TEG: The ABCs of Implementing Thromboelastography in a Trauma Center

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Neuro/Critical Care CNS
Mission Hospital
Learning Objectives

- Implement TEG into a Trauma Center
- Describe the normal/abnormal dynamic clotting parameters of Thromboelastography (TEG) and propose treatment using an algorithm
- Strategize treatment options involving actual cases of hemorrhage
Disclosure Statement

- Bader
  - Board of Directors: Secretary
    - Neurocritical Care Society
  - Honorarium
    - Bard
    - Integra
  - Medical Advisory Board
    - Brain Trauma Foundation and Neuroptics
  - Scientific Advisory Board
    - Cerebrotech
  - Stock options
    - Neuoptics and Cerebrotech
Hemorrhage States

- Trauma
  - Traumatic Brain Injury
- Intracranial Hemorrhage
  - ICH
  - SAH
- GI Bleeding
- Liver disease/disorders
- OB Hemorrhage
- Ruptured vessels
Trauma Injury, Hemorrhage, & TBI

• Trauma/Injury is the 2\textsuperscript{nd} leading cause of death globally
  – 40\% of mortality associated with injury due to uncontrollable hemorrhage

• 1/3 of severely injured trauma patients sustain Trauma Induced coagulopathy (TIC)
  – Poorly understood mechanisms
  – Several theories

• Coagulopathy of TBI (CTBI) is a component of TIC
  – Multiple theories contribute to early platelet dysfunction
  – Correlation between severity of TBI and platelet dysfunction
Coagulopathy of TBI (CTBI)

- Presence of CTBI ranges 10-97% in ROL due to many factors
  - Heterogeneity of patients, types of lab tests, timing of tests, and lack of clear defined consensus to define CTBI
  - Associated with poor outcomes
  - Blunt TBI: coagulopathy increases mortality (50% vs 17.3%) compared to no coagulopathy
  - Factors increase risk include GCS<8, ISS>16, hypotension on admit, cerebral edema, SAH, shift
Coagulopathy of TBI (CTBI)

- Platelets & Platelet Activating Factor Theories
  - TBI may result in platelet hyperactivity
  - Platelet activating factor (PAF) induces aggregation and contributes to hypoxia-induced breakdown of the BBB
  - Tissue Factor normally not exposed to circulating blood volume...in TBI brain tissue (rich in TF) & platelets (breakdown) release TF in response to the injury and other cellular dynamics
Exhausted Platelet Dysfunction

• BBB disruption releasing TF (Castellino et al 2014)
  – Qualitatively different form that found in most tissues (unexposed to soluble clotting factors – unsaturated by factor VII)
  – Liberation of free TF into circulation, provokes TF binding to VIIa on a massive scale
    • Results in stimulation of thrombin production in the initiation phase
    • Flood of TF – generated thrombin results in platelet exhaustive syndrome
    • Large numbers of circulating platelets exist in a refractory state
      – Leads to Platelet inhibition at the ADP receptor site (Davis et al 2013)
      – Platelets incapable of stimulation and cannot form a stable thrombus through usual pathways
      – Platelet count usually normal (Davis et al 2013)
    • No evidence of fibrinolysis (Davis et al 2013)
Traumatic brain injury causes platelet adenosine diphosphate and arachidonic acid receptor inhibition independent of hemorrhagic shock in humans and rats

METHODS—We used thrombelastography with platelet mapping as a measure of platelet function, assessing the degree of inhibition of the adenosine diphosphate (ADP) and arachidonic acid (AA) receptor pathways. First, we studied the early effect of TBI on platelet inhibition by performing thrombelastography with platelet mapping on rats. We then conducted an analysis of admission blood samples from trauma patients with isolated head injury (n = 70). Patients in shock or on clopidogrel or aspirin were excluded.

RESULTS—In rats, ADP receptor inhibition at 15 minutes after injury was 77.6% ± 6.7% versus 39.0% ± 5.3% for controls (p < 0.0001). Humans with severe TBI (Glasgow Coma Scale [GCS] score ≤ 8) showed an increase in ADP receptor inhibition at 93.1% (interquartile range [IQR], 44.8–98.3%; n = 29) compared with 56.5% (IQR, 35–79.1%; n = 41) in milder TBI and 15.5% (IQR, 13.2–29.1%) in controls (p = 0.0014 and p < 0.0001, respectively). No patient had significant hypotension or acidosis. Parallel trends were noted in AA receptor inhibition.

CONCLUSION—Platelet ADP and AA receptor inhibition is a prominent early feature of CTBI in humans and rats and is linked to the severity of brain injury in patients with isolated head trauma. This phenomenon is observed in the absence of hemorrhagic shock or multisystem injury. Thus, TBI alone is shown to be sufficient to induce a profound platelet dysfunction. *J Trauma Acute Care Surg.* 2014;76: 1169–1176.
WHY TEG?
Assessing Coagulopathy

Coagulopathy after traumatic brain injury: incidence, pathogenesis, and treatment options

Fig. 2. Laboratory tests currently available to assess the coagulopathy after TBI (modified from 11).
Measuring TIC and CTBI

Value of Viscoelastic Analysis

• Viscoelastical Hemostatic Assays (VHAs) tests that reflect the new understanding of hemostasis
  – Initiation – Amplification – Propagation
  – TEG and ROTEM

• VHAs assess properties of coagulation in whole blood
  – Can differentiate between low fibrinogen and reduced platelet function as the cause of impaired clot strength as well as systemic hyperfibrinolysis
  – Clinical value of VHA is corroborated by > 30 clinical studies on patients with massive hemorrhage—
    • Demonstrates Superiority over conventional coagulation tests
Hemostasis Monitoring:
TEG Hemostasis System

- Whole blood test
- Measures hemostasis
  - Clot initiation through clot lysis
  - Net effect of components
- TEG system
  - Laboratory based
  - Point of care
  - Remote, can be networked
  - Flexible to institution
TEG Technology: How It Works

- Cup oscillates
- Pin is attached to a torsion wire
- Clot binds pin to cup
- Degree of pin movement is a function of clot kinetics
- Magnitude of pin motion is a function of the mechanical properties of the clot
- System generates a hemostasis profile
  - From initial formation to lysis
TEG Parameter Summary

- **Platelet function**
  - Clotting time: 5-10 min
  - Clot kinetics: $\alpha$ (Angle) 53-72°
  - Clot stability: LY30 = 0-8%
  - MA = 50-70 mm

Coagulation | Fibrinolysis

- Enzymatic (R)
- Fibrinogen (K, $\alpha$)
- Thrombolysins (Ly30, EPL)
Standard TEG Tracing

<table>
<thead>
<tr>
<th>SP</th>
<th>R</th>
<th>K</th>
<th>Angle</th>
<th>MA</th>
<th>G</th>
<th>EPL</th>
<th>LY30</th>
<th>TEG ACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>min</td>
<td>min</td>
<td>min</td>
<td>deg</td>
<td>mm</td>
<td>d/sc</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>11.1</td>
<td>11.8</td>
<td>1.7</td>
<td>65.4</td>
<td>62.9</td>
<td>8.5K</td>
<td>0.0</td>
<td>0.0</td>
<td>0—8</td>
</tr>
<tr>
<td>5—10</td>
<td>1—3</td>
<td>53—72</td>
<td>50—70</td>
<td>4.5K—11.0K</td>
<td>0—15</td>
<td>0—8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Fibrinolytic Abnormalities
LY30 Parameter: Primary Fibrinolysis

When fibrinolysis is greater than the rate of clot formation, or when it causes the breakdown of new clots, bleeding typically occurs. This condition is primary fibrinolysis and is identified with the TEG analyzer by an LY30 value of greater than 7.5% (or EPL > 15%), combined with a CI value of less than or equal to 1.0.

- Possible causes:
  - Excessive rate of fibrinolysis

- Possible etiologies:
  - High levels of tPA

- Common treatments:
  - Anti-fibrinolytic agent
Mortality rate by percent fibrinolysis

Mortality rate (%)

LY-30%
Fibrinolysis greater than 3% is the critical value for initiation of antifibrinolytic therapy

Michael P. Chapman, MD, Ernest E. Moore, MD, Christopher R. Ramos, MD, Arsen Ghasabyan, MPH, CCRC, Jeffrey N. Harr, MD, MPH, Theresa L. Chin, MD, John R. Stringham, MD, Angela Sauaia, MD, PhD, Christopher C. Silliman, MD, PhD, and Anirban Banerjee, PhD, Aurora, Colorado
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WHAT ABOUT RAPID TEG?
Rapid TEG

• Jeger and colleagues evaluated Rapid TEG

• r-TEG utilizes tissue factor in addition to kaolin for activation of the clotting cascade

• 20 trauma patients: r-TEG results available < 20 min. vs. > 30 min. for TEG, PT/PTT

_Jeger V et al J Trauma_  2009
Normal TEG vs r-TEG

Courtesy: Dr. Bryan Cotton
Rapid TEG predicting coagulopathy

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACT &gt;128 s</td>
<td>5.15</td>
<td>1.361–19.494</td>
<td>0.016</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>1.00</td>
<td>0.974–1.043</td>
<td>0.636</td>
</tr>
<tr>
<td>Male gender</td>
<td>0.56</td>
<td>0.139–2.319</td>
<td>0.431</td>
</tr>
<tr>
<td>Blunt mechanism of injury</td>
<td>0.43</td>
<td>0.128–1.473</td>
<td>0.475</td>
</tr>
<tr>
<td>White race</td>
<td>0.65</td>
<td>0.353–0.1233</td>
<td>0.191</td>
</tr>
<tr>
<td>ED systolic blood pressure</td>
<td>0.99</td>
<td>0.970–1.011</td>
<td>0.378</td>
</tr>
<tr>
<td>ED heart rate</td>
<td>0.98</td>
<td>0.968–1.017</td>
<td>0.548</td>
</tr>
<tr>
<td>Positive FAST examination</td>
<td>1.59</td>
<td>0.466–5.148</td>
<td>0.181</td>
</tr>
</tbody>
</table>
r-TEG predicting NO blood

### TABLE 5. Multivariate Logistic Regression Model Predicting No PRBC Transfusions in the First 6 h

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACT &lt;105 s</td>
<td>1.85</td>
<td>1.069–3.185</td>
<td>0.028</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>0.99</td>
<td>0.978–1.007</td>
<td>0.340</td>
</tr>
<tr>
<td>Male gender</td>
<td>0.88</td>
<td>0.486–1.606</td>
<td>0.686</td>
</tr>
<tr>
<td>Blunt mechanism of injury</td>
<td>1.56</td>
<td>0.868–2.835</td>
<td>0.136</td>
</tr>
<tr>
<td>White race</td>
<td>0.60</td>
<td>0.355–1.037</td>
<td>0.068</td>
</tr>
<tr>
<td>ED systolic blood pressure</td>
<td>1.00</td>
<td>0.985–1.027</td>
<td>0.558</td>
</tr>
<tr>
<td>ED heart rate</td>
<td>0.98</td>
<td>0.976–0.998</td>
<td>0.020</td>
</tr>
<tr>
<td>Positive FAST examination</td>
<td>0.62</td>
<td>0.313–1.238</td>
<td>0.117</td>
</tr>
</tbody>
</table>

Courtesy: Dr. Bryan Cotton
Platelets
## Measuring Platelet Dysfunction

<table>
<thead>
<tr>
<th>Device</th>
<th>Technique</th>
<th>Antiplatelet Medication Detection</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFA 100</td>
<td>Cessation of blood flow by occlusion of aperture through platelet plug</td>
<td>Aspirin GpIIb/IIIa antagonists</td>
<td>Closure Time</td>
</tr>
<tr>
<td>Multiplate</td>
<td>Altered electrical impedance through platelet aggregation</td>
<td>Aspirin Thienopyridines GpIIb/IIIa antagonists</td>
<td>Aggregation Unit</td>
</tr>
<tr>
<td>Verify Now</td>
<td>Altered light transmission through platelet aggregation</td>
<td>Aspirin Thienopyridines GpIIb/IIIa antagonists</td>
<td>Aspirin Reaction unit P2Y&lt;sub&gt;12&lt;/sub&gt; reaction unit Platelet aggregation unit</td>
</tr>
<tr>
<td>TEG-PM</td>
<td>Platelet effects on clot strength</td>
<td>Aspirin Thienopyridines GpIIb/IIIa antagonists</td>
<td>% Platelet inhibition Measured levels of clot strength MA&lt;sub&gt;ADP&lt;/sub&gt; and MA&lt;sub&gt;AA&lt;/sub&gt;</td>
</tr>
</tbody>
</table>
TEG with Platelet Mapping

- Platelet function is analyzed using the TEG/PM assay.
  - Four individual samples of 360 µL of whole blood are placed into separate specialized cups from blue-capped collection tubes. Next, 10 µL of the prepared activator solution, comprised of reptilase, factor XIIIa, and phospholipids are added to three of the cups.
  - Cup 1: Kaolin (TEG Tracing – MA$_{\text{Thrombin}}$)
  - Cup 2: MA Fibrin (MA$_{\text{Fibrin}}$)
  - Cup 3: MA$_{\text{ADP}}$ (adenosine diphosphate) (MA$_{\text{ADP}}$)
  - Cup 4: MA$_{\text{AA}}$ (arachidonic acid) (MA$_{\text{AA}}$)
Platelet Mapping Values

% inhibition: 11.4
Sample: 8/28/2015 16:21-17:13

PM

% Inhib. 11.4
% Agg 88.6

MA (K) 60.2
MA (A) 6.5
MA (ADP) 54.1

Kd/sc
mm

% inhibition: 55.4

PM

% Inhib. 55.4
% Agg 44.6

MA (CK) 62.6
MA (A) 4.1
MA (AA) 30.2

Kd/sc
mm

Platelet Mapping: Tx Thresholds

MA\textsubscript{ADP} or MA\textsubscript{AA} absolute values should be interpreted in correlation with the MA

- MA\textsubscript{ADP} > 50 less likely to bleed
- MA\textsubscript{ADP} 35-50 moderate chance of bleeding
- MA\textsubscript{ADP} < 35 high chance of bleeding

<table>
<thead>
<tr>
<th>% Inhibition</th>
<th>Platelet Mapping Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADP or AA %</td>
<td>0-40%</td>
</tr>
<tr>
<td>Critical Value</td>
<td>&gt; 60%</td>
</tr>
</tbody>
</table>
Platelets are more inhibited:
TEG/PM tracing with platelet inhibition greater than normal.
A patient can have a normal Platelet count but the platelets are not functioning properly.
ABCs of TEG: Where to start?

• Become the Expert or Find a Nurse Colleague who wants to be content expert
  – Review/Read the literature on the use of TEG
  – Attend a lecture on how it is applied
  – Visit a center that has implemented a program
  – Become the expert!

• Find a Physician Champion
  – Get Physician BUY IN from the surgeons, intensivists, and Anesthesia
  – Find a champion from each area of expertise
    • Trauma, Neurosurgery, Neuro Critical Care, Intensivists, ED, Anesthesia

• Make friends with the Lab Manager or Perfusionist
ABCs of TEG: Where to start?

• Budget?
  – Donors are nice!
  – Build it into the budget cycle

• Once purchased: Form a MD team to build a hospital based protocol
  – Start with another hospital based protocol or develop one
  – Gain consensus: 2-3 meetings

• Educate staff
  – Physicians: Bring in physician content expert (national)
  – Nurses: Provide 1 – 1/2 hour lecture on TEG for key staff

• Get BUY IN from the rest of the hospital
  – Engage key nurses from ED/ICU, Laboratory personnel, OR personnel, and IT

• Provide 24/7 support
Thromboelastography (TEG) Protocol for Monitoring/Treatment of Coagulation Alterations

I. Responsibility: Executive Director, Critical Care Services

II. Scope:
Emergency Department Physicians, General Surgeons, Neurosurgeons, Cardiologists, Critical Care Physicians, Cardiovascular Surgeons, Nurses, Pharmacists, and Laboratory Personnel

III. Key Words: @TEG, @hemorrhage, @neurotrauma, @life threatening Hemorrhage, @Fibrinolysis

IV. General Description:
Patients presenting to the Emergency Department with trauma may sustain massive bleeding. Trauma induced coagulopathy (TIC) is a complication of severe hemorrhage requiring blood products to reverse the coagulopathy. Patients presenting with severe traumatic brain injury are at risk for refractory intracranial hemorrhage from platelet dysfunction or the concurrent use of anticoagulants or anti-platelet medications. In addition, patients presenting with massive hemorrhage require targeted blood product administration to halt the hemorrhagic processes.

Thromboelastography (TEG, Haemonetics Corporation, Braintree, MA) testing provides a more predictive and accessible point-of-care (POC) measurement of clot formation and strength, platelet function, and fibrinolytic activity that the critical care team needs to guide effective hemostatic therapy for TIC as well as excessive hemorrhage.

IV. Purpose:
1. This protocol will define the assessment, diagnostic workup, and treatment choices to reverse the hemorrhagic state in patients with trauma, severe TBI, uncontrolled bleeding, and/or reversal of anticoagulants/anti-platelet medications.
2. Define the parameters associated with TEG
3. Define the parameters associated with TEG with platelet mapping.
4. Provide treatment recommendations for abnormal TEG/TEG with Platelet Mapping results.
**Table 1: Algorithm for TEG-Guided Blood Component Therapy**

Note: Gray tracing overlapping diagram represents normal TEG tracing

<table>
<thead>
<tr>
<th>TEG Normal/Abnormal Value</th>
<th>Blood Component Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal 5-10 min</strong></td>
<td>1) Prothrombin Complex Concentrate (PCC) Preferred as #1</td>
</tr>
<tr>
<td>Prolonged R &gt; 10 min</td>
<td>2) Fresh Frozen Plasma (FFP) alternative</td>
</tr>
<tr>
<td><strong>Critical Value &gt;10 Minutes</strong></td>
<td>3) Protamine if Heparin Present</td>
</tr>
<tr>
<td><strong>Normal K 1-3 min</strong></td>
<td>4) Factor VIIa if Jehovah’s Witness</td>
</tr>
<tr>
<td>Normal α-angle 53-72 degrees</td>
<td>1) Cryoprecipitate and/or</td>
</tr>
<tr>
<td>Prolonged K time and/or reduced α-angle (&lt;53°)</td>
<td>2) FFP</td>
</tr>
<tr>
<td><strong>Critical Value &lt; 53 degrees</strong></td>
<td></td>
</tr>
</tbody>
</table>
### Table 1: Algorithm for TEG-Guided Blood Component Therapy

**Note:** Gray tracing overlapping diagram represents normal TEG tracing

<table>
<thead>
<tr>
<th>TEG Normal/Abnormal Values</th>
<th>Blood Component Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal MA 50-70 mm</strong></td>
<td>1) Platelets</td>
</tr>
<tr>
<td>Low MA (&lt; 50 mm)</td>
<td>2) Consider DDAVP if going to OR stat</td>
</tr>
<tr>
<td><strong>Critical Value &lt; 50 mm</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Normal LY30% 0-8%</strong></td>
<td>1) <strong>Primary Fibrinolysis</strong> LY30% &gt; 8% with Cl of &lt; 1: TXA</td>
</tr>
<tr>
<td>Elevated LY 30% (≥ 8%)</td>
<td></td>
</tr>
<tr>
<td><strong>Critical Value &gt; 15%</strong></td>
<td>2) <strong>Secondary Fibrinolysis</strong> LY30% &gt; 8% with Cl of &gt; 3: Consider Anticoagulation</td>
</tr>
</tbody>
</table>
21 year old Male- Ped vs Train

- Red Trauma Alert...1035
  - GCS 1-4-2
  - VS HR 160 BP 92/50 R28
  - O2 saturation 60%
  - Hgb 11.9/Lactate 8.4
  - Diagnostics
    - Left chest pulmonary contusion, fx clavicle, scapulae, Left Rib fractures (1-3, 5, 7, 8-9) hemopneumothorax
    - Pelvic left side rami fractures/acetabular fx, Right sacral fx
    - Facial fractures: R maxillary sinus, right zygoma/nasal fx, orbital emphysema, fx anterior right orbital floor;
    - CT abdomen: active hemorrhage within the left flank, left gluteal region, near the left sacroiliac joint, near the left medial gluteal muscle, suspected mesenteric and retroperitoneal contusions, severe left hydronephrosis from uteropelvic junction obstruction, right adrenal contusion.
Other injuries

• CT brain: bilateral apical parasagittal parenchymal hemorrhages, SDH, contusions, and cerebral edema
  – ICP opening pressure 30s

• Intervventional OR: embolization of internal iliac artery
What is this?
Platelet Mapping
Massive Transfusion Protocol

- TXA completed at 1500
Post TXA

Given 2 units FFP
Post op 1710
% inhibition: 42.9
Sample: 11/11/2016 17:10-18:10

% inhibition: 6.1
Sample: 11/11/2016 17:10-18:10
Discussion

Ratio-driven Resuscitation vs Goal-driven Resuscitation

– Use Point of care testing and patient vitals to guide initial care in major trauma
– Look at your patient (bleeding sources, vitals, etc)
– MTP and damage control surgery

• Using TEG in major trauma
  – “Mop up” once patient stabilized
  – Tailor the products to what the patient needs
  – Limitations (length of time to run test)
Conclusion
End Points of Resuscitation

- The MTP should be discontinued when there is recognition that further resuscitation is futile.

- The following should be used as guides to cease therapy with blood and blood components in a patient who is (1) not actively bleeding and (2) still in the acute resuscitation phase:
  - RBC transfusions for **hemoglobin** $\geq 10$ g/dL
  - Plasma transfusion for **prothrombin time (PT)** $< 18$ seconds
  - Plasma transfusion for activated **partial thromboplastin time (aPTT)** $< 35$ seconds
  - Platelet transfusions for **platelet count** $> 150 \times 10^9$
  - Cryoprecipitate or fibrinogen concentrate for **fibrinogen level** $> 180$ g/L

- If standard thrombelastography (TEG®) is available, the following cut-points for transfusion triggers may also be used:
  - Plasma for **r-value** $> 9$ minutes
  - Plasma and/or cryoprecipitate (fibrinogen concentrate) for **k-time** $> 4$ minutes
  - Cryoprecipitate (or fibrinogen concentrate) and/or plasma for **$\alpha$-angle** $< 60^\circ$
  - Platelets for **mA** $< 55$ mm
  - Anti-fibrinolytics for LY30$_1$ $> 7.5$ percent