Thromboelastograph (TEG ®) Utilization in Blood Management

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Firelands Regional Medical Center, Sandusky, OH
TEG® Hemostasis System
ROTEM® Delta

- Whole blood Hemostasis Analyzer
- Personalized Treatment
- Point of Care Test
- Comprehensive blood management program to reduce allogeneic transfusions
Platelet Issues…Why TEG ®?

- Availability of Resources?
- Size of Institution?
- Time frame for Delivery of Blood Products?
- Physical Location from Blood Supply?
- Expiration Date?
- How many to order?
- Are Platelets always Available?
- Release to other Patients?
- How many expire and are wasted?
- Platelet Medications/Platelet inhibition?
Improve Outcomes

- Develop a Comprehensive Blood Management Program
- Individualized Hemostasis assessment
- Decrease allogenic transfusions
- Decrease Transfusion Reactions
- Implement Ordering Strategies to reduce waste
- Develop Protocols to Release “on hold” platelets
- Implement Platelet Mapping on patients to determine platelet inhibition
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
Monitoring Hemostasis

• Need whole blood sample
  – TEG® analysis uses whole blood
  – PT, aPTT, TT, D-DIMER, platelet counts use plasma
  – Measure interaction of components
  – TEG® analysis reflects interaction
  – PT, aPTT, TT, D-DIMER, platelet counts isolate components

• Measure dynamic changes from start to finish of process
  – TEG® analysis reflects dynamic changes
  – PT, aPTT, TT, D-DIMER, platelet counts reflect one point in time
Monitoring Insights

• Results are used in conjunction with patient status:
  – Patient clinical condition (bleeding/not bleeding)
  – Phase in medical intervention
  – Type and dose of drug therapy
  – Patient history

• TEG ® testing shows net effect “whole picture” of hemostasis at that point in time:
  – Identifies a “factor deficiency,” but not which factor
  – Identifies a platelet defect, but does not distinguish between platelet deficiency and platelet dysfunction
Formal Definition of TEG®
Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>R is the time of latency from the time that the blood was placed in the TEG® analyzer until the initial fibrin formation.</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>The $\alpha$ value measures the rapidity (kinetics) of fibrin build-up and cross-linking, that is, the speed of clot strengthening.</td>
</tr>
<tr>
<td>K</td>
<td>K time is a measure of the rapidity to reach a certain level of clot strength</td>
</tr>
<tr>
<td>MA</td>
<td>MA, or Maximum Amplitude, is a direct function of the maximum dynamic properties of fibrin and platelet bonding via GPIIb/IIIa and represents the ultimate strength of the fibrin clot.</td>
</tr>
<tr>
<td>CI</td>
<td>Coagulation Index is linear combination of the above parameters.</td>
</tr>
<tr>
<td>LY30</td>
<td>LY30 measures the rate of amplitude reduction 30 minutes after MA. This measurement gives an indication of the stability of the clot.</td>
</tr>
</tbody>
</table>
TEG ® Parameter Summary

Coagulation

- Enzymatic (R)
- Fibrinogen (K, α)

Fibrinolysis

- Platelets (MA)
- Thrombolysins (Ly30, EPL)

Platelet function

Clot strength (G)

Clotting time

Clot kinetics

Clot stability

Clot breakdown
Thrombin Formation Abnormalities

The R Parameter: **Elongated R**

- Possible causes of imbalance:
  - Slow enzymatic reaction

- Possible etiologies:
  - Factor deficiency/dysfunction
  - Residual heparin

- Common treatments:
  - FFP
  - Protamine

Initial fibrin formation

Pin is stationary
Pin is engaged
Fibrinogen Abnormalities

The $\alpha$ (Angle) Parameter: \textbf{Low }$\alpha$

- Possible causes of imbalance:
  - Slow rate of fibrin formation
- Possible etiologies:
  - Low fibrinogen levels or function
  - Insufficient rate/amount of thrombin generation
  - Platelet deficiency/dysfunction
- Common treatments:
  - FFP
  - Cryoprecipitate

Baseline

Pin is engaged

Fibrin increases
Platelet Function Abnormalities
The MA Parameter: Low MA

Possible causes:
- Insufficient platelet-fibrin clot formation

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

Common treatments:
- Platelet transfusion
Platelet Function Abnormalities

The MA Parameter: High MA

- Possible causes:
  - Excessive platelet activity

- Possible etiologies:
  - Platelet hypercoagulability

- Common treatments:
  - Antiplatelet agents
  - Note: Should be monitored for efficacy and/or resistance
Assessing Risk of Thrombosis: General Surgical Patients

McGrath DJ et al. Anesth Analg 2005

<table>
<thead>
<tr>
<th>TEG MA range (mm)</th>
<th>% with thrombotic complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>16 – 63 (n = 47)</td>
<td>4%</td>
</tr>
<tr>
<td>63 – 67 (n = 47)</td>
<td>3%</td>
</tr>
<tr>
<td>67 – 72 (n = 56)</td>
<td>16%</td>
</tr>
<tr>
<td>72 – 95 (n = 56)</td>
<td>32%</td>
</tr>
</tbody>
</table>
# Suggested Treatment

## Treatment protocol

<table>
<thead>
<tr>
<th>TEG® value</th>
<th>Clinical cause</th>
<th>Suggested Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>R between 7 - 10 min</td>
<td>↓ clotting factors</td>
<td>x 1 FFP or 4 ml/kg</td>
</tr>
<tr>
<td>R between 11-14 min</td>
<td>↓↓ clotting factors</td>
<td>x 2 FFP or 8 ml/kg</td>
</tr>
<tr>
<td>R greater than 14 min</td>
<td>↓↓↓ clotting factors</td>
<td>x 4 FFP or 16 ml/kg</td>
</tr>
<tr>
<td>MA between 49 -54 mm</td>
<td>↓ platelet function</td>
<td>0.3mcg/kg DDAVP</td>
</tr>
<tr>
<td>MA between 41 -48 mm</td>
<td>↓↓ platelet function</td>
<td>x5 platelet units</td>
</tr>
<tr>
<td>MA at 40 mm or less</td>
<td>↓↓↓ platelet function</td>
<td>x10 platelet units</td>
</tr>
<tr>
<td>θ less than 45°</td>
<td>↓↓ fibrinogen level</td>
<td>.06 u/kg cryo</td>
</tr>
<tr>
<td>LY30 at 7.5% or greater, C.I. less than 3.0</td>
<td>Primary fibrinolysis</td>
<td>antifibrinolytic of choice</td>
</tr>
<tr>
<td>LY30 at 7.5% or greater, C.I. greater than 3.0</td>
<td>Secondary fibrinolysis</td>
<td>anticoagulant of choice</td>
</tr>
<tr>
<td>LY30 less than 7.5%, C.I. greater than 3.0</td>
<td>Prothrombotic state</td>
<td>anticoagulant of choice</td>
</tr>
</tbody>
</table>

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Baseline TEG with Platelet Mapping

BASELINE TEG

• Citrated tube
• Recalcified before analysis
• Activated with Kaolin
• standardized time (maximum of 2 hours) between blood draw and test

BASELINE TEG with Platelet Mapping

• Citrated tubes and Heparin (Non-Gel)
• Specific platelet activators are required to demonstrate effect of antiplatelet agents
TEG Platelet Mapping ADP Assay

Antiplatelet drugs

- ADP receptor inhibitors
  - Examples: clopidogrel, ticlopidine
- Arachidonic acid pathway inhibitors
  - Example: aspirin
- GPIIb/IIIa inhibitors
  - Examples: abciximab, tirofiban, eptifibatide, Prasugrel

- Measures the effect of antiplatelet agents on platelet function
- Measures the patient’s maximum platelet function as a reference point
- Measures the percentage of inhibition relative to the patient’s reference point
Assay with Citrated Thrombin Sample

*Citrated kaolin sample can also be run using 360μL blood and has been validated.
Antiplatelet Therapy and Coronary Surgery

Clopidogrel Responsiveness Regardless of the Discontinuation Date Predicts Increased Blood Loss and Transfusion Requirement After Off-Pump Coronary Artery Bypass Graft Surgery

Young-Lan Kwak, MD, PhD,* †Jong-Chan Kim, MD,* Yong-Seon Choi, MD,* Kyung-Jong Yoo, MD, PhD,‡ Young Song, MD,* Jae-Kwang Shim, MD, PhD*

Seoul, South Korea
Patients on Plavix who have high platelet inhibition by TEG are at increased risk of postop bleeding and transfusion, regardless of discontinuation date of Plavix.

Prospective, observational trial.

Paper states: “Regardless of time of discontinuation of Plavix, patients with platelet inhibition < 70% by TEG PlateletMapping can safely undergo OPCABG”
GPIIb/IIIa Inhibitors

- All PlateletMapping Assays are sensitive to GPIIb/IIIa inhibitors
  - Abciximab (ReoPro®)
  - Tirofiban (Aggrastat®)
  - Eptifibatide (Integrilin®)
  - Prusagrel (effient®)
Patient A: 50% platelet inhibition does not provide sufficient reduction of the risk of a thrombotic or ischemic event

Patient B: 50% platelet inhibition provides antithrombotic protection without risk of bleeding

Patient C: 50% platelet inhibition increases risk of bleeding
Platelet Mapping Assay

TEG Analysis: Clopidogrel Resistance

% Inhibition = 8.5
% Aggregation = 91.5

% inhibition = 100 - \[ \frac{(MA_{pi} - MA_f)}{(MA_t - MA_f)} \times 100 \]
TEG Hemostasis Summary

Clinical
- Assess risk of bleeding or thrombosis
- Personalize hemostatic therapy
- Monitor efficacy of hemostatic therapy

Administrative
- Improve patient care
- Use hemostatic drugs appropriately
- Lower costs
  - Reduce blood product use
  - Reduce re-operations
  - Reduce thrombotic events
  - Reduce length of stay
Clinical Scenario
Platelet Mapping

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>R min</td>
<td>5.6</td>
</tr>
<tr>
<td>K min</td>
<td>1.4</td>
</tr>
<tr>
<td>Angle deg</td>
<td>68.7</td>
</tr>
<tr>
<td>MA mm</td>
<td>66.8</td>
</tr>
<tr>
<td>CI</td>
<td>1.4</td>
</tr>
<tr>
<td>EPL %</td>
<td><em>0</em></td>
</tr>
<tr>
<td>LY30 %</td>
<td><em>0</em></td>
</tr>
<tr>
<td>G d/sc</td>
<td>10.1K</td>
</tr>
<tr>
<td>A mm</td>
<td>67.2</td>
</tr>
<tr>
<td>A30 mm</td>
<td><em>66.2</em></td>
</tr>
</tbody>
</table>

% inhibition: 54.3

Sample: 7/7/2011 12:24PM-12:56PM

54.3% Inhibition
Clinical Scenario
Post Bypass after Protamine

Normal TEG Heparin Reversed
CK/CKH samples
Clinical Scenario
Effect of Bypass surgery on Platelets

Pre-Bypass compared to post bypass ck samples/Platelet function decreased
Clinical Scenario
Effect of Heparin Rebound in ICU

Prolonged R-Time
Heparin rebound and low MA
Clinical Scenario
Post ICU 12 Hr

TEG tracing after 50 mg protamine and 1 Platelet
Clinical Scenario
Baseline

<table>
<thead>
<tr>
<th>R min</th>
<th>K min</th>
<th>Angle</th>
<th>MA</th>
<th>CI</th>
<th>EPL</th>
<th>LY30</th>
<th>G d/sec</th>
<th>A mm</th>
<th>A30 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.7</td>
<td>1.4</td>
<td>69.7</td>
<td>60.8</td>
<td>0.7</td>
<td><em>0</em></td>
<td><em>0</em></td>
<td>7.7K</td>
<td>61.0</td>
<td><em>60.5</em></td>
</tr>
<tr>
<td>5 — 10</td>
<td>1 — 3</td>
<td>53 — 72</td>
<td>50 — 70</td>
<td>-3 — 3</td>
<td>0 — 15</td>
<td>0 — 8</td>
<td>4.6K — 10.9K</td>
<td></td>
<td></td>
</tr>
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</table>

Normal Baseline Tracing
Clinical Scenario
Post Bypass

Sample: 11/16/2009 03:17PM-04:13PM

Prolonged R - Low MA
Clinical Scenario

After 50 mg additional Protamine

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value 1</th>
<th>Value 2</th>
<th>Value 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>R (min)</td>
<td>9.2</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>K (min)</td>
<td>2.3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Angle (deg)</td>
<td>58.1</td>
<td>53</td>
<td>72</td>
</tr>
<tr>
<td>MA (mm)</td>
<td>40.2</td>
<td>50</td>
<td>70</td>
</tr>
<tr>
<td>CI</td>
<td>-4.4</td>
<td>-3</td>
<td>-3</td>
</tr>
<tr>
<td>EPL (%)</td>
<td>3.8</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>LY30 (%)</td>
<td>3.8</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>G (d/sec)</td>
<td>4.7K</td>
<td>4.6K</td>
<td>10.9K</td>
</tr>
<tr>
<td>A (mm)</td>
<td>46.0</td>
<td>46.0</td>
<td>46.0</td>
</tr>
</tbody>
</table>
Case Report:

Thromboelastograph Guided Management of A Patient Requiring Abiomed Bi-Ventricular Support with Consumptive Coagulopathy.

Patient Information

• 69 yrs old male, BSA 1.74 m^2
• Patient presented with severe 3-vessel coronary artery diseases with no valve dysfunction (LAD, Circ, RCA)
• At the time of admission: Unstable angina
• History: HTN, Renal insufficiency, Ejection fraction 65%
Procedure

- CABG X 4 w/ TLMR (obtuse marginal region)
- Patient had tolerated procedure well and was transferred to the ICU in a stable condition
- Later in ICU (same day) patient became asystolic and was emergently placed on ECMO in ICU
- ECMO was converted to cardiopulmonary bypass in the OR. (CABG x 1 Aorta to LAD)
- After unsuccessful attempts to wean, patient was placed on LVAD and then RVAD (ABIOMED BVS 5000)
- Patient was transported to ICU with BIVAD functioning well.
ABIOMED: BVS 5000

• USE:
  – Ventricular dysfunction/ Postcardiotomy shock
  – acute heart disorders (eg. viral myocarditis)
  – Any Cardiac disorder where native heart recovery is likely
  – In patients whose hearts have not recovered after temporary support, the BVS 5000 may be used as a bridge to another device or as a bridge to heart transplantation.

• Max Flow: Up to 6 LPM
• How many days: 5 to 10 days
Patient: Coagulopathy (Uncontrolled bleeding)

- Patient had developed coagulopathy.
- Possible causes: may be Cardiogenic shock, massive transfusion reaction, long pump run, exposure to foreign surfaces such as Heart-Lung machine, ECMO, ABIOMED; trauma, surgical incision, decrease and imbalance in levels of clotting factor.
- Currently, medical management of DIC is controversial because there is no set treatment model.
- Usually: FFP, Platelets, and Cryo are given for DIC
Patient: ICU

- BiVad was functioning well.
- Patient was bleeding
- Blood products were administered to maintain stable output for Abiomed.
- TEG tracing was used as a guiding tool and obtained to measure whole blood coagulation on per-need basis.
TEG Tracing

Baseline

Post Bypass

71% down (MA)

Post BiVAD

<table>
<thead>
<tr>
<th>R</th>
<th>K</th>
<th>Angle</th>
<th>MA</th>
<th>PMA</th>
<th>G</th>
<th>EPL</th>
<th>A</th>
<th>CI</th>
<th>LY30</th>
</tr>
</thead>
<tbody>
<tr>
<td>min</td>
<td>min</td>
<td>deg</td>
<td>mm</td>
<td></td>
<td>d/sc</td>
<td>%</td>
<td>mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.5</td>
<td>1.3</td>
<td>70.7</td>
<td>59.9</td>
<td>0.0</td>
<td>7.5K</td>
<td><em>0</em></td>
<td>59.9</td>
<td>0.8</td>
<td><em>0</em></td>
</tr>
<tr>
<td>2 — 8</td>
<td>1 — 3</td>
<td>55 — 78</td>
<td>51 — 69</td>
<td></td>
<td>4.6K — 10.9K</td>
<td>0 — 15</td>
<td></td>
<td>-3 — 3</td>
<td>0 — 8</td>
</tr>
</tbody>
</table>
TEG Tracing overtime

24 Hrs Post BiVAD

48 Hrs Post BiVAD

Post BiVAD

<table>
<thead>
<tr>
<th>R</th>
<th>K</th>
<th>Angle</th>
<th>MA</th>
<th>PMA</th>
<th>G</th>
<th>EPL</th>
<th>A</th>
<th>CI</th>
<th>LY30</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.3</td>
<td>2.3</td>
<td>56.7</td>
<td>63.0</td>
<td>0.0</td>
<td>8.5K</td>
<td>0.0</td>
<td>65.1</td>
<td>-0.1</td>
<td>0.0</td>
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<tr>
<td>2 — 8</td>
<td>1 — 3</td>
<td>55 — 78</td>
<td>51 — 69</td>
<td>4.6K — 10.9K</td>
<td>0 — 15</td>
<td>-3 — 3</td>
<td>0 — 8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
TEG Tracing Comparison

Baseline

Prior to transfer

<table>
<thead>
<tr>
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<th>Value</th>
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<tbody>
<tr>
<td>R min</td>
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</tr>
<tr>
<td>PMA</td>
<td>0.0</td>
</tr>
<tr>
<td>G d/sc</td>
<td>9.9K</td>
</tr>
<tr>
<td>EPL %</td>
<td>0.0</td>
</tr>
<tr>
<td>A mm</td>
<td>67.9</td>
</tr>
<tr>
<td>CI</td>
<td>-0.4</td>
</tr>
<tr>
<td>LY30 %</td>
<td>0.0</td>
</tr>
</tbody>
</table>
TEG Guided management

- NovoSeven: Total 12 mg to Decrease time to maximum rate of thrombus from 17.6 to 9.92 min
TEG Guided management

- NovoSeven: Total 12 mg to increase thrombus generation from 391 to 563 over time
Summary

• Abiomed BVS 5000 was successful in providing a support to native recovery
• TEG provided a means to manage DIC and transfuse blood products.
• Significance: able to correct coagulopathy in a patient with Bi Ventricular Assist Device.
References