Managing Acute Exsanguinating Coagulopathy in Trauma

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Patients with massive blood loss succumb to coagulopathy despite surgical control
# Probability of Developing Life-Threatening Coagulopathy

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Conditions</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>No risk factor</td>
<td></td>
<td>1%</td>
</tr>
<tr>
<td>ISS &gt; 25</td>
<td></td>
<td>10%</td>
</tr>
<tr>
<td>ISS &gt; 25</td>
<td>SBP &lt; 70 mm Hg</td>
<td>39%</td>
</tr>
<tr>
<td>ISS &gt; 25</td>
<td>pH &lt; 7.10</td>
<td>58%</td>
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<tr>
<td>ISS &gt; 25</td>
<td>Temp &lt; 34°C</td>
<td>49%</td>
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<tr>
<td>ISS &gt; 25</td>
<td>SBP &lt; 70 mm Hg + Temp &lt; 34°C</td>
<td>85%</td>
</tr>
<tr>
<td>ISS &gt; 25</td>
<td>SBP &lt; 70 mm Hg, + pH &lt; 7.10 + Temp &lt; 34°C</td>
<td>98%</td>
</tr>
</tbody>
</table>
Bloody Lethal Triad

Acidosis

Hypothermia

Coagulopathy
New Understandings about Coagulopathy

• Initiated immediately after tissue injury
• Independent of clotting factor deficiency
Coagulation Cascade

- **Initiation**
  - Building the clot

- **Amplification**
  - Growing the clot

- **Propagation**
  - Making more clot
Thrombogenic Phase: Primary Hemostasis

- Animal cellular and protein components react with damaged endothelial cell wall and tissue factor
- Thrombin generated
- Platelets adhere to vessel wall
Thrombogenic Phase: Secondary Hemostasis

- Thrombin works on IIb-IIIa receptors on platelets
- Thrombin burst
- Platelet activation & aggregation
- Clot propagation
- Factor VII/TF complex stabilizes clot
- Cross linking of fibrin & fibrin deposition
Look Familiar?
Fibrinolytic Phase

- Normal response becomes pathologic
- "Auto-anticoagulation" protects critical tissue beds from thrombosis
Life-threatening trauma

Imunoactivation

Tissue Injury

Activation/Consumption of Complement

Massive RBC tx

Pre-existing Diseases

Clotting Factor Deficiencies

Acute Endogenous Coagulopathy

Progressive Systemic Coagulopathy
Hypothermia principles

- Normal body temperature 37°C
- Normal diurnal variation 0.7-2.0°C
- Hypothermia in trauma: < 34.5°C
- Thermoregulation
Temperature Sensors

- Pre-optic hypothalamus
- Deep body
- Skin
Thermoregulatory Responses

Posterior hypothalamus

Autonomic responses
Behavioral responses
Detrimental Effects of Hypothermia

![Graph showing mortality at different temperatures by Luna, Jurkovich, and Psarras.](image-url)
Incidence of Hypothermia in Trauma

- Pre-hospital study of 302 injured patients, it was found that almost **every 2nd** patient was hypothermic.

- Entrapped patients were at highest risk (98% vs 35%) as were patients older than 65 years.

- 12% of patients arrived in the ED hypothermic, 92% lost temperature during the initial evaluation.
Incidence of Mortality in Trauma Hypothermia

- Hypothermia is associated with increased morbidity and mortality with a dramatic decrease in survival at core temperatures <34°C (93.2°F) (Tsuel, 2004)

- Admission hypothermia is associated with greater mortality, increased ISS and acidosis (Martin, 2005)

- Hypothermic trauma patients have significantly higher mortality than trauma patients with the same ISS who were normothermic. (Shafi, 2005)
Consequences of Hypothermia

- Cardiac depression
- Myocardial ischemia
- Arrhythmias
- Peripheral vasoconstriction
- Cellular hypoxia
- Decreased hepatic flow and metabolism
- Decreased renal blood flow
- Suppression of neutrophils
Significance of hypothermia in major trauma

- Left shift of oxy-hgb dissociation curve
- Coagulopathy at < 34°C
  - slowing of coagulation enzymes
  - platelet dysfunction
  - platelet sequestration
  - enhanced fibrinolysis
Acidosis

• A reflection of inadequate oxygen delivery to the tissues

• Risk factors
Causes of decreased delivery

Poor cardiac output (poor pump)

Decreased hemoglobin

Pulmonary dysfunction
Results of inadequate DO$_2$

- Lactic acidosis
  - cardiac irritability
  - left ventricular failure
  - poor coronary perfusion
  - altered glucose metabolism
  - cerebral swelling
  - impaired systemic O$_2$ utilization
Results of Inadequate $\text{DO}_2$

- **Cellular death**
  - increase in cellular permeability
  - interstitialization of fluids
  - release of intracellular toxins into circulation
  - entrance of toxins into cells
  - ARDS
  - obstruction of capillary beds
  - multiple organ failure
Life-threatening trauma

- Blood Loss
  - Iatrogenic Factors
  - Core Hypothermia
    - Metabolic Acidosis
    - Hypocalcemia
  - Cellular Shock
    - Progressive Systemic Coagulopathy
    - Acute Endogenous Coagulopathy
Life-threatening trauma

Blood Loss

Immunoactivation

Tissue Injury

Iatrogenic Factors

Core Hypothermia

Metabolic Acidosis

Hypocalcemia

Cellular Shock

Acute Endogenous Coagulopathy

Activation/Consumption of Complement

Massive RBC tx

Progressive Systemic Coagulopathy

Clotting Factor Deficiencies

Pre-existing Diseases
Bloody Lethal Triad Revisited

- Acidosis
- Hypothermia
- Coagulopathy

Decreased Oxygen Delivery
Reverse hypothermia

Standardized rewarming methods
- Passive external
- Active external
- Active internal
After-drop Phenomenon

Initial active external rewarming leads to

Peripheral vasodilation (BP drops)

Cold blood from dilated peripheral vessels carries high lactic acid levels to core vessels

Cold acidotic blood causes drop in core temp

Temperature drop and acidosis provoke serious arrhythmias
Reverse hypothermia

• Rapid Infusers
  - Fast, efficient, use familiar equipment
  - Decrease costs
Correct oxygen delivery

- Appropriate fluid resuscitation
- Replace oxygen carrying capacity
- Correct electrolytes
- Hemodynamic monitoring to guide resuscitation
- Laboratory assessments
Reverse Coagulopathy
Changing Transfusion Practices

- Hemostatic dressings, injectables & sealants
- Ratios of FFP: PRBC
- Whole Blood
- Platelets
- Recombinant Factor VIIa (rVIIa)
- Fibrinogen Concentrate
- Prothrombin Complex Concentrates (PCC)
- Tranexamic Acid (TXA)
Hemostatic Strategies

• Hemostatic dressings
  - Dry Fibrin Sealant Dressing
  - Rapid Deployment Hemostat
  - Chitosan
  - Quickclot

• Topical hemostatic agents
Chitosan
FFP:PRBC Ratios

- European guidelines recommend FFP 10-15 ml/kg for INR > 1.5
- Thawed Frozen Plasma available, but rapidly loses coagulation function
- Ratios are faster than waiting for labs
  - “High” : 1:1, 1:2
  - “Moderate”: 1:3, 2:3

Platelets

- Platelet COUNT does not reflect platelet FUNCTION
- Traditional transfusion triggers are 50-100K
- No specific tx trigger for platelets
  - MD preference
  - Clinical situation
- Immunologic complications
Fibrinogen

- Cryo rich in Factors VIII, XIII, VWF, fibrinogen
- Fibrinogen > 50 mg/dL required for physiologic hemostasis
- No recommendations for pre-emptive transfusion of cryo
- Fibrinogen found in other blood products
  - 4 u FFP contains 1500 mg Fibrinogen (1 pooled cryo pack)
  - 10 pk platelets = 300 mg Fibrinogen
Fibrinogen Concentrate

- Lyophilized fibrinogen concentrate (Factor I)
- Virus inactivated, antibody free
- 50 mL reconstituted
- Monitor for thrombotic reactions
Recombinant Factor VIIa

• Use well established in patients with baseline coagulopathy requiring surgery

• Pro-coagulant: reduces blood loss and restores normal coag state (↓PT within 5 mins after injection)

• Binds to surface of activated platelets
  - promotes Factors IX and X
  - increases thrombin generation from platelets at a site of injury

• Increases platelet function, independent of temperature
Factor VIIa (Novoseven)

- 50% reduction of blood loss in animal trauma studies
- Affects the site of injury, and does not cause systemic hypercoagulability
- Does not transmit disease
- Does not require Blood Bank resources
- 180 mcg/kg single infusion
Prothrombin Complex Concentrate (PCC)

- Clotting factors II, IX, X
- Replaces factor deficiency
- Advantages over FFP include more timely correction, absence of volume overload and potentially more complete correction.

PCC for Coumadin Reversal

- Reverses effect of Coumadin Used in patients on oral anticoagulants
  - 500 IU of PCC is likely an optimal dose of PCC for emergent reversal of INR in patients requiring rapid correction of INR below 5.0
  - 500 IUS is inadequate dose in patients with INR of 5.0 or more.

- Administration with vitamin K can reverse INR rapidly within 10 min and keep the reversed INR values for 12-24 h
Tranexamic Acid (TXA)

- European CRASH-2 study showed improved mortality and decreased blood loss if given within first 8 hours of injury
  - 1 gm over 10 minutes, followed by 1 gm over 8 hours
  - 15-20 mg/kg
- No risk of vascular occlusive events if given within 6-8 hours
- Potential use in, TBI with ICH, Post-partum, Liver tx
- Recommended for inclusion on the WHO List of Essential Medicines

How do we guide therapy?
Problems with traditional labs

- Static measurements
- Delayed
- Measured in plasma, not whole blood
- Don’t consider cellular influences on coag
- Don’t measure clot strength
- Require normal pH and temperature
Viscoelastography
TEG®   ROTEM®

- Provides information on the balance between thrombosis and thrombolysis
- Considers the interaction of the entire clotting cascade and platelet function in whole blood
- Point of Care testing
- For use in Trauma, Open-Heart, and Liver Transplant surgeries
• Pin rotates 4.75°
• Fibrin strands form, increases torque between pin and cup surface
• Dissociation of fibrin strands from the cup wall (clot retraction) or degradation of fibrin by fibrinolysis decreases torque
ROTEM® Waveform

- **CT (clotting time):** Time from start of measurement until initiation of clotting
  - Initiation of clotting, thrombin formation, start of clot polymerisation

- **CFT (clot formation time):** Time from initiation of clotting until a clot firmness of 20mm is detected
  - Fibrin polymerisation, stabilisation of the clot with thrombocytes and F XIII

- **MCF (maximum clot firmness):** Firmness of the clot
  - Increasing stabilisation of the clot by the polymerised fibrin, thrombocytes as well as F XIII

- **ML (maximum lysis):** Reduction of the clot firmness after MCF in relation to MCF
  - Stability of the clot (ML < 15%) or fibrinolysis (ML > 15% within 1h)
Normal Patient
ROTEM Guided Management of Coagulopathy

Clinical Bleeding

- EXTEM, FIBTEM, INTEM, APTEM & Coagulation Tests
  - All Normal
  - Clinical Management as Appropriate

Platelet Deficit
- Either EXTEM MCF < 48 mm with FIBTEM MCF ≥ 10 mm
  - or EXTEM A10 < 40 mm with FIBTEM A10 > 12 mm
  - and/or Platelets < 100 x 10^9

Fibrinogen Deficit
- FIBTEM MCF < 10 mm
  - and/or Fibrinogen < 150 mg/dL

Thrombin Generation Deficit
- EXTEM CT > 100 sec
  - and EXTEM CT = APTEM CT and/or INTEM CT > 240 sec
  - and/or PT/aPTT > 1.5 x normal
  - and/or INR > 1.5

Hyperfibrinolyis
- EXTEM ML > 15%
  - and EXTEM CT > APTEM CT

Severe Clot Deficiency
- EXTEM A10 < 30 mm

Recent heparin exposure
- INTEM CT > HEPTEM CT

ROTEM
- Plateletpheresis 1-2 units

COAG
- RBC concentrate (RiaSTAP) 15-25 mg/kg
  - and/or Cryoprecipitate 2 pools of 5 units

TREATMENT
- TXA 1 gm IV over 10 mins followed by 1 gm IV over 3 hrs Q 24 hrs
- PCC 15-20 Units/kg (if obese, use adjusted body wt) and/or 2-4 units FP
- TXA 1 gm IV over 10 mins followed by 1 gm IV over 8 hrs (2 mg/min)
  - RBC concentrate 70 mg/kg
  - (or Cryo 2-4 pools of 5 units)
  - PCC 20-30 U/kg
  - (or FP 4-6 units)
  - Plateletpheresis 1-2 units to keep plt > 100k

TXA = Tramoxenic acid (dosing per CRASH-2 study)
PCC = Prothrombin Complex Concentrate

Repeat ROTEM tests should be ordered based on clinical response

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End points of resuscitation

• Temp > 35°C or normothermic

• Hemostasis:
  - INR < 1.5 without ongoing bleeding
  - Plts > 50,000 if no longer bleeding

• Adequate tissue oxygenation
  - How to assess?
Concluding remarks

- Presence of hypothermia, acidosis and coagulopathy in any critically ill patient lead to poor oxygen delivery
- The combination of the 3 contributes to higher patient mortality
- Proper assessment and treatment of each component is essential for positive patient outcomes
- Rapidly changing information, so stay informed of current research findings