparin or factor deficiency
K=4
MA= 55
Angle= 54.5

Example 2

Value	Normal Range
R	4 – 8 min
K	1 – 4 min
α angle	47° – 74°
MA	50 – 70 mm
G	6.0K – 13.2K
EPL	0 – 15
LY30	0 – 8%

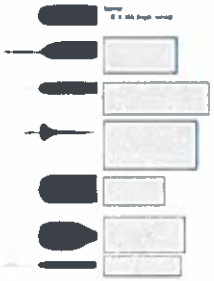
R=8.5
K=2
MAx 79.5 Hypercoagulable state
Angle= 78

Example 3

Value	Normal Range
R	4 – 8 min
K	1 – 4 min
α angle	47° – 74°
MA	50 – 70 mm
G	6.0K – 13.2K
EPL	0 – 15
LY30	0 – 8%

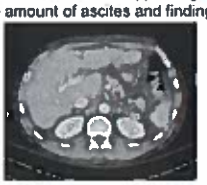
R=4.8
K=25.5 Low fibrinogen/insufficient thrombin. Suspect platelet dysfunction, thrombocytopenia.
MAx 55
Angle= 34.9

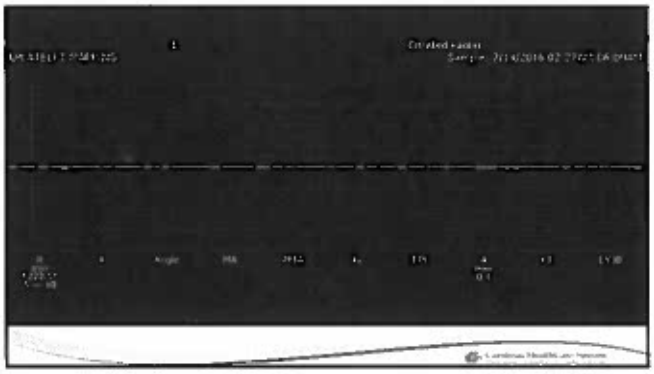
More Examples

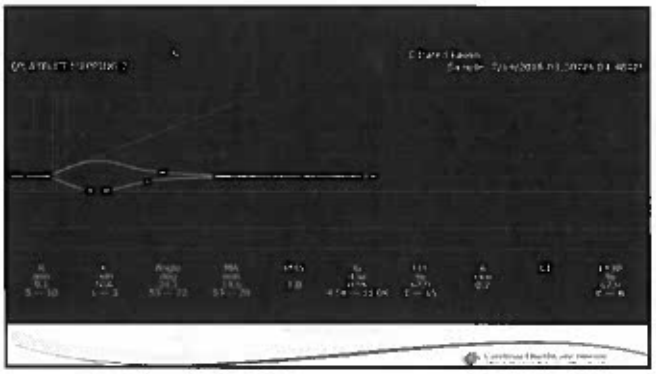


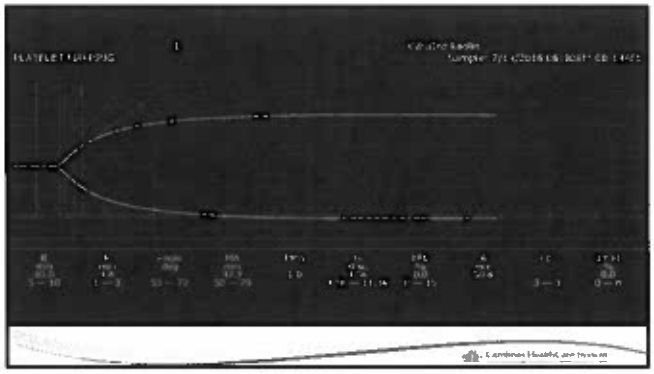
Case Study

- 61 year-old gentleman with hepatitis C, pulmonary stenosis, and HTN presents after 20 foot fall from ladder
- Left femur fracture
- CT Abdomen: Cirrhotic appearing liver. Recannulized periumbilical vein. Trace amount of ascites and findings of portal HTN









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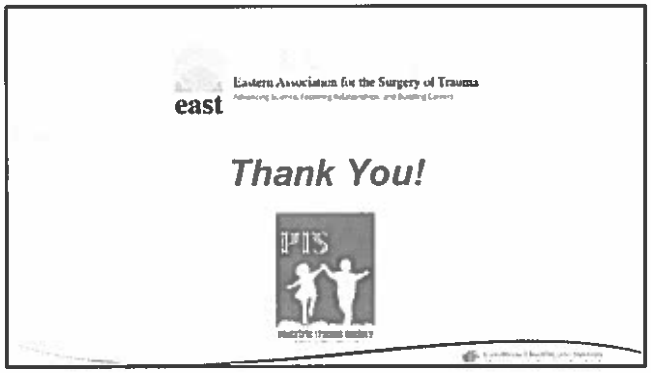
east
Eastern Association for the Surgery of Trauma
Thank You!
PTS