IS IT TIME FOR HEMATOLOGISTS TO START EMBRACING THE TEG?

Sarah Buckley
Discussant: David Garcia
March 10th, 2016
“We need an urgent consult to figure out why this patient is bleeding in the OR. We’ve transfused him, and his CBC, BUN, and coags are fine, but the oozing won’t stop.”

“What’s his fibrinogen?”

“It’s 400.”
Quiz Time: “the bleeding won’t stop”

A. “It will eventually.”
B. “Just keep transfusing and trend the fibrinogen, and if that drops give cryoprecipitate.”
C. “Dr. Gernsheimer says to give him Amicar.”
D. “Check a TEG.”

LY30 = 9.5%
Outline

• What is TEG?
• Cardiac and trauma surgery
• Liver surgery / liver disease
• Case: bleeding history with “normal labs”
• Case: bleeding risk in hemophilia
• Take-home points
Thromboelastography

• A holistic measure of clotting parameters
• Rapidly available (some results in <5 min)
Thromboelastogram

R = Reaction time (5-10 minutes)
K = Kinetic time (1-3 minutes)
α = Angle (53-72 degrees)
MA = Max amplitude (50-70 mm)
LY30 = Lysis at 30 minutes (0-3%)
Normal

**Anticoagulants, Hemophilia, Factor deficiency**
- Prolonged R, K
- Some decrease in α, MA

**Platelet blockers, thrombocytopenia**
- Normal R, K
- Decrease α, MA

**Fibrinolysis, presence of t-PA**
- Normal R, K
- Declining amplitude, LY30 >7.5%

**Hypercoagulability**
- Decreased R, K
- Increased α, MA

**Early DIC – hypercoaguability with fibrinolysis**
- As above with increased lysis

**Late DIC – hypocoagulable state**
- All metrics affected

TEG-based Transfusion

- Multiple guidelines, all similar (for cardiac surgery)
  - For example:

<table>
<thead>
<tr>
<th>TEG Value</th>
<th>Transfuse</th>
</tr>
</thead>
<tbody>
<tr>
<td>R time &gt;10 min</td>
<td>FFP</td>
</tr>
<tr>
<td>K time &gt;3 min</td>
<td>Cryoprecipitate</td>
</tr>
<tr>
<td>α angle &lt;53°</td>
<td>Cryoprecipitate ± platelets</td>
</tr>
<tr>
<td>MA &lt;50 mm</td>
<td>Platelets</td>
</tr>
<tr>
<td>LY30 &gt;3%</td>
<td>Tranexamic acid</td>
</tr>
</tbody>
</table>
TEG in Cardiac Surgery

<table>
<thead>
<tr>
<th>TEG-based transfusion</th>
<th>Clinician-directed transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1995 study (n=1079)</strong></td>
<td></td>
</tr>
<tr>
<td>Transfusions</td>
<td>78%</td>
</tr>
<tr>
<td>Need for re-exploration</td>
<td>1.5%</td>
</tr>
<tr>
<td><strong>2009 study (n=224)</strong></td>
<td></td>
</tr>
<tr>
<td>RBC transfusion</td>
<td>52%</td>
</tr>
<tr>
<td>PLT transfusion</td>
<td>17%</td>
</tr>
<tr>
<td>FFP transfusion</td>
<td>19%</td>
</tr>
<tr>
<td>Excessive bleeding</td>
<td>9.4%</td>
</tr>
<tr>
<td>Need for re-exploration</td>
<td>4.5%</td>
</tr>
</tbody>
</table>

1. Can TEG predict trauma-induced coagulopathy / hemorrhage?

   2015 Cochrane review – too little evidence to recommend

2. Can TEG-guided transfusions help in trauma surgery?

<table>
<thead>
<tr>
<th></th>
<th>TEG-based transfusion</th>
<th>Clinician-directed transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015 study (n=111)</td>
<td>80%</td>
<td>66% (P=0.027)</td>
</tr>
<tr>
<td>28 day survival</td>
<td>4.5 units</td>
<td>5 (ns)</td>
</tr>
<tr>
<td>RBC transfusion</td>
<td>0 units</td>
<td>0-1 (P=0.041)</td>
</tr>
<tr>
<td>FFP transfusion</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Quiz Time: Predict the Hemorrhage
Liver Transplant

- Three patients with ESLD getting OLT. One had severe post-op bleeding. Which one?

<table>
<thead>
<tr>
<th></th>
<th>PRE OLT #1</th>
<th>POST OLT #1</th>
<th>PRE OLT #2</th>
<th>POST OLT #2</th>
<th>PRE OLT #3</th>
<th>POST OLT #3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.6</td>
<td>2.0</td>
<td>1.8</td>
<td>2.2</td>
<td>3.4</td>
<td>3.7</td>
</tr>
<tr>
<td>Fbgn:</td>
<td>131</td>
<td>104</td>
<td>221</td>
<td>140</td>
<td>100</td>
<td>123</td>
</tr>
<tr>
<td></td>
<td>84</td>
<td>64</td>
<td>76</td>
<td>79</td>
<td>84</td>
<td>60</td>
</tr>
</tbody>
</table>
Case: liver transplants

Three patients with ESLD getting OLT. One had severe post-op bleeding. Which one?

<table>
<thead>
<tr>
<th></th>
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<th>POST OLT #1</th>
<th>PRE OLT #2</th>
<th>POST OLT #2</th>
<th>PRE OLT #3</th>
<th>POST OLT #3</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>12</td>
<td>5.2</td>
<td>4.2</td>
<td>5.4</td>
<td>3.8</td>
<td>5.2</td>
</tr>
<tr>
<td>K</td>
<td>4</td>
<td>4</td>
<td>1.9</td>
<td>2.7</td>
<td>1.8</td>
<td>2</td>
</tr>
<tr>
<td>α</td>
<td>44</td>
<td>53</td>
<td>67</td>
<td>59</td>
<td>70</td>
<td>66</td>
</tr>
<tr>
<td>MA</td>
<td>39</td>
<td>32</td>
<td>50</td>
<td>49</td>
<td>48</td>
<td>43</td>
</tr>
<tr>
<td>LY30</td>
<td>0%</td>
<td>56%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>11%</td>
</tr>
</tbody>
</table>
# TEG in Liver Surgery

## 2015 study (n=200)

<table>
<thead>
<tr>
<th></th>
<th>ROTEM-based transfusion</th>
<th>Clinician-directed transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC transfusions</td>
<td>3%</td>
<td>5% (P&lt;0.001)</td>
</tr>
<tr>
<td>FFP transfusion</td>
<td>0%</td>
<td>2% (P&lt;0.001)</td>
</tr>
<tr>
<td>PLT transfusion</td>
<td>0%</td>
<td>1% (P&lt;0.001)</td>
</tr>
<tr>
<td>Tranexamic acid</td>
<td>4%</td>
<td>0% (P&lt;0.05)</td>
</tr>
<tr>
<td>Massive transfusion</td>
<td>2%</td>
<td>13% (P=0.005)</td>
</tr>
<tr>
<td>Re-exploration needed</td>
<td>5%</td>
<td>13% (P=0.048)</td>
</tr>
<tr>
<td>Kidney injury</td>
<td>16%</td>
<td>29% (P=0.028)</td>
</tr>
</tbody>
</table>

What’s going on in liver disease?

- ↑ factor VIII
- ↑ vW
- ↓ protein C/S
- ↓ antithrombin
- ↓ plasminogen
- ↑ PAI
- ↓ factor II, V, VII, IX, X, XI
- ↓ factor XIII
- ↓ fibrinogen
- ↑ t-PA
- ↓ platelets

- TEG usually **normal** with compensated cirrhosis
- In advanced cirrhosis, MA is low (relates to thrombocytopenia)
RCT of 153 patients with ESLD, INR >1.8 or PLT <50k, pre-procedure

Standard of care group
- FFP for INR >1.8
- PLT for PLT <50k

TEG group
- FFP for long R time
- PLT for low MA

- Fewer transfusions in TEG group (17% vs 100%)
- Post-procedure bleeding in only 1 patient

Case: “normal labs”

- 30 year old woman with 5 weeks of gross hematuria, worsened after cystoscopy / ureteroscopy. She recalls having a GI bleed at age 23.

Fbg: 500

\[ \begin{align*}
12.7 & \downarrow \\
1.0 & \downarrow \\
\text{Fbgn: 500} & \\
\end{align*} \]

\[ \begin{align*}
R & 5.2 \\
K & 1.6 \\
\alpha & 68 \\
\text{MA} & 32 \downarrow \\
\text{LY30} & 0\% \quad \text{---PLTs---> 37} \text{ [+ anti-2b3a inhibitor]} \\
\end{align*} \]
TEG in Hemophilia
“Novo Seven doesn’t work on my son”
“Novo Seven doesn’t work on my son”
• TEG characteristics in 47 children with hemophilia (18 on ppx)
• TEG correlated with bleeding phenotype
TEG Takeaways

• **TEG can add information to standard labs** and may be faster and/or more accessible than other tests currently available

• TEG may be helpful in guiding **management in the OR**

• The utility of TEG in other medical settings (e.g., **chronic liver disease**, **hemophilia**) may be worth exploring in a more systematic fashion

• **We should also continue to investigate other measures of coagulation**... (e.g., clot lysis time)
Thank you....

- David Garcia
- Terry Gernsheimer
- Monica Pagano
- Sioban Keel
- Barb Konkle
Thank you....

- David Garcia
- Terry Gernsheimer
- Monica Pagano
- Sioban Keel
- Barb Konkle

- Some of the 1st year fellows...

Message from Colin:

Just ordered a TEG. Thought you should know.

That's good. Ideally I'd like to get a push notification anytime someone orders one but this is good too. I'm
Thank you....

- David Garcia
- Terry Gernsheimer
- Monica Pagano
- Sioban Keel
- Barb Konkle

- Some of the 1st year fellows...
EXTRA SLIDES
Case: elevated INR

- 18 year old woman admitted for urgent C-section. Procedure is uncomplicated, healthy twins delivered. Post op labs show elevated INR. She has no bleeding history. Is it safe to remove her epidural? What is her bleeding risk?

TT: 15
Fbgn: 645
Factor VII activity: 7%

R  4.6
K  0.8
α  81
MA  79.9
LY30 6.4%

UHH problem – if this is regular TEG, R time is measuring intrinsic clotting, so it’s missing factor 7 😞 But factor 7 generates thrombin, so maybe when severe R time is longer?
“Hypercoagulable” = all 3 abnormal.

- 28% of PBC
- 43% of PSC
- 5% of non-cholestatic cirrhotics
- 0% of normal controls
TEG in Trauma: prognostication

Meta analysis of accuracy of TEG / ROTEM in predicting trauma-induced coagulopathy.

- Too little evidence to recommend

Black = MA at 5 min
Red = MA at 10 min
Green = MA at 15 min

Case: TEG in hemophilia

<table>
<thead>
<tr>
<th></th>
<th>R, min</th>
<th>K, min</th>
<th>MA, mm</th>
<th>G, dyn/cm²</th>
<th>EPL, %</th>
<th>Ly 30, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.0</td>
<td>5.0</td>
<td>65.2</td>
<td>9.4</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>2</td>
<td>9.4</td>
<td>N/A</td>
<td>13.3</td>
<td>0.8</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>3</td>
<td>10.7</td>
<td>9.1</td>
<td>53.4</td>
<td>5.7</td>
<td>10.5</td>
<td>10.5</td>
</tr>
<tr>
<td>4</td>
<td>7.8</td>
<td>4.1</td>
<td>66.1</td>
<td>9.7</td>
<td>0.2</td>
<td>0.2</td>
</tr>
</tbody>
</table>
Ex-vivo addition of rFVIIa to blood of a patient with hemophilia (+inhibitor).

→ Shows dose-responsiveness

Dose-response effect on TEG R time for each of 10 patients with hemophilia (+inhibitor).

→ Large inter-subject variation
→ Probably harder to standardize

Does INR predict bleed in liver disease?

<table>
<thead>
<tr>
<th>Reference/Procedure</th>
<th>Abnormal tests n/N</th>
<th>Normal tests n/N</th>
<th>Risk difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>angiography</td>
<td>1/85</td>
<td>15/915</td>
<td></td>
</tr>
<tr>
<td>angiography</td>
<td>0/9</td>
<td>0/200</td>
<td></td>
</tr>
<tr>
<td>bronchoscopy</td>
<td>3/28</td>
<td>28/218</td>
<td></td>
</tr>
<tr>
<td>bronchoscopy</td>
<td>1/14</td>
<td>43/412</td>
<td></td>
</tr>
<tr>
<td>liver biopsy</td>
<td>0/27</td>
<td>0/9</td>
<td></td>
</tr>
<tr>
<td>liver biopsy</td>
<td>4/76</td>
<td>4/100</td>
<td></td>
</tr>
<tr>
<td>liver laparoscopy</td>
<td>4/93</td>
<td>4/85</td>
<td></td>
</tr>
<tr>
<td>liver laparoscopy</td>
<td>0/29</td>
<td>1/50</td>
<td></td>
</tr>
<tr>
<td>transjugular liver</td>
<td>0/112</td>
<td>0/45</td>
<td></td>
</tr>
<tr>
<td>transjugular liver</td>
<td>0/31</td>
<td>0/19</td>
<td></td>
</tr>
<tr>
<td>transjugular liver</td>
<td>3/203</td>
<td>0/168</td>
<td></td>
</tr>
<tr>
<td>para/thoracocentesis</td>
<td>1/42</td>
<td>18/556</td>
<td></td>
</tr>
<tr>
<td>transjugular kidney</td>
<td>2/10</td>
<td>0/15</td>
<td></td>
</tr>
<tr>
<td>kidney biopsy</td>
<td>1/9</td>
<td>33/110</td>
<td></td>
</tr>
</tbody>
</table>

TEG in Glanzmann’s Disease

• 30 year old woman with 5 weeks of gross hematuria, worsened after cystoscopy / ureteroscopy. She recalls having a GI bleed at age 23.

Baseline Glanzmann’s Thrombasthenia

10 minutes after rFVIIa 90 mcg/kg bolus (normalization of R time)

What does TEG show in liver disease?

• TEG usually normal with compensated cirrhosis
• In advanced cirrhosis, MA is low (relates to thrombocytopenia)
• Is TEG predictive of outcomes?

**BLEEDING:** the case of variceal re-bleed

**CLOTTING:** the case of cholestatic liver disease

Stravitz TF. Gastroenterol Hepatol 2012.