Use of Thromboelastography in the Management of the Trauma Patient

Rio Grande Trauma Conference

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Double Whammy....

• Diagnosis and Management of Traumatic Coagulopathy

  • Use of Thromboelastography in the Management of the Trauma Patient

  • Use of Prothrombin Complex Concentrate to Reverse Coagulopathy
Background - History

• Physiology of Traumatic Coagulopathy
• Diagnostic Considerations
  • Clinical
  • Laboratory tests
  • Point of Care tests
• (Therapeutic Strategies)
Coagulation Models

Fig. 1. The blood coagulation system. (TF, tissue factor; PL, anionic phospholipid.)
Damage Control
Damage Control

- Control of mechanical bleeding, limit contamination
- Restore physiology
- Staged definitive repairs

- Coagulopathy
  - Hypothermia
  - Metabolic Acidosis
  - Clotting factor dilution
  - (Circulating Anticoagulants vs. dilution → Mixing studies)
Figuring it out and treating it....

• Traumatic Coagulopathy
  • Diagnosed clinically – setting and seeing the bleeding
  • Diagnosed by laboratory tests
    • PT, PTT, Fibrinogen, FDP, ACT, TEG, TEM, (H & H)

• Treatment strategies
  • Treating the bleeding
  • Treating the shock
  • Treating the tests

• Treatment options
  • PRBC, FFP, Platelets, Cryoprecipitate, PCC, rFVIIa, TXE (Heparin, tPA)(FWB)
What is our tolerance for...

- Anemia?
- Hypothermia?
- Factor Dilution?
- Fibrinolysis?

What is the natural history of TC?
Laboratory Tests – PT, PTT, Fibrinogen, FDP

• Drawn into a reversible anticoagulant
• Transport to lab, run test, report
• Run on plasma at 37 degrees C
• Correlation with bleeding?
Point of Care Tests- ACT, TEG, rTEG, TEM

• Needs incorporation into work flow
• Procedural violations – Result Variance
• Equipment QA
• Run on whole blood at 37 degrees C
• Correlation with bleeding?

Lab tests ↔ POC tests
Point of Care Test

• ACT (1966) Activated Clotting Time
  • Used for Heparin Monitoring; Trauma?

• TEG (1948) Thromboelastography
  • Used for medical coagulation diagnosis; Trauma?

• rTEG  Rapid TEG
  • Kaolin activated TEG

• TEM  Thromboelastometry (ROTEM)
  • TEG with numbers
Traumatic Coagulopathy

ACT Protocol

• Inclusion Criteria
  • Hypotensive trauma operated STAT (n=8) (7)
  • Expanded to include urgent (n = 32) (27)
  • Excluded major head injury

• Methods
  • Serial ACT (q 15 min intra op)
  • Blood usage, Temp, pH
  • Clinical coagulopathy ---> Damage Control
### Traumatic Coagulopathy

#### Intraoperative ACT

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean ACT +/- SD</th>
<th>Groups</th>
<th>ANOVA</th>
<th>Multiple Range Test</th>
<th>Variance Check †</th>
<th>Kruskall - Wallace</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 n= 7</td>
<td>180 +/- 63</td>
<td>1,3</td>
<td>p=0.0002</td>
<td>‡</td>
<td>p=0.0001</td>
<td>p=0.005</td>
</tr>
<tr>
<td>2 (n=21)*</td>
<td>136 +/- 15</td>
<td>1,2,3</td>
<td>p&lt;0.0001</td>
<td>‡</td>
<td>p&lt;0.0001</td>
<td>p=0.001</td>
</tr>
<tr>
<td>3 n= 24</td>
<td>118 +/- 20</td>
<td>1,2</td>
<td>p=0.0028</td>
<td>‡</td>
<td>P&lt;0.0001</td>
<td>p=0.031</td>
</tr>
</tbody>
</table>

* Normal volunteers, International Technidyne Corporation package insert.
† Cochran’s C, Bartlett’s & Hartley’s tests confirmed ANOVA despite large variance.
‡ Significant above 95 % confidence interval

Traumatic Coagulopathy

Intraoperative ACT

Bench Model-Methods
Type Matched PRBC + FFP; POC outcome measures

PRBC

FFP

37 Degree C

Citrated Mixture

Whole Blood Equivalent

iSTAT

2.5 M Calcium Chloride

Recalcified

Whole Blood Equivalent

37 Degree C

ACT-LR

ACT+

iSTAT
Classic vs. Microsample ACT


Thromboelastography/Thromboelastometry
Thromboelastography

- Kinetics of clot development
- Angle
- LY30
- Reaction time, first significant clot formation
- Achievement of certain clot firmness
- Maximum amplitude – maximum strength of clot
- Percent lysis 30 minutes after MA

Characteristic Thromboelastograph Tracings
- Normal
- Thrombocytopenia
- Severe Platelet Dysfunction
- Coagulation Factor Deficiency
- Fibrinolysis
- Hypercoagulable State
# TEG Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Definition</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clotting Time CT (sec)</strong></td>
<td>Time to reach 20 mm amplitude from beginning of test</td>
<td>Speed of fibrin formation; influenced by clotting factors, anti-coagulants</td>
</tr>
<tr>
<td><strong>Clot Formation Time CFT (sec)</strong></td>
<td>Time to reach 20 mm amplitude from the time of 2mm amplitude</td>
<td>Kinetics of clot formation; influenced by platelet level/ function and fibrinogen level/ability to polymerize</td>
</tr>
<tr>
<td><strong>Maximum Clot Firmness, MCF</strong></td>
<td>Maximum amplitude (in mm)</td>
<td>Firmness of clot, i.e., clot quality; influenced by platelets, fibrinogen (concentration and ability to polymerize), Factor XIII, fibrinolysis</td>
</tr>
<tr>
<td><strong>Maximum Lysis, ML (% of MCF)</strong></td>
<td>Percent of clot firmness lost during measurement</td>
<td>Abnormal ML at 30 minutes likely indicates fibrinolysis</td>
</tr>
</tbody>
</table>
# ROTEM Variations

<table>
<thead>
<tr>
<th>ASSAY</th>
<th>Activator/ Inhibitor</th>
<th>Information provides</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTEM</td>
<td>Contact activation</td>
<td>Fast assessment of clot formation, fibrin polymerisation and fibrinolysis via the intrinsic pathway.</td>
</tr>
<tr>
<td>HEPTEM</td>
<td>Contact activation + heparinase</td>
<td>ROTEM® analysis without heparin influence: Specific detection of heparin (compared to INTEM), assessment of clot formation in heparinised patients.</td>
</tr>
<tr>
<td>EXTEM</td>
<td>Tissue factor activation</td>
<td>Fast assessment of clot formation, fibrin polymerisation and fibrinolysis via the extrinsic pathway.</td>
</tr>
<tr>
<td>FIBTEM</td>
<td>Tissue factor activation and platelet inhibition</td>
<td>ROTEM® analysis without platelets: Qualitative assessment of fibrinogen status.</td>
</tr>
<tr>
<td>APTEM</td>
<td>Tissue factor activation + aprotinin</td>
<td>In-vitro fibrinolysis inhibition: Fast detection of lysis when compared to EXTEM.</td>
</tr>
<tr>
<td>NATEM</td>
<td>Recalcification only = classical TEM (Thromboelastometry)</td>
<td>Very sensitive assessment of the equilibrium of coagulation activation or inhibition.</td>
</tr>
</tbody>
</table>
Validating TEG/TEM

• Define Normal and Standard Deviation
• Compare to standard coagulation tests
• Validate against clinical bleeding
"thrombelastography"[MeSH Terms] 3332
Oldest 1962

"thrombelastography"[MeSH Terms] AND "wounds and injuries"[MeSH Terms] 196 (5.9%)
TEG and ROTEM, side by side

• 184 Trauma patients; 3 hospitals, Denmark, USA, Norway
• Mean ISS 17; Mortality 16.5 %
• Correlation Coefficient (r) =
  • R-time vs. CT 0.24
  • K-time vs. CFT 0.48
  • Alpha angle 0.44
  • MA vs. MCF 0.76 *less than 10% deviation at 1 center
• Concluded that inter-changeability is limited in the trauma setting and validation parameters need to be defined separately

ROTEM to detect TC

• 48 Severe Trauma Victims (39 Battlefield casualties) 51 % TC

• Sensitivity of A5 and A10 against
  1) MCF of < 40
  2) “2/3 rule” Deficient initiation, dynamics, and strength (2 out of 3)
  3) Conventional testing: PT > 1.5 X normal
  4) Normal volunteers (n= 50)

ROTEM to detect TC

• EXTEM at 5 and 10 min compared to MCF < 40 (51% of samples)
  • A5 and A10- sensitivities/specificities of: 0.96/0.58  1.00/0.70

• EXTEM at 5 and 10 min compared to “2/3 rule” (58% o samples)
  • A5 and A10 - sensitivities/specificities of: 0.97/0.68  0.98/0.80

• ROTEM MCF vs. Abnormal PT agreed only 58 %
  • Of remaining 42%, half abnormal by 1 test only

Comparing TEG and rTEG

• Simultaneous TEG and rTEG measurements on 190 trauma patients
  • Strong correlation for overall clot strength and platelet function
  • Moderate correlation in assessing the degree of fibrin cross-linking
  • Poor correlation in evaluating thrombolysis

Correlation of conventional thrombelastography and rapid thrombelastography in trauma.
rTEG to Predict Mortality

- Measured rTEG in ED and correlate to occurrence of massive transfusion (MT) and coagulation related death (MT-D)
  - 80 patients
  - 41% MT
  - 21% MT-D

Fig 1. Algorithm for goal-directed massive transfusion. The transfusion algorithm relies on thrombelastography (TEG) tracing variables to direct blood component therapy. r-TEG, Rapid TEG; ACT, activated clotting time; MA, maximum amplitude; EPL, estimated per cent lysis; FFP, fresh frozen plasma; CRYO, cryoprecipitate; PLT, platelet; ACA, aminocaproate.

Viscoelastic clot strength predicts coagulation-related mortality within 15 minutes.

Table IV. Independent predictors of massive transfusion and coagulation-related death*

<table>
<thead>
<tr>
<th></th>
<th>Model AUC</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ROC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Massive transfusion (MT)</td>
<td>0.92</td>
<td>0.86–0.97</td>
<td>.026</td>
</tr>
<tr>
<td>ISS</td>
<td></td>
<td></td>
<td>.013</td>
</tr>
<tr>
<td>INR, s</td>
<td></td>
<td></td>
<td>.019</td>
</tr>
<tr>
<td>G, dynes/cm²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coagulation-related death (MT + death)</td>
<td>0.93</td>
<td>0.87–0.98</td>
<td>.057</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td>.118</td>
</tr>
<tr>
<td>ISS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td></td>
<td></td>
<td>.027</td>
</tr>
<tr>
<td>G, dynes/cm²</td>
<td></td>
<td></td>
<td>.004</td>
</tr>
</tbody>
</table>

*Variables entered: Age, ISS, SBP, BD, INR, PTT, and G.

AUC ROC, Area under the receiver operating characteristic curve; CI, confidence interval; ISS, injury severity score; INR, international normalized ratio; G, clot strength; SBP, systolic blood pressure.

Viscoelastic clot strength predicts coagulation-related mortality within 15 minutes.
TEG the Test

A
INTTEM
CT: 142 s (121-229) CA\textsubscript{A1}: 56 mm (51-64) CLI\textsubscript{A1}: 98% (95-98)
MCF: 62 mm (54-66) CLI\textsubscript{MCF}: 98% (84-96)
CT: 78 s (47-100)

EXTEM
CT: 52 s (30-81) CA\textsubscript{A1}: 56 mm (47-64) CLI\textsubscript{A1}: 98% (97-98)
MCF: 62 mm (52-66) CLI\textsubscript{MCF}: 97% (83-96)
CT: 92 s (60-115)

FIBTEM
CT: 55 s (39-76) CA\textsubscript{A1}: 13 mm (7-18)
MCF: 16 mm (8-20)
CT: 62 s (44-89) CA\textsubscript{A1}: 54 mm (46-63) CLI\textsubscript{A1}: 98% (97-98)
MCF: 61 mm (51-65) CLI\textsubscript{MCF}: 98% (86-96)
CT: 102 s (66-149) MCF: 61 mm (51-65)
CT: >8027 s (39-76) CA\textsubscript{A1}: 0 mm (7-18)
MCF: 0 mm (8-20)

B
INTTEM
CT: 293 s (121-229) CA\textsubscript{A1}: 0 mm (51-64) CLI\textsubscript{A1}: 5% (95-98)
MCF: 17 mm (54-66) CLI\textsubscript{MCF}: 6% (84-96)
CT: >7875 s (47-100)

EXTEM
CT: 167 s (30-81) CA\textsubscript{A1}: 0 mm (47-64) CLI\textsubscript{A1}: 0% (97-98)
MCF: 13 mm (52-66) CLI\textsubscript{MCF}: 0% (83-96)
CT: >7815 s (60-115)

C
INTTEM
CT: 272 s (121-229) CA\textsubscript{A1}: 33 mm (51-64) CLI\textsubscript{A1}: 98% (95-98)
MCF: 43 mm (54-66) CLI\textsubscript{MCF}: 98% (84-96)
CT: 309 s (47-100)

EXTEM
CT: 122 s (30-81) CA\textsubscript{A1}: 30 mm (47-64) CLI\textsubscript{A1}: 98% (97-98)
MCF: 42 mm (52-66) CLI\textsubscript{MCF}: 97% (83-96)
CT: 396 s (60-115)

FIBTEM
CT: >9274 s (39-76) CA\textsubscript{A1}: 0 mm (7-18)
MCF: 0 mm (8-20)
CT: 149 s (44-89) CA\textsubscript{A1}: 30 mm (46-63) CLI\textsubscript{A1}: 96% (97-98)
MCF: 41 mm (51-65) CLI\textsubscript{MCF}: 98% (86-96)
CT: 395 s (66-149)

D
INTTEM
CT: >7342 s (121-229) CA\textsubscript{A1}: 0 mm (51-64) CLI\textsubscript{A1}: % (97-98)
MCF: 0 mm (54-66) CLI\textsubscript{MCF}: % (83-96)
CT: >7190 s (30-81)

EXTEM
CT: >7190 s (30-81) CA\textsubscript{A1}: 0 mm (47-64) CLI\textsubscript{A1}: % (97-98)
MCF: 0 mm (52-66) CLI\textsubscript{MCF}: % (83-96)
CT: >7150 s (60-115)

FIBTEM
CT: >7092 s (39-76) CA\textsubscript{A1}: 0 mm (7-18)
MCF: 0 mm (8-20)
CT: 699 s (44-89) CA\textsubscript{A1}: 0 mm (46-63) CLI\textsubscript{A1}: % (97-98)
MCF: 0 mm (51-65) CLI\textsubscript{MCF}: % (86-96)
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