Managing Hemostasis in Trauma-induced Coagulopathy

TIC-TIC
Timing is Everything

George A. Fritsma, MS MLS
www.fritsmafactor.com; george@fritsmafactor.com
Overview

• Pathophysiology of trauma and shock
• Traditional trauma management
• Current trauma management
• Massive transfusion protocol
• Balanced blood product therapy
• Antifibrinolytics and components
US Injury Incidence

- In the USA, 36,000,000/y (1/7) suffer significant injury
- 27,000,000 injury-related doctor or hospital visits
- 1,700,000 injury-related hospital admissions
- 1,000,000 are transferred to trauma centers
- 10,000 require massive transfusion
- Extent of injury is determined by whole body CT scan or focused abdominal sonography for trauma (FAST)

Death by Trauma

- Unintended or intentional injury is the most common cause of death in N Americans age 1–45
  - 93,000/y in the USA, up 20% since 2005
  - 3,000,000/y worldwide, exceeded only by AIDS deaths

- 50% of trauma deaths are caused by neurological displacement and occur before reaching hospital

- 20,000 die in hospital of *exsanguination* in 48 h
  
  - 30–35% with blood loss & uncompensated shock expire
  
  - 3–4,000 of US hemorrhage deaths are preventable
  
  - Coagulopathy, failure to achieve hemostasis

## Years of Potential Life Lost (YPLL) Before Age 65

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>YPLL</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Causes</td>
<td>948,426</td>
<td>100.0%</td>
</tr>
<tr>
<td>Unintentional Injury</td>
<td>199,903</td>
<td>21.1%</td>
</tr>
<tr>
<td>Suicide</td>
<td>52,265</td>
<td>5.5%</td>
</tr>
<tr>
<td>Homicide</td>
<td>48,190</td>
<td>5.1%</td>
</tr>
<tr>
<td>Malignant Neoplasms</td>
<td>137,221</td>
<td>14.5%</td>
</tr>
<tr>
<td>Heart Disease</td>
<td>107,009</td>
<td>11.3%</td>
</tr>
<tr>
<td>Perinatal Period</td>
<td>75,496</td>
<td>8.0%</td>
</tr>
<tr>
<td>Congenital Anomalies</td>
<td>43,615</td>
<td>4.6%</td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>21,817</td>
<td>2.3%</td>
</tr>
<tr>
<td>HIV</td>
<td>21,508</td>
<td>2.3%</td>
</tr>
<tr>
<td>Liver Disease</td>
<td>21,352</td>
<td>2.3%</td>
</tr>
<tr>
<td>All Others</td>
<td>220,050</td>
<td>23.2%</td>
</tr>
</tbody>
</table>

31.7%
<table>
<thead>
<tr>
<th>Rank</th>
<th>&lt;1</th>
<th>1-4</th>
<th>5-9</th>
<th>10-14</th>
<th>15-24</th>
<th>25-34</th>
<th>35-44</th>
<th>45-54</th>
<th>55-64</th>
<th>65+</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Congenital Anomalies 4,746</td>
<td>Unintentional Injury 1,216</td>
<td>Unintentional Injury 730</td>
<td>Unintentional Injury 11,836</td>
<td>Unintentional Injury 17,357</td>
<td>Unintentional Injury 16,048</td>
<td>Malignant Neoplasms 44,834</td>
<td>Malignant Neoplasms 115,282</td>
<td>Heart Disease 499,722</td>
<td>Heart Disease 614,748</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Short Gestation 4,123</td>
<td>Congenital Anomalies 399</td>
<td>Malignant Neoplasms 435</td>
<td>Suicide 425</td>
<td>Suicide 5,079</td>
<td>Suicide 6,669</td>
<td>Malignant Neoplasms 11,267</td>
<td>Heart Disease 34,791</td>
<td>Heart Disease 74,473</td>
<td>Malignant Neoplasms 412,385</td>
<td>Malignant Neoplasms 561,269</td>
</tr>
<tr>
<td>3</td>
<td>Maternal, Fetal, Perinatal 1,574</td>
<td>Homicide 364</td>
<td>Congenital Anomalies 192</td>
<td>Malignant Neoplasms 416</td>
<td>Homicide 4,144</td>
<td>Homicide 4,159</td>
<td>Heart Disease 10,566</td>
<td>Unintentional Injury 20,610</td>
<td>Unintentional Injury 16,030</td>
<td>Chronic Low. Respiratory Disease 124,693</td>
<td>Chronic Low. Respiratory Disease 147,101</td>
</tr>
<tr>
<td>4</td>
<td>SIDS 1,545</td>
<td>Malignant Neoplasms 321</td>
<td>Homicide 123</td>
<td>Congenital Anomalies 156</td>
<td>Malignant Neoplasms 1,569</td>
<td>Malignant Neoplasms 3,624</td>
<td>Suicide 6,706</td>
<td>Suicide 6,767</td>
<td>Unintentional Injury 113,308</td>
<td>Unintentional Injury 150,653</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Unintentional Injury 1,101</td>
<td>Heart Disease 149</td>
<td>Heart Disease 69</td>
<td>Homicide 156</td>
<td>Heart Disease 963</td>
<td>Heart Disease 3,341</td>
<td>Homicide 2,590</td>
<td>Liver Disease 8,327</td>
<td>Diabetes Mellitus 13,342</td>
<td>Diabetes Mellitus 13,342</td>
<td>Unintentional Injury 150,653</td>
</tr>
<tr>
<td>6</td>
<td>Placenta Cord, Membranes 965</td>
<td>Influenza &amp; Pneumonia 109</td>
<td>Chronic Low. Respiratory Disease 68</td>
<td>Heart Disease 122</td>
<td>Congenital Anomalies 377</td>
<td>Liver Disease 725</td>
<td>Liver Disease 2,582</td>
<td>Diabetes Mellitus 6,062</td>
<td>Liver Disease 12,792</td>
<td>Diabetes Mellitus 54,161</td>
<td>Unintentional Injury 48,295</td>
</tr>
<tr>
<td>7</td>
<td>Bacterial Sepsis 544</td>
<td>Chronic Low. Respiratory Disease 52</td>
<td>Influenza &amp; Pneumonia 57</td>
<td>Chronic Low. Respiratory Disease 71</td>
<td>Influenza &amp; Pneumonia 199</td>
<td>Diabetes Mellitus 709</td>
<td>Diabetes Mellitus 1,999</td>
<td>Corpuscostal 5,349</td>
<td>Corpuscostal 11,727</td>
<td>Corpuscostal 48,295</td>
<td>Diabetes Mellitus 76,488</td>
</tr>
<tr>
<td>8</td>
<td>Respiratory Distress Syndrome 440</td>
<td>Septicemia 19</td>
<td>Severe Neoplasms 38</td>
<td>Severe Neoplasms 45</td>
<td>Severe Neoplasms 43</td>
<td>Diabetes Mellitus 181</td>
<td>HIV 583</td>
<td>Corpuscostal 1,417</td>
<td>Corpuscostal 4,402</td>
<td>Corpuscostal 48,295</td>
<td>Diabetes Mellitus 76,488</td>
</tr>
<tr>
<td>9</td>
<td>Circulatory System Disease 444</td>
<td>Septicemia 33</td>
<td>Severe Neoplasms 38</td>
<td>Influenza &amp; Pneumonia 41</td>
<td>Chronic Low. Respiratory Disease 176</td>
<td>Septicemia 579</td>
<td>Heart Disease 1,174</td>
<td>Septicemia 2,751</td>
<td>Septicemia 5,709</td>
<td>Septicemia 39,557</td>
<td>Septicemia 48,145</td>
</tr>
<tr>
<td>10</td>
<td>Neonatal Hemorrhage 441</td>
<td>Perinatal Period 38</td>
<td>Septicemia 33</td>
<td>Severe Neoplasms 38</td>
<td>Severe Neoplasms 177</td>
<td>Severe Neoplasms 649</td>
<td>Septicemia 1,125</td>
<td>Septicemia 2,514</td>
<td>Septicemia 5,290</td>
<td>Septicemia 29,124</td>
<td>Septicemia 42,773</td>
</tr>
</tbody>
</table>

## 10 Leading Causes of Injury Deaths by Age Group Highlighting Unintentional Injury Deaths, United States – 2014

<table>
<thead>
<tr>
<th>Rank</th>
<th>Age Group</th>
<th>Causes</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;1</td>
<td>Unintentional Suffocation 991</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Drowning 386</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional MV Traffic 345</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional MV Traffic 384</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional MV Traffic 6,531</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Poisoning 9,334</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional MV Traffic 9,116</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Poisoning 11,009</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Poisoning 7,013</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Fall 27,044</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Poisoning 42,937</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1-4</td>
<td>Homicide Unspecified 119</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional MV Traffic 293</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Drowning 125</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Suffocation 225</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Homicide Firearm 3,587</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Firearm 3,309</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Firearm 2,430</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Firearm 9,453</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Fall 5,567</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5-9</td>
<td>Homicide Other Spec., Classifiable 83</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Homicide Unspecified 189</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Fire/Burn 69</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Firearm 174</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Firearm 3,489</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Homicide Firearm 3,360</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Firearm 2,830</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Fall 2,957</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10-14</td>
<td>Unintentional MV Traffic 61</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Suffocation 126</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Homicide Firearm 86</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Homicide Firearm 115</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Firearm 2,270</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Firearm 2,629</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Firearm 2,057</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Fall 2,321</td>
<td></td>
</tr>
<tr>
<td></td>
<td>25-34</td>
<td>Unintentional MV Traffic 128</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Suffocation 105</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Suffocation 2,109</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Suffocation 2,492</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Homicide Firearm 1,835</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Poisoning 1,795</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Poisoning 1,529</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Suffocation 3,682</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Suffocation 1,847</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Poisoning 1,958</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Firearm 10,945</td>
<td></td>
</tr>
<tr>
<td></td>
<td>35-44</td>
<td>Unintentional MV Traffic 61</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Suffocation 34</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Suffocation 507</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Poisoning 800</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Poisoning 1,274</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Poisoning 1,340</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Suffocation 1,059</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Poisoning 1,935</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Homicide Firearm 10,945</td>
<td></td>
</tr>
<tr>
<td></td>
<td>45-54</td>
<td>Unintentional MV Traffic 61</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Suffocation 34</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Suffocation 507</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Poisoning 800</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Poisoning 1,274</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Poisoning 1,340</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Suffocation 1,059</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Poisoning 1,935</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Homicide Firearm 10,945</td>
<td></td>
</tr>
<tr>
<td></td>
<td>55-64</td>
<td>Unintentional MV Traffic 61</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Suffocation 34</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Suffocation 507</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Poisoning 800</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Poisoning 1,274</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Poisoning 1,340</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Suffocation 1,059</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Poisoning 1,935</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Homicide Firearm 10,945</td>
<td></td>
</tr>
<tr>
<td></td>
<td>65+</td>
<td>Unintentional MV Traffic 61</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Suffocation 34</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Suffocation 507</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Poisoning 800</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suicide Poisoning 1,274</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Poisoning 1,340</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Suffocation 1,059</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintentional Poisoning 1,935</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Homicide Firearm 10,945</td>
<td></td>
</tr>
</tbody>
</table>

Data Source: National Center for Health Statistics (NCHS), National Vital Statistics System.
Produced by: National Center for Injury Prevention and Control, CDC using WISQARS™.
Idaho Injury Death Rates/100,000

2004-2010, Idaho
Death Rates per 100,000 Population
All Injury, All Intents, All Races, All Ethnicities, Both Sexes, All Ages
Annualized Crude Rate for Idaho: 64.23

Reports for All Ages include those of unknown age.
*Rates based on 20 or fewer deaths may be unstable. These rates are suppressed for counties (see legend above); such rates in the title have an asterisk.

Produced by: the Statistics, Programming & Economics Branch, National Center for Injury Prevention & Control, CDC
Data Sources: NCES National Vital Statistics System for numbers of deaths; US Census Bureau for population estimates.
The Fritsma Factor
A 24-YO male arrived in the ED with a shotgun wound causing massive abdominal trauma. He had received three units of Dextran® balanced 5% glucose-electrolyte crystalloid in transit to achieve fluid resuscitation but was hemorrhaging. ED personnel ordered and administered four RBC units. Upon the second RBC four-unit batch order the transfusion service director recommended one plasma and one pheresis platelet concentrate. After 8 RBCs, she ordered 1 more plasma and 1 more platelet, but the patient was still bleeding.

Labs:
PT: 20.8 s (MRI 12.9); PTT: 82.5 s (MRI 30.1)
FG: 130 mg/dL (RI 225–498); PLTs: 70,000/uL (RI 150–450,000)
24-YO ♂, GSW in ED, 2008

Patient BP was 70/40, temp 32°C, pH 7.30. In surgery, major vessels were tied, but the field was obscured by microvascular bleeds. The patient survived surgery but expired in the recovery room.

Thanks to Margaret Fritsma, Mary Anne Krupsky, Michelle Brown, Birmingham, AL and Jose De Jesus, Tuscaloosa, AL for information on which this case is based.
Traditional TIC Management

• If no coagulopathy is suspected…
  – Ligate and treat with crystalloids and RBCs
  – Discourage plasma and platelets

• If coagulopathy is suspected…
  – Plasma to replenish multiple coagulation factors
  – Platelet concentrate for thrombocytopenia
  – Coagulation factor concentrates: VIII, IX
  – Replenish FG with CRYO or RiaSTAP (2009)
  – Activated PCC (FEIBA)
  – Four-factor PCC (KCentra)
  – NovoSeven® recombinant activated factor VII
American Society of Anesthesiologists 2006 Practice Guidelines

• Use no plasma to augment volume, use colloid or crystalloid expanders (5% dextrose: Dextran®)
  – Plasma only if microvascular bleeding…
  – And PT >1.5X “normal” or PTT >2X “normal”

• Use RBCs when HGB <6 g/dL

• “Usually” give platelets if <50,000/uL, unless…
  – Limited blood loss is anticipated based on type of surgery
  – Thrombocytopenia is associated with HIT, ITP, or TTP, where platelets may be ineffective

2004 Baghdad Case

- An IED-injured US soldier received 18 RBC units and died of dilutional coagulopathy before plasma could be thawed.
- Surgeons and BB director agreed to keep 4 units of thawed AB plasma available at all times.
- Initiated 1:1 plasma/RBC Rx; improved resuscitation, reduced hemorrhage, added PLT concentrate 2006.
- Reduced crystalloids (Dextran, 5% glucose), reduced lung and tissue edema.
- 2006: Joint Theatre Trauma System Guidelines.
- 2012: Joint Trauma System Clinical Practice Guidelines.

Bottom Line At the Start (BLATS)

- Crystalloid (Dextran®) resuscitation raises blood loss, transfusion requirements, edema, and mortality
- Balanced blood product (BBP) resuscitation reduces blood loss, Tx requirements, and improves survival
- Thawed plasma in the ER (or EMT), time is critical

TIC: Massive Trauma
Hematoma or Hemorrhage

Figure 2. Severely injured patients can present with coagulopathy at the time of hospital admission. This soldier arrived in hemorrhagic shock and required massive transfusion with packed red blood cells (pRBC), coagulation products, and whole blood. Tourniquets were placed on the patient’s thighs in the field to minimize blood loss.
The Fritsma Factor

Your Interactive Hemostasis Resource

TIC Initial Management

**Record** hypothermia, hypotension, acidosis (base deficit), coagulopathy

**Surgery**: use warmed room, warmed fluids & RBCs, close large vessels, control for microvascular bleeding

**Hypothermia**: remove wet clothing, cover with blanket, peritoneal lavage, extracorporeal arteriovenous warming

**Lab**: PT, PTT, CBC w/ PLTs, FG, D-D, ABG, Lytes, TEG, TEM

**Coagulopathy Rx**: RBC, PLT, plasma 1:1:1; FG, FEIBA or PCC, TXA, factors, rFVIIa

**Acidosis**: shock resuscitation, normal saline, correct base deficit, maintain moderate target BP: systolic >70


The Fritsma Factor
TIC Mechanisms

- Hypoperoxidation (shock)
- Hypothermia (shock)
- Acidosis (shock)
- Hyperfibrinolysis
- Coagulopathy
- Protein C activation
- Hemodilution & hypothermia by fluid resuscitation

Inflammation
Tissue factor activation
Platelet activation
Surgical damage
RBCs

Coagulation Pathway

**Extrinsic**
- Initiation: exposed TF binds VIIa, activates IX→IXa and X→Xa
- TF

**Intrinsic**
- Pre-K
- HMWK

**Common**
- Propagation: phosphatidyl serine on activated PLTs
- IXa
- VIIIa
- Xa
- Va
- Thr
- XIIIa

**Fibrinogen** → **Fibrin Polymer** → **Crosslinked Fibrin**


So why do we bleed?
Lost Clotting Ability

- Half of FG and PLT pools exsanguinate and are lost in massive hematoma or hemorrhage
- Factor VII is lost to exposed tissue factor
- Factor V and VIII depletion
- Nerve tissue emboli from injured brain, fat emboli from broken bones, and amniotic fluid emboli in pregnancy cause DIC with defibrination
  - Especially thromboplastin-rich brain tissue
Coagulant Deficit Upon Arrival Injury Severity Score >16

<table>
<thead>
<tr>
<th>Clotting factors</th>
<th>Critical deficit ≤30% clotting factor activity</th>
<th>22 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor II (n=105)</td>
<td>2 (9.1%)</td>
<td>2</td>
</tr>
<tr>
<td>Factor V (n=105)</td>
<td>22 (100%)</td>
<td>22</td>
</tr>
<tr>
<td>Factor VII (n=108)</td>
<td>1 (4.5%)</td>
<td>1</td>
</tr>
<tr>
<td>Factor VIII (n=110)</td>
<td>4 (18.2%)</td>
<td>4</td>
</tr>
<tr>
<td>Factor IX (n=105)</td>
<td>2 (10%)</td>
<td>2</td>
</tr>
<tr>
<td>Factor X (n=96)</td>
<td>2 (10%)</td>
<td>2</td>
</tr>
<tr>
<td>Factor XI (n=99)</td>
<td>3 (15%)</td>
<td>3</td>
</tr>
<tr>
<td>Factor XII (n=97)</td>
<td>2 (10%)</td>
<td>2</td>
</tr>
</tbody>
</table>

Clotting Factor Dilution

- Hypotension leaves plasma colloid osmotic pressure unopposed. Protein-poor fluid seeps into vasculature, diluting coagulation factors and PLTs
- Crystalloids like 5% dextrose further dilute blood
- Whole blood?
  - Donor whole blood is diluted with 67 mL A/C per 450 mL TV
  - Whole blood theoretical best HCT is 28%

- Red cells?
  - Coagulation factor activity is diminished to 60%
  - PLT count averages 90,000/uL

Hypothermia, Acidosis, Fibrinolysis

- All enzyme activity slows at <37°C
- PLT activation slows at 32–34°C (?)
- Platelets cease to bind VWF at 30°C
- Vitamin K-dependent factors II, VII, IX, and X fail to bind phospholipid in acidosis
- Thrombomodulin exposure activates & consumes protein C
- α₂-antiplasmin loss prolongs free plasmin life
- Decreased plasminogen activator inhibitor (PAI-1) prolongs tissue plasminogen activator (TPA) life
- Thrombin consumption lowers TAFI activation
  - Thrombin-activatable fibrinolysis inhibitor
- Factor XIII dilution causes inadequate fibrin crosslinking
  - Fibrin strands are thin, easily digested
The Protein C Control Pathway

- Thrombin
- TM
- Endothelial Cell
- EPCR-1
- APC
- PC
- Excess activation
- Excess destruction
- C4b-BP
- 60% Bound PS
- 40% Free PS
- PS

Thrombomodulin overexpressed in hypoperfusion

- Va
- VIIIa
- Vi
- VIIIi

ACPC: Activated protein C
C4b-BP: Complement C4b binding protein
EPCR-1: Endothelial cell protein C receptor
PC: Protein C
PS: Protein S
TM: Thrombomodulin
Va, VIIIa: Activated V and VIII
Vi, VIIIi: Inactivated V and VIII


Coagulopathy
VWF Synthesis, Reduced ADAMTS13

(a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13)

Endothelial cell & megakaryocyte production

2050 aa monomers

20m D multimers

5–20m D multimers

Plasma

α-granule and Weibel-Palade body storage

20m Dalton VWF multimers

VWF-cleaving protease ADAMTS-13

↓ ADAMTS13
## Injury Severity Score (ISS)

<table>
<thead>
<tr>
<th>Region</th>
<th>Description (Examples)</th>
<th>Injury Score (1–6)</th>
<th>Highest 3 Squared</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head &amp; neck</td>
<td>Cerebral contusion</td>
<td>3 (Serious)</td>
<td>9</td>
</tr>
<tr>
<td>Face</td>
<td>Scratches</td>
<td>1 (Minor)</td>
<td></td>
</tr>
<tr>
<td>Chest</td>
<td>Sucking wound</td>
<td>4 (Severe)</td>
<td>16</td>
</tr>
<tr>
<td>Abdomen</td>
<td>Liver contusion</td>
<td>2 (Moderate)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spleen rupture</td>
<td>5 (Critical)</td>
<td>25</td>
</tr>
<tr>
<td>Extremity</td>
<td>Fractured femur</td>
<td>3 (Serious)</td>
<td></td>
</tr>
<tr>
<td>External</td>
<td></td>
<td>1 (Minor)</td>
<td>1</td>
</tr>
<tr>
<td>Sum</td>
<td></td>
<td>ISS:</td>
<td>50</td>
</tr>
</tbody>
</table>

Maximum is 75. If injury is assigned a score of 6 (unsurvivable), the ISS is automatically 75. ISS correlates linearly with mortality, morbidity and hospital stay. See also automated revised ISS, TRISS, which incorporates respiration and BP.


---

**Coagulopathy**

---

The Fritsma Factor
## Probability of Life-threatening Coagulopathy in Trauma

<table>
<thead>
<tr>
<th>Condition:</th>
<th>% Coagulopathy*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injury severity score (ISS) &gt;25 alone</td>
<td>10%</td>
</tr>
<tr>
<td>ISS &gt;25 &amp; systolic BP &lt;70 mm Hg</td>
<td>39%</td>
</tr>
<tr>
<td>ISS &gt;25 &amp; body temp &lt;34°C</td>
<td>49%</td>
</tr>
<tr>
<td>ISS &gt;25 &amp; pH &lt;7.10</td>
<td>58%</td>
</tr>
<tr>
<td>ISS &gt;25; SBP &lt;70 mm Hg; body temp &lt;34°C</td>
<td>85%</td>
</tr>
<tr>
<td>ISS &gt;25; SBP &lt;70 mm Hg; temp &lt;34°C; pH &lt;7.10</td>
<td>98%</td>
</tr>
</tbody>
</table>

*Life-threatening coagulopathy defined as PT and PTT ≥ 2X mean of reference interval (MRI)*

Coagulopathy in Trauma

<table>
<thead>
<tr>
<th>ISS &amp; Coagulopathy n = 1088</th>
<th>% Coagulopathy by Lab Assay*</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISS &gt;15; median 20</td>
<td>57.7%</td>
</tr>
<tr>
<td>ISS &lt;15</td>
<td>10.9%</td>
</tr>
</tbody>
</table>

Coagulopathy at Admission | % Mortality
---|---
Yes (24.4%) | 46%
No | 10.9%
Overall mortality | 19.5%

*Coagulopathy defined independent of fluid replacement as: PT ≥18s, 16.3%; PTT ≥60s, 24.4%; or thrombin time ≥15s, 14.2%

PT and PTT Predict Mortality

• Review of 7638 level I trauma admissions
  • Initial PT >14s: 28% of admissions
    – 6.3% of patients with PT <14s died
    – 19.3% of patients with PT >14s died
    – Independent mortality increase 35%; OR, 3.6; \( p < 0.0001 \)
      • Controlled for age, ISS, BP, HCT, pH, and head injury
  • Initial PTT >34s: 8% of admissions
    – Independent mortality increase 326%; OR 7.8; \( p < 0.001 \)

Definition and “Drivers” of TIC

- Retrospective cohort study
  - 3646 trauma patients at five international trauma centers
  - TIC = PTR >1.2; correlates with ISS and shock

- Prothrombin time ratio (PTR) >1.2
  - Mortality 22.7%
    Vs. 7.0%, p <0.001
  - RBC use 3.5 versus 1.2 units, p <0.001
  - Plasma use 2.1 versus 0.8 units, p <0.001

The Fritsma Factor

Mortality rises with PTR >1.2

RBC and plasma demand rise with PTR >1.2
PTR rise depends upon both ISS and acidosis (base deficit).

Mortality mirrors PTR as it also depends upon both ISS and acidosis.

Base deficit (mmol/L) mirrors shock.

Coagulopathy
Massive Transfusion Protocol (MTP)

- Major hemorrhage defined by blood usage
  - Retrospective: ≥ 10 RBC units in 24h
    - Or ≥ 50 total component units in 24h
    - 1 blood volume replaced in 70 kg patient
- Ongoing: 3 units RBCs/h; 5 units/3h
- Why give RBCs first?
  - Patient loses “red stuff,” needs “red stuff.”
  - But HCT unchanged, though volume lost

Massive Transfusion in Young, Healthy Combat Casualties

• Systolic <110 mm Hg
• Pulse >110 BPM
• Acidosis: pH <7.25 or base deficit >6 mM
• HGB <11 g/dL
• PT >1.5 x mean of reference interval (MRI)

MTP in ER: Civilian Casualties

- Penetrating Vs. blunt mechanism
- focused abdominal sonography for trauma (FAST)
  - Peritoneal fluid, organ rupture, internal bleeding
- Arrival systolic BP <90 mmHg, pulse >120

ER use of uncrossmatched RBCs predicts 3X the incidence of MTP

# Intraoperative RBC Transfusion Risks

<table>
<thead>
<tr>
<th>Independent Outcome</th>
<th>RBCs</th>
<th>No RBCs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>16.4%</td>
<td>9.8%</td>
</tr>
<tr>
<td>Pulmonary complication</td>
<td>12.6%</td>
<td>6.0%</td>
</tr>
<tr>
<td>Wound complications</td>
<td>9.2%</td>
<td>4.7%</td>
</tr>
<tr>
<td>Mortality</td>
<td>6.4%</td>
<td>4.4%</td>
</tr>
<tr>
<td>Thromboembolic disease</td>
<td>4.0%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Renal complications</td>
<td>2.7%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Cardiac complications</td>
<td>2.1%</td>
<td>1.4%</td>
</tr>
</tbody>
</table>

30-day outcomes, all but the last two significant at p < 0.05

RBC Transfusion Risks in Trauma

- Tx predicts MOF when victim survives >24 h
- Transfusion-associated circulatory overload (TACO)
- Tx correlates with 4X rise in ICU admission
- Mortality rises with each RBC unit
- No patient >75 who gets >12 RBC units survives
- Tx infection odds ratio 5.26 versus no Tx
- Composite risk of TRALI* and ARDS* 1:5000
  - *Transfusion-related acute lung injury
  - *Acute respiratory distress syndrome

RBC Transfusion Risks in Context

Transfusion-related acute lung injury

Transfusion-associated circulatory overload

Risk

- HIV
- HCV
- HBV
- TRALI
- Life-threatening reaction
- Fatal hemolysis

1 in 100 million
1 in 10 million
1 in 1 million
1 in 100,000
1 in 10,000
1 in 1,000
1 in 10
1 in 1

Motor vehicle fatalities
Firearm homicide
Airplane fatalities
Lightning fatalities

Fever

Death from medical error

# RBC Risks and Indications

<table>
<thead>
<tr>
<th>Risk</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABO Incompatibility*</td>
<td>Fever, hemoglobinuria, hemoglobinemia</td>
</tr>
<tr>
<td>TRALI* or TACO</td>
<td>Respiratory distress, hypoxemia</td>
</tr>
<tr>
<td>Bacterial contamination</td>
<td>Fever, hypotension</td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>Urticaria</td>
</tr>
<tr>
<td>Citrate toxicity</td>
<td>Hypocalcemia</td>
</tr>
</tbody>
</table>

*Observe for delayed TRALI and Tx reaction; terminate Tx and start diagnostic tests*
Platelet Concentrate

- Clinicians discouraged from giving platelets
  - Why? “Platelets are a precious commodity.”
- Use early anyway, they stabilize the coagulopathy
  - PLT concentrate has all the “good stuff” that is in plasma

What Does “Plasma” Mean?

• Fresh frozen plasma (FFP)
  – Plasma processed and placed at ≤ −18C within 8 h of collection
  – Plasma from males or nulligravida females to avoid TRALI
  – Largely discontinued 2000–2010, though name lives on

• 24-h plasma (PF24)
  – WB ambient ≤8 h → 1–6C ≤16 h → processed → −18C in 24 h
  – Most common prep, mis-named FFP by most health care pros

• 24-h plasma (PF24RT24)
  – WB held ambient, processed and placed at −18C within 24 h
  – Approved 4/1/2014 for replacement of non-labile coagulation factors

• All preparations stored frozen up to 12 months

• Thawed AB plasma: stored at 1–6C; 5 d if closed
Mean Factor V, VIII and Protein S Levels in FFP, PF24, and PF24RT24

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Factor V</th>
<th>Factor VIII</th>
<th>Protein S</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFP at thaw</td>
<td>85%</td>
<td>81%</td>
<td>97%</td>
</tr>
<tr>
<td>FFP 5d post-thaw</td>
<td>67%</td>
<td>43%</td>
<td>92%</td>
</tr>
<tr>
<td>PF24 at thaw</td>
<td>86%</td>
<td>66%</td>
<td>90%</td>
</tr>
<tr>
<td>PF24 5d post-thaw</td>
<td>59%</td>
<td>48%</td>
<td>78%</td>
</tr>
<tr>
<td>PF24RT24 at thaw</td>
<td>90%</td>
<td>86%</td>
<td>82%</td>
</tr>
<tr>
<td>PF24RT24 5d post-thaw</td>
<td>89%</td>
<td>86%</td>
<td>73%</td>
</tr>
</tbody>
</table>

RBC/Plasma 1:1

• USA hospital in Baghdad Green Zone
  – Tx >2000 wounded, massively Tx >600 wounded
  – Retrospective w/o controls but extensive, careful documentation

• Receiving ≤1 plasma per 4 RBCs: 65% mortality
  – Confounding data: soldiers who received >10 RBC units but died before plasma could thaw are counted in this arm

• Receiving 2 plasma for every 3 RBCs: 19% mortality
  – Confounded: survivors receive more plasma Vs. those who die
  – Requires ~15 h to resolve coagulopathy
  – Surgeons report less bleeding and edema

• Anticipated adverse effects
  – Plasma supply—yes
  – TACO—yes
  – No TRALI, anaphylaxis, ARDS, MOF, or thrombosis

ASA 2015 Plasma Indications

- Manage preoperative or bleeding pts who require replacement of multiple coagulation factors (eg, liver disease, DIC).
- Manage patients undergoing massive transfusion who have clinically significant coagulation deficiencies.
- Manage bleeding patients taking warfarin or who need an invasive procedure before vitamin K could reverse the warfarin effect (but 4-factor PCC is better).
- Transfusion or plasma exchange in patients with thrombotic thrombocytopenic purpura (TTP)
- Manage patients with congenital or acquired factor deficiencies for which there are no specific coagulation concentrates
  - FP24RT24 not indicated for factor VIII or protein S deficiency

Plasma Reduces EC Permeability

- Barrier dysfunction, interstitial edema, tissue hypoxia, inflammatory cells
- Infiltration, detached pericytes, extracellular matrix breakdown, apoptosis, exposed subendothelium
- Stabilizes ECs through junction protein regulation

Group AB Plasma When ABO is Unknown

• Group AB from males & nulligravida females
  – Pre-restrictions: odds of AB plasma TRALI 14.5 X higher than A, B, or O
  – TRALI restrictions first applied 4/1/2014
  – AB = 2.6% of active donors before TRALI restriction
  – AB availability now cut by 33%

• AB demand raised
  – New massive Tx protocols raise plasma demand
  – Maintaining thawed plasma supply in ER
  – Thawed AB diverted to non-ABs on 5th day to avoid waste

• Solution: group A plasma

Group A Plasma When ABO is Unknown

- Most recipients are A and O, compatible w/ A plasma
- Anti-B titers low in TRALI-restricted population
- B substance in secretors neutralizes anti-B
- PTs may be receiving massive O RBCs anyway
- U Mass, 2008–13 (similar data from Mayo)
  - Emergency release of 358 A plasmas
  - 84% of recipients turned out to be A or O, compatible
  - 23 recipients were B or AB, 11 of these received O RBCs
  - No acute hemolytic transfusion reactions
  - Three weak positive post-transfusion DATs
  - Reduced AB plasma usage 97%

Group AB Plasma When ABO is Unknown

- 76 U of Cincinnati PTs received 76 gender-nonspecific group AB plasma transfusions, and compared to Mayo trial they had...
  - Lower ratios of arterial O₂ partial pressure to fractional inspired oxygen.
  - Higher rates of sepsis (p=0.024), acute renal failure (p = 0.003), DVT (p = 0.021), and PE (p = 0.013).
  - Longer ICU stays.

PROMMOTT Study

- 34,362 trauma admissions, 10 centers 58 wks
- 10% transfused within 6 hours
- 7% received ≥ 3 RBCs
- Overall mortality 25%
  - 94% of hemorrhagic deaths occurred within 24 hours
  - Median time to hemorrhagic death 2.6 h, range, 1.7–5.4 h

PROMMT Plasma:RBC Ratio

PRospective Observational Multicenter Massive Transfusion sTUdy

UTHealth
The University of Texas Health Science Center at Houston

Plasma:RBC ratio
- -1:2
- ≥1:2 to <1:1
- ≥1:1

Hem death at 2.6 hrs

Patients, %

Time Interval, h

0.5 1 2 3 6 24
PROMMT Platelet:RBC Ratio

Earlier and higher ratios of plasma and platelets associated with decreased in-hospital mortality in the first 6 hours.
Reduced Crystalloids

- 17 YO GSW to liver, 60/30, base deficit –17
- 11 RBC, 10 plasma, 2 PLTs, 3 L crystalloid
- 3 surgeries, home in 10 days
TRALI Versus CRALI

• Crystalloid-related acute lung injury (CRALI)
• The amount of crystalloid versus blood products transfused during the first day of care seems to be the modifiable risk factor for lung injury
• TRALI, 0; vs CRALI, 505

Updated TIC Rx

- Minimize crystalloids by targeting low BP
- Use thawed plasma in EMS, not crystalloids
- Rewarm patient intensively, warm components
- In relatively stable patients, guide Rx w/ repeated CBCs, PTs, PTTs, TEG or TEM
- Rx: BBP: Plasma, PLTs, FG, RBCs 1:1:1:1
- Europe, 4-factor PCC, factor VIII, FG concentrate, rFVIIa (NovoSeven), tranexamic acid (TXA)

PROPPR Trial: Group A Plasma

- 12 level I trauma centers
- Balanced BPs randomized: 1:1:1 or 1:1:2
  - Plasma : platelet concentrate : red blood cells
- All but 1 center delivered 6 u universal donor plasma and 6 of UD RBCs in 10 minutes
- 3 sites provided 141 group A plasma to AB and B patients, 97 units untitered anti-B
  - No transfusion reactions

PROPPR Outcomes

- **1:1:1 vs 1:1:2 plasma/PLT concentrate/RBCs**
  - 338 vs 342 severely injured patients in hemorrhagic shock
  - 12 sites, 9 used thawed AB, 3 added thawed A plasma

- **FDA-required primary outcomes**
  - 24-h and 30-d mortality no differences
  - Reduced 3-h mortality
    real measure of
    trauma resuscitation
  - 1:1:2 patients required
    "catch-up" products

Fresh Whole Blood—Why Not?

- FWB provides plasma:RBC:PLTs in a 1:1:1 ratio
- FWB improved survival compared to stored components.
- FWB is available in austere conditions
- No cold storage loss of clotting factor or platelet function.
- No RBC storage lesion. Butt…
- Lack of screening: transfusion-transmitted infections
  - HBV, HCV, HIV, HTLV, syphilis
- Grouping error and hemolytic transfusion risk
  - Crossmatch required
- Bacterial contamination

Joint Theater Trauma System Clinical Practice Guideline: Fresh whole blood transfusion, 2012
Tranexamic Acid (Cyclokapron) Rx

- Synthetic lysine blocks plasminogen binding sites, reduces fibrinolysis
- Reduces Tx requirements in surgery without raising mortality
- Around since 1968, cheap

Tranexamic Acid Death by Cause

<table>
<thead>
<tr>
<th>CRASH-2</th>
<th>IV TXA</th>
<th>Placebo</th>
<th>RR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 g TXA bolus + 1 g/8h</td>
<td>n = 10060</td>
<td>n = 10067</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Any cause of death</strong></td>
<td>1463 (14.5%)</td>
<td>1613 (16%)</td>
<td>0.91</td>
<td>0.0035</td>
</tr>
<tr>
<td><strong>Bleeding death</strong></td>
<td>489 (4.9%)</td>
<td>574 (5.7%)</td>
<td>0.85</td>
<td>0.0077</td>
</tr>
<tr>
<td><strong>Thrombosis death</strong></td>
<td>33 (0.3%)</td>
<td>48 (0.5%)</td>
<td>0.69</td>
<td>0.096</td>
</tr>
</tbody>
</table>

No significant differences in myocardial infarct, stroke, VTE, blood product volumes

### All-cause Mortality by Subgroup

Tranexamic Acid Versus Placebo

<table>
<thead>
<tr>
<th>Time from injury (h)</th>
<th>Tranexamic acid allocated</th>
<th>Placebo allocated</th>
<th>Risk ratio (99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1</td>
<td>509/3347 (15.6%)</td>
<td>581/3704 (15.7%)</td>
<td>0.87 (0.75-1.00)</td>
</tr>
<tr>
<td>&gt;1-≤3</td>
<td>463/3037 (15.2%)</td>
<td>528/2996 (15.6%)</td>
<td>0.87 (0.75-1.00)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>491/3272 (15.0%)</td>
<td>502/3362 (14.9%)</td>
<td>1.00 (0.86-1.17)</td>
</tr>
</tbody>
</table>

χ² = 4.411; p = 0.11

<table>
<thead>
<tr>
<th>Systolic blood pressure (mm Hg)</th>
<th>Tranexamic acid allocated</th>
<th>Placebo allocated</th>
<th>Risk ratio (99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥90</td>
<td>702/6878 (10.2%)</td>
<td>736/6761 (10.9%)</td>
<td>0.94 (0.82-1.07)</td>
</tr>
<tr>
<td>76-89</td>
<td>280/1609 (17.5%)</td>
<td>313/1689 (18.5%)</td>
<td>0.94 (0.78-1.14)</td>
</tr>
<tr>
<td>≤75</td>
<td>478/1562 (30.6%)</td>
<td>562/1599 (35.1%)</td>
<td>0.87 (0.76-0.99)</td>
</tr>
</tbody>
</table>

χ² = 1.345; p = 0.51

<table>
<thead>
<tr>
<th>GCS</th>
<th>Tranexamic acid allocated</th>
<th>Placebo allocated</th>
<th>Risk ratio (99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe (3-8)</td>
<td>796/1789 (44.5%)</td>
<td>860/1830 (47.0%)</td>
<td>0.95 (0.86-1.04)</td>
</tr>
<tr>
<td>Moderate (9-12)</td>
<td>219/1349 (16.2%)</td>
<td>249/1344 (18.5%)</td>
<td>0.88 (0.70-1.09)</td>
</tr>
<tr>
<td>Mild (13-15)</td>
<td>447/6915 (6.5%)</td>
<td>502/6877 (7.3%)</td>
<td>0.88 (0.75-1.04)</td>
</tr>
</tbody>
</table>

χ² = 1.387; p = 0.50

<table>
<thead>
<tr>
<th>Injury type</th>
<th>Tranexamic acid allocated</th>
<th>Placebo allocated</th>
<th>Risk ratio (99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blunt</td>
<td>1134/6788 (16.7%)</td>
<td>1233/6817 (18.1%)</td>
<td>0.92 (0.83-1.02)</td>
</tr>
<tr>
<td>Penetrating</td>
<td>329/3272 (10.1%)</td>
<td>380/3250 (11.7%)</td>
<td>0.86 (0.72-1.03)</td>
</tr>
</tbody>
</table>

χ² = 0.791; p = 0.37

<table>
<thead>
<tr>
<th>All patients</th>
<th>Tranexamic acid allocated</th>
<th>Placebo allocated</th>
<th>Risk ratio (99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1463/10060 (14.5%)</td>
<td>1613/10067 (16.0%)</td>
<td>0.91 (0.85-0.97)</td>
<td></td>
</tr>
</tbody>
</table>

Two-sided p = 0.0035
CRASH 2 on Public Media
Use TXA, CRYO, and PCC

• Rapid, effective, predictable rise in factor activity
• Activated PCC, 4-factor PCC; low volume vs. plasma
• RiaSTAP® FG; low volume vs. CRYO, no TACO
• Avoid 58% of massive transfusions
  – “Massive transfusion avoidance protocol”
• No risk of incompatible transfusion
• Reduce plasma Tx by 90%
• Effective viral inactivation
• Reduce RBC Tx by 8.4%
• No risk of TRALI
• “Never” use rVIIa?
CRASH-2 Weaknesses

- Subject selection based upon “uncertainty” principle
- Most subjects in countries with austere trauma care
  - Benefits could be lost in mature facilities with BBP protocols
- No laboratory monitoring: TEG, TEM
- TXA antifibrinolytic mechanism poorly defined
- No effort to measure thrombosis except for death
  - Other studies report 13% DVT/PE prevalence in TXA Rx
- Small subject cohort who required blood
  - Blood product usage equivalent in TXA and control arm
- Several new trials in progress
- MATTER reported better outcomes than CRASH-2
  - Number needed to treat: 7 versus 67

Thromboelastograph

1946

Pen displacement by viscoelastic changes
Rotational Thromboelastometry

The Fritsma Factor

TEG and TEM 64
Thromboelastograph

Coagulation

Fibrinolysis

TIME

R

K

MA

α

Normal R & MA

Hypocoagulable

Hyperfibrinolysis

Thrombocytopenia
TEG 6s

- Small volume
- Cartridge
- Stable
TEM Monitor, No Transfusion, No rFVIIa

Surgical intervention: suture, divert, compress, and pack

T <37°C; pH <7.2; HGB <8 mg/dL, Ca++ <1 mmol/L

hypocoag: RiaSTAP®

hyperfibrinolysis: tranexamic acid

aspirin, clopidogrel, coumadin, heparin

Bottom Line At the End (BLATE)

- Thawed A plasma on site, no crystalloids
- Treat shock: warm patient, pH
- BBP: 1:1:1:1 plasma, RBCs, FG, PLTs
- Factors VIII and IX when necessary
- Tranexamic acid, 4-factor PCC
- Monitor with ROTEM
  - PT and PTT if ROTEM not available
Questions?