Managing Hemostasis in Trauma-induced Coagulopathy

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

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Sponsored by the Robert B. Adams Foundation
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
  - 3,000,000/y worldwide, exceeded 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>

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

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.

American Society of Anesthesiologists
2006 Practice Guidelines

- Do not use 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”
- 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

Standard (Old) 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®
  - Activated PCC (FEIBA®)
  - Four-factor PCC (KCentra®)
  - NovoSeven® recombinant activated factor VII

Bottom Line At the Start (BLATS)

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

The Fritsma Factor

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.

**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, PLTs, FG, D-D, ABG, Lytes, TEG, TEM, PAI-1

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

**Acidosis**: shock resuscitation, normal saline, correct base deficit, maintain low target BP


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**Trauma-induced Coagulopathy**

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**TIC Mechanisms**

**Hypoperfusion (shock)**

**Hypothermia (shock)**

**Acidosis (shock)**

**Hyperfibrinolysis**

**Coagulopathy**

**Protein C activation**

**RBCs**

**Hemodilution & hypothermia by fluid resuscitation**

**Surgical damage**

**Tissue factor activation**

**Platelet activation**

**Inflammation**


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**Coagulation Pathway**

**Initiation:** exposed TF binds VIIIa, activates IX → IXa and X → Xa

**Propagation:** phosphatidyl serine on activated PLTs

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Lost Clotting Ability

- Half of FG and PLT pool exsanguinate and are lost in massive hematoma or hemorrhage
- Nearly all of factor VII is lost to exposed tissue factor
- 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

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
- Combination of RBCs, plasma, and PLTs at 1:1:1…
  - Donor whole blood is diluted with 67 mL A/C per 450 mL TV
  - Whole blood theoretical best HCT is 28%
  - 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
- $\alpha_2$-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

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**The Protein C Control Pathway**


- APC: 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

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The Fritsma Factor

**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>4</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: 50</td>
<td></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.


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**The Fritsma Factor**

The Fritsma Factor

Fibrinolysis in Hypoperfusion
### 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 is arbitrarily defined as PT and PTT >2X mean of reference interval (MRI)

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### 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>

<table>
<thead>
<tr>
<th>Coagulopathy at Admission</th>
<th>% Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes (24.4%)</td>
<td>46%</td>
</tr>
<tr>
<td>No</td>
<td>10.9%</td>
</tr>
<tr>
<td>Overall mortality</td>
<td>19.5%</td>
</tr>
</tbody>
</table>

*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 5 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, \( p < 0.001 \)

Mortality rises with PTR

RBC and plasma demand rise with PTR

PTR rise depends upon both ISS and acidosis (base deficit)

Mortality mirrors PTR as it also depends upon both ISS and hypoperfusion

Base deficit (mmol/L) mirrors shock
Massive Transfusion Protocol (MTP)

- Major hemorrhage defined by blood loss
- 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?
  - HCT unchanged, though volume lost
  - Patient loses “red stuff,” needs “red stuff.”


Massive Transfusion in Young, Healthy Combat Casualties

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

MTP in ER: Civilian Casualties

- Penetrating Vs. blunt mechanism
- Focused abdominal sonography for trauma (FAST)
  - Peritoneal fluid, organ rupture, internal bleeding
- Arrival BP <90 mmHg, pulse >12

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 significant at p <0.05

RBC Transfusion Risks in Trauma

- Tx predicts MOF* when victim survives >24 h
  - *Multiple organ failure
- Tx correlates with 4X rise in ICU admission
- Mortality rises with each RBC unit
- No patient >75 who gets >12 RBC units survived
- 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
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>

Terminate transfusion and start diagnostic tests

*Observe for delayed TRALI and transfusion reaction

Platelet Concentrate

- Clinicians discouraged from giving platelets
  - Why? "Platelets are a precious commodity."
- Use early anyway, they stabilize the coagulopathy
  - They've got 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
  - Released 4/1/2014 for replacement of non-labile coagulation factors
- All preparations stored frozen up to 12 months
- Thawed AB plasma: kept at 1–6C; 5 d if closed

Mean Factor V, VIII and Protein S Levels in FFP, PF 24, 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)
  - Transfusion-associated circulatory overload (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
  - 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 A 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 $O_2$ 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.

PROPPR Trial: Group A Plasma

- 12 level I trauma centers
- Balanced blood products: 1:1:1 or 1:1:2
  - Plasma : platelet concentrate : red blood cells
- All but 1 delivered 6 u UD 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


Plasma Efficacy in Adults

<table>
<thead>
<tr>
<th>INR</th>
<th>Median FFP (mg/kg)</th>
<th>Median Change</th>
<th>Median FFP (mg/kg)</th>
<th>Median Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>11.4</td>
<td>-0.2</td>
<td>11.4</td>
<td>-2.6</td>
</tr>
<tr>
<td>≤1.5</td>
<td>10.9</td>
<td>0.0</td>
<td>11.0</td>
<td>+2.8</td>
</tr>
<tr>
<td>1.6–1.7</td>
<td>10.9</td>
<td>-0.2</td>
<td>10.8</td>
<td>-1.3</td>
</tr>
<tr>
<td>1.8–1.9</td>
<td>12.1</td>
<td>-0.3</td>
<td>11.7</td>
<td>-5.8</td>
</tr>
<tr>
<td>2.0–2.1</td>
<td>11.4</td>
<td>-0.4</td>
<td>12.6</td>
<td>-19</td>
</tr>
<tr>
<td>2.2–2.5</td>
<td>11.6</td>
<td>-0.6</td>
<td>12.3</td>
<td>-0.9</td>
</tr>
<tr>
<td>2.6–2.9</td>
<td>12.3</td>
<td>-1.8</td>
<td>11.5</td>
<td>-1.8</td>
</tr>
<tr>
<td>3.0–4.9</td>
<td>11.5</td>
<td>-2.0</td>
<td>10.5</td>
<td>-2.0</td>
</tr>
</tbody>
</table>

- "The median reductions in INR were greater when the pre-plasma Tx INRs were higher."
- "The median reduction in PTT was greater when the pre-plasma Tx PTTs were higher."

Updated TIC Rx

- Minimize crystalloids by targeting low BP
- Use plasma, 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)


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
PROMMT 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


The Fritsma Factor

PROMMT Plasma:RBC Ratio

UTHealth The University of Texas
Health Science Center at Houston

Hem death at 2.6 hrs

The Fritsma Factor
PROMMT Platelet:RBC Ratio

Earlier and higher ratios of plasma and platelets were associated with decreased in-hospital mortality in the first 6 hours. 1:1:1 is superior to 1:1:2

TRALI Versus CRALI

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

Tranexamic Acid (Cyclokapron) Rx

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


<table>
<thead>
<tr>
<th>CRASH-2</th>
<th>TXA</th>
<th>Placebo</th>
<th>RR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 10060</td>
<td>n = 10067</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any cause of death</td>
<td>1463 (14.5%)</td>
<td>1613 (16%)</td>
<td>0.91</td>
<td>0.0035</td>
</tr>
<tr>
<td>Bleeding death</td>
<td>489 (4.9%)</td>
<td>574 (5.7%)</td>
<td>0.85</td>
<td>0.0077</td>
</tr>
<tr>
<td>Thrombosis death</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 products

All-cause Mortality by Subgroup
Tranexamic Acid Versus Placebo

<table>
<thead>
<tr>
<th>Time from Injury (h)</th>
<th>TXA</th>
<th>Placebo</th>
<th>Risk ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>56.9 (3.92-7.94)</td>
<td>59.7 (3.96-7.94)</td>
<td>0.92 (0.71-1.20)</td>
</tr>
<tr>
<td>3-6</td>
<td>54.9 (3.92-7.94)</td>
<td>59.7 (3.96-7.94)</td>
<td>0.92 (0.71-1.20)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>54.9 (3.92-7.94)</td>
<td>59.7 (3.96-7.94)</td>
<td>0.92 (0.71-1.20)</td>
</tr>
</tbody>
</table>

The Fritsma Factor

Thromboelastograph

Pen displacement by viscoelastic changes

1946
Rotational Thromboelastometry

Thromboelastograph

Normal R & MA

Hypocoagulable

Hyperfibrinolysis

Thrombocytopenia
Trauma-induced Coagulopathy

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**Thromboelastometry**


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**TEM Monitor, No Transfusion, No rFVIIa**

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource

CRASH 2: 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?

Bottom Line
• 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
• New study: PROPPR