Management of Non-Compressible Hemorrhage in TCCC

Frank Butler, MD
John Holcomb, MD
30 March 2017
The Goal

ZERO Preventable Deaths from Trauma
Preventable Death on the Battlefield: OEF and OIF

Eastridge 2012 Study

- **4,596** U.S. deaths
- **87%** of combat fatalities were pre-hospital
- **24%** of the prehospital deaths potentially preventable
- **50%** of in-hospital deaths potentially preventable
Noncompressible hemorrhage is the NUMBER ONE cause of preventable death in US combat fatalities.
Compressible
- Tourniquets
- Hemostatic Dressings
- Junctional Tourniquets
- XStat

Non-Compressible
- Pelvic Binders

Both
- Minimize Evacuation Time to Surgical Capability
- Optimize TXA Use
- Prehospital Damage Control Resuscitation
- Avoidance of Platelet-impairing NSAIDs
- TCCC Triple-Option Analgesia Plan
- Hypothermia Prevention
Noncompressible Hemorrhage in TCCC

Can Be Done **Now**

- Minimize evacuation time to surgical capability
- Pelvic Binders
- Far-Forward Whole Blood
- Optimize TXA use; administer it immediately when indicated
- Avoidance of platelet-impairing NSAIDs
- Triple-Option Analgesia
- Hypothermia Prevention
COL (Ret) Russ Kotwal

The Effect of a Golden Hour Policy on the Morbidity and Mortality of Combat Casualties
Introduction

With the premise that battlefield casualties would benefit from reduced time between injury and care, and a firm belief that one hour was a matter of “morale and moral obligation to the troops,”...

...on June 15, 2009, SecDef Robert M. Gates directed a ≤60-minute standard, from call to treatment facility arrival, for prehospital helicopter transport of U.S. military casualties with critical injury...cutting in half the previous goal of two hours, and aligning with the “Golden Hour” concept.

The DoD Joint Trauma System evaluated compliance with this new ≤60-minute mandate and described patient injury, treatment, and transport time relative to morbidity and mortality outcomes.
TIME IS IMPORTANT!

RESULTS:

- In the total 21,089 casualty population:
  - %KIA (16.0 vs. 9.9; p<0.001) and CFR (13.7 vs. 7.6; p<0.001) were higher pre- vs. post-mandate, while
  - %DOW (4.1 vs. 4.3; p=0.712) remained relatively unchanged.

- Post-mandate CFR decline was associated with increasing % casualties transported ≤60-minutes (regression coefficient=-0.141; p<0.001), with projected vs. actual CFR equating to 359 lives saved.

- Among 4,542 casualties (mean ISS=17.3, mortality=10.1%) with detailed data, there was:
  - a decrease in pre- vs. post-mandate median transport time (90min vs. 43min; p<0.001), and
  - an increase in missions achieving ≤60-minute prehospital helicopter transport (24.8% [181/731] vs. 75.2% [2867/3811]; p<0.001).
CONCLUSION:

- A mandate by Secretary of Defense Gates reduced time between critical injury and definitive care for combat casualties in Afghanistan.

- Reduced prehospital transport time and increased treatment capability are likely contributors of casualty survival.
For NCH, Sooner Is Better. Period.

- Study Design: NTDBR Data Set
- Very large (2.5 million+) retrospective study
- Patients with significant TBI excluded
- Prehospital time and mortality
For NCH, Sooner Is Better. Period.

“In this analysis, we noted a precipitous incremental rise in patient mortality in patients with high-grade injuries at prehospital times 0-15 and 16-30 min, irrespective of mechanism.”
For NCH, Sooner Is Better. Period.

- 2 very large RCTs (total of 1925 trauma patients)
- Overall mortality rate at 1 hour is 4.6%
- Overall mortality rate at 2 hours is 2.5%
- Note exponential shape of curve between 1-3 hours
For NCH, Sooner Is Better. Period.

The University Hospital at this point in time had refused to staff the new ORs in Shock Trauma, requiring trauma patients to be moved to main hospital’s ORs.

“In one eight-month period I lost 15 patients just trying to get them from here over to the main hospital…”

Dr. Catherine Musemeche

R. Adams Cowley

P85 – R. Adams Cowley
Baltimore Shock Trauma
1969
Can Be Done **Now**

Minimize evacuation time to surgical capability

Pelvic Binders

Far-Forward Whole Blood

Optimize TXA use; administer it immediately when indicated

Avoidance of platelet-impairing NSAIDs

Triple-Option Analgesia

Hypothermia Prevention
TFC and TACEVAC

4. Bleeding
c. A pelvic binder should be applied for cases of suspected pelvic fracture - Severe blunt force or blast injury with one or more of the following indications:
   - Pelvic pain
   - Any major lower limb amputation or near amputation
   - Physical exam findings suggestive of a pelvic fracture
   - Unconsciousness
   - Shock
Pelvic Fractures in Combat Casualties

- Most commonly associated with dismounted IED attacks accompanied by amputations
- May also occur in severe blunt trauma (such as motor vehicle crashes and falls)
- 26% of service members who died in OEF/OIF had a pelvic fracture
- Bleeding pelvic fractures with hemodynamic instability have up to 40% mortality
Pelvic Fractures and Lower Limb Amputations Due to Dismounted IEDs

• 77 consecutive patients with traumatic lower limb amputation
  – 22% had associated pelvic fracture
    • Unilateral amputation: 10%
    • Bilateral amputation: 30%
    • Bilateral above knee amputation: 39%

• “This study demonstrates a high incidence of pelvic fractures in patients with traumatic lower limb amputations, supporting routine pre-hospital application of pelvic binders in this patient group”

Cross 2014
Does a pelvic binder control bleeding from a fractured pelvis?

- Prospective study of 585 patients with unstable pelvic fractures requiring transfer to a trauma center.
  - Those who received pre-transfer PCCD
    - required fewer blood transfusions (400 ml vs. 2000 ml)
    - Shorter LOS (6.6 vs. 11.8 days)
  » Fu 2013 Am J Emerg Med
What Exam Findings Are Suggestive of a Pelvic Fracture?

Exam Findings:

- Pelvic pain
- Laceration or bruising at bony prominences of the pelvic ring
- Deformed or unstable pelvis
- Unequal leg length
- Scrotal, perineal, or perianal bruising
- Blood at the urethral meatus
- Massive hematuria
- Blood in the rectum or vagina
- Neurologic deficits in lower extremities

Durkin – Am J Surg - 2006
Noncompressible Hemorrhage in TCCC

Can Be Done Now

Minimize evacuation time to surgical capability
Pelvic Binders
Far-Forward Whole Blood
Optimize TXA use; administer it immediately when indicated
Avoidance of platelet-impairing NSAIDs
Triple-Option Analgesia
Hypothermia Prevention
Fluid Resuscitation from Hemorrhagic Shock

“The historic role of crystalloid and colloid solutions in trauma resuscitation represents the triumph of hope and wishful thinking over physiology and experience.”

COL Andre Cap
J Trauma, 2015

There is an increasing awareness that fluid resuscitation for casualties in hemorrhagic shock is best accomplished with fluid that is identical to that lost by the casualty - whole blood.
## Characteristics of an Ideal Resuscitation Fluid

<table>
<thead>
<tr>
<th></th>
<th>Volume</th>
<th>Hemostatic</th>
<th>O2 Carrying Capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystalloid</td>
<td>Y</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Colloid</td>
<td>Y</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Plasma</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>1:1:1</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Whole Blood</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>
Damage Control Resuscitation

• 354 combat casualties transfused > 1 unit PRBCs
• 30-day mortality
• Similar ISS
• 100 got warm fresh whole blood – 95% survival
• 254 did not – 82% survival
• $P = 0.002$
Damage Control Resuscitation

The Ratio of Blood Products Transfused Affects Mortality in Patients Receiving Massive Transfusions at a Combat Support Hospital

Matthew A. Borgman, MD, Philip C. Spinella, MD, Jeremy G. Perkins, MD, Kurt W. Grathwohl, MD, Thomas Repine, MD, Alec C. Beekley, MD, James Sebesta, MD, Donald Jenkins, MD, Charles E. Wade, PhD, and John B. Holcomb, MD

• 246 combat casualties with massive transfusions
• Mortality at hospital D/C by plasma to RBC ratio
  • Low ratio (1:8) – Mortality was 65%
  • Medium ratio (1:2.5) – Mortality was 34%
  • High ratio (1:1.4) – Mortality was 19%
• P < 0.001
Advocates for:

- FWB as the optimal prehospital choice for hem. Shock
- TXA as adjunct to whole blood
- Balanced blood components if FWB not feasible
What do you mean you don’t have a whole blood program!!

CDR Geir Strandenes - THOR 2016
Optimal fluid resuscitation in trauma: type, timing, and total

Marcie Feinman\textsuperscript{a}, Bryan A. Cotton\textsuperscript{b}, and Elliott R. Haut\textsuperscript{a}

**KEY POINTS**

- Crystalloids should be limited in trauma patients.
- Damage control resuscitation with blood products that approximate whole blood is the current best practice for acutely injured patients until bleeding is controlled.
- Thrombelastography can help guide the use of blood products to ensure judicious administration.
- Targeted resuscitation using global and regional endpoints should be employed once hemostasis is achieved.
Forrest Gump on Normal Saline

I AM NOT A SMART MAN

BUT TOO MUCH SALINE SEEMS LIKE A BAD IDEA IN PENETRATING TRAUMA

Slide:
Dr. Marty Schreiber
Fluid Resuscitation for Hemorrhagic Shock in Tactical Combat Casualty Care

TCCC Guidelines Change 14-01 – 2 June 2014

Frank K. Butler, MD; John B. Holcomb, MD; Martin A. Schreiber, MD; Russ S. Kotwal, MD; Donald A. Jenkins, MD; Howard R. Champion, MD, FACS, FRCS; F. Bowling; Andrew P. Cap, MD; Joseph J. Dubose, MD; Warren C. Dorlac, MD; Gina R. Dorlac, MD; Norman E. McSwain, MD, FACS; Jeffrey W. Timby, MD; Lorne H. Blackbourne, MD; Zsolt T. Stockinger, MD; Geir Strandenes, MD; Richard B. Weiskopf, MD; Kirby R. Gross, MD; Jeffrey A. Bailey, MD
Updated Fluid Resuscitation Plan

Order of precedence for fluid resuscitation of casualties in hemorrhagic shock

1. Whole blood
2. 1:1:1 plasma:RBCs:platelets
3. 1:1 plasma: RBCs
4. (tie) Plasma (liquid, thawed, dried) or RBCs alone
8. Hextend
9. (tie) Lactated Ringers or Plasma-Lyte A

Butler et al – JSOM 2014
#9 (Tie)

- Study methods for increasing the availability, safety, efficacy, and shelf life of cold stored plasma, platelets, and whole blood in the deployed combat environment; in particular, a cryoprotective agent to allow Type O Low Titer Whole Blood to be frozen for storage, then used later with full hemostatic function of plasma and platelets.
Type O Low Titer Whole Blood with a Prolonged Shelf Life

• The “Holy Grail” of prehospital fluid resuscitation options?
• Identify Type O Low donors
• Collect the blood CONUS or closer to theater
• Screen for pathogens – FDA compliant
• New technology for cryopreservation to enable prolonged storage without loss of efficacy
• Move far-forward with electrically powered blood coolers (Wild 2013)
• 50-hour blood container now available (no power required)
• FWB is the best prehospital resuscitation fluid
• 75th Ranger Regiment program
• Type O – Low Titer Anti-A, Anti-B abs
• Donors pre-screened for type, titers, and infectious diseases
• Use donor pool to transfuse casualties in shock
Tactical DCR in 75th RR
Fisher et al 2015
28 January 2016
Somewhere in Theater

• 2 GSW to the chest – entered above the chest plates
• 2+ liters of blood from chest tube
• Resuscitated with thawed FFP, freeze-dried plasma, and PRBCs
• “Not a drop of crystalloid”
• Ketamine for pain – not opioids
• Found at surgery to have a right pulmonary vein injury
• Arrested on the table – revived successfully
• Survived and is doing well
• Great save!
MEMORANDUM FOR: Army Blood Program  
Navy Blood Program  
Air Force Blood Program

SUBJECT: Low Titer Group O Whole Blood for Contingency Support
1. Low titer Group O Whole Blood (WB) is a blood product which has been tested and found to have anti-A/anti-B antibody titers of <1:256. This product may be given to a recipient of any ABO type during damage control resuscitation based on the Tactical Combat Casualty Care (TCCC) guidelines dated 2 June 2014. Low titer Group O WB may be supplied to far forward special operations medical teams or to Role of Care 2/3 facilities which lack apheresis platelets.

2. ASBPO requests each Service Blood Program to be capable of producing FDA licensed low titer Group O Whole Blood NLT 1 Oct 2016 at one or more of their blood donor centers to support our blood program. Each donated unit of whole blood must be tested and found to have anti-A and anti-B titers of <1:256 as per current guidelines. While ASBPO is not requesting the Service Blood Programs maintain a whole blood inventory for routine mission support, the Services have the discretion to utilize this product to augment local facility massive transfusion protocols when deemed appropriate by the medical director and service transfusion medical consultant.

3. ASBPO point of contact for this action is Lt Col Jerome Vinluan at DSN 761-8011, commercial (703) 681-8011, or via email at Jerome.L.Vinluan.mail@email.mil.

ROLAND L. FAHIE, CAPT, MSC, USN
Director
**Hypotensive Resuscitation**

**Goals of Fluid Resuscitation**

- Improved state of consciousness (if no TBI)
- Normal radial pulse corresponds roughly to systolic blood pressure of 80 mm Hg
- Resuscitate to normal radial pulse
- BP targets: 80-90 mmHg SBP if no TBI
  - Minimum of 90 mmHg SBP in TBI Casualties
- Avoid over-resuscitation of shock from torso wounds - too much fluid volume may make internal hemorrhage worse by “Popping the Clot.”
Noncompressible Hemorrhage in TCCC

Can Be Done Now

- Minimize evacuation time to surgical capability
- Pelvic Binders
- Far-Forward Whole Blood
- Optimize TXA use; administer it immediately when indicated
- Avoidance of platelet-impairing NSAIDs
- Triple-Option Analgesia
- Hypothermia Prevention
Tranexamic Acid (TXA)

- Non-compressible hemorrhage is the leading cause of preventable death on the battlefield
- Tourniquets and Combat Gauze do not work for *internal* bleeding
- **TXA does!**
TXA Update

Beyond CRASH-2 and MATTERS

Frank Butler, MD
21 April 2016

The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial

- Subgroup analysis of 20,211 trauma patients based on time of administration of TXA
- Time of 1st TXA dose; only deaths due to bleeding
- 3076 overall deaths; 1063 due to bleeding
- Risk of death due to bleeding was significantly reduced (5.3% vs 7.7%) if TXA given within 1 hour of injury. At 1-3 hrs after injury, also significant (4.8 vs 6.1%) At times > 3 hrs, mortality increased.
• 896 consecutive combat casualties: TXA or no-TXA
• First report of TXA use in combat casualties
• TXA group had lower mortality (17.4% vs 23.9%; \(P=0.03\)) despite TXA group being more severely injured (ISS 25.2 vs 22.5)
• Benefit greatest in casualties who received a MT: mortality with TXA was 14.4% vs 28.1 % in the no-TXA group (\(p=0.004\))
• Both DVT and PE were increased in the TXA group, (PE in TXA MT group 3.2% vs 0% in no-TXA MT group); no PE fatalities in the study
FOR: JONATHAN WOODSON, M.D., ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)

SUBJECT: Recommendations Regarding the Addition of Tranexamic Acid to the Tactical Combat Casualty Care Guidelines 2011-06

EXECUTIVE SUMMARY

Traumatic hemorrhage is the leading cause of preventable death on the battlefield. A comprehensive review of the literature (as provided in this report) found that the antifibrinolytic tranexamic acid (TXA) has proven to decrease all cause mortality following major trauma. In trauma patients experiencing severe hemorrhage on the battlefield, tranexamic acid has the potential to reduce both mortality and morbidity. In light of these findings, the Defense Health Board recently approved a recommendation for the addition of tranexamic acid to the Tactical Combat Casualty Care (TCCC) guidelines.

Col Warren Dorlac
The use of tranexamic acid to reduce blood loss and transfusion in major orthopedic surgery: a meta-analysis

Fei Huang, MD, a,1 Dan Wu, PhD, b,1 Guangwen Ma, MD, a Zongsheng Yin, MD, c,* and Qing Wang, MD a

a Department of Orthopaedics, The Fourth Affiliated Hospital of Anhui Medical University, Hefei, Anhui, People’s Republic of China
b Department of Scientific Research and Medical Education, The First Affiliated Hospital of Anhui Medical University, Hefei, Anhui, People’s Republic of China
c Department of Orthopaedics, The First Affiliated Hospital of Anhui Medical University, Hefei, Anhui, People’s Republic of China

• Results: “A total of 46 randomized controlled trials involving 2925 patients were included. The use of TXA reduced total blood loss by a mean of 408.33 mL….“

Conclusions: TXA significantly reduced blood loss and blood transfusion requirements in patients undergoing orthopedic surgery, and did not appear to increase the risk of DVT.
TXA in Spine Surgery

A Systematic Review of the Effectiveness of Intravenous Tranexamic Acid Administration in Managing Perioperative Blood Loss in Patients Undergoing Spine Surgery

Jennifer Badeaux, DNP, CRNA, Diane Hawley, PhD, RN, ACNS-BC, CCNS, CNE

Conclusion:
“The results of this the meta-analysis suggest that TXA is effective in the reduction of intraoperative and postoperative blood loss for patients undergoing spine surgery.”
The best way to prevent death from hemorrhage is to PREVENT blood loss.

There is Level A evidence that TXA reduces blood loss in elective surgery patients.

There is Level A evidence that TXA does not increase the risk of thromboembolic complications in elective surgery patients.

TXA is given BEFORE the bleeding starts in elective surgery.
“Currently, TXA may be the best pharmacologic option for prehospital hemostatic interventions, and its administration in the field has been shown to be feasible in both military and civilian settings.”

TAMPIT Study looking at 2 and 4 mg dosing
Battlefield administration of tranexamic acid by combat troops: a feasibility analysis

Chris Wright

Quote: “Morphine auto-injectors are the obvious model for this drug.”

Data on IM TXA?
ASDHA Letter on TXA
9 October 2013

MEMORANDUM FOR ASSISTANT SECRETARY OF THE ARMY (MANPOWER AND RESERVE AFFAIRS)
ASSISTANT SECRETARY OF THE NAVY (MANPOWER AND RESERVE AFFAIRS)
ASSISTANT SECRETARY OF THE AIR FORCE (MANPOWER AND RESERVE AFFAIRS)
DIRECTOR, JOINT STAFF

SUBJECT: Use of TXA in Combat Casualty Care

- Response to CENTCOM Surgeon request
- TXA use no longer restricted to SOF and MTFs
- Need to accumulate data; monitor outcomes
“Traumatic hemorrhage remains the leading cause of death on the battlefield..... Joint Theater Trauma experts recommended adding TXA as an adjunct to severe hemorrhage management. Presently, TXA is not FDA-approved for this indication, and as such is considered an off-label use subject to a provider’s clinical judgment in a practitioner-patient relationship.”
“The Military Services and the Combatant Commands may authorize such use of TXA in the combat environment, consistent with current clinical practice guidelines and appropriate clinical oversight. The Services will accumulate outcome data and monitor adverse events. The Services will establish Service-specific policies regarding TXA administration, develop training and education plans, and assume all costs for implementation. TXA may be obtained through normal class VIII channels.”
TRAUAMA/BEST AVAILABLE EVIDENCE

Does the Use of Tranexamic Acid Improve Trauma Mortality?

Virginia Harvey, MD; JeanMarie Perrone, MD; Patrick Kim, MD

0196-0644/$-see front matter
Copyright © 2013 by the American College of Emergency Physicians.
http://dx.doi.org/10.1016/j.annemergmed.2013.08.028

BOTTOM LINE

According to the available evidence, tranexamic acid has been shown to significantly decrease mortality in bleeding trauma patients, with no significant increase in serious prothrombotic complications if administered within 3 hours of injury. There is, however, no evidence of benefit in patients with traumatic brain injury. As such, we recommend early treatment with tranexamic acid in trauma patients without isolated brain injuries who have or are at risk for significant hemorrhage and in patients who receive resuscitation with blood products, particularly if they require massive transfusion or have a high risk of death at baseline.
Question

• For a trauma patient with ongoing life-threatening extremity hemorrhage – what is the best time to apply a tourniquet?

  • Within 1 hour?
  • Within 3 hours?
  • RIGHT NOW?

• So – for a patient with non-compressible torso hemorrhage – when should you give TXA?

Illustration: Dr. Lenworth Jacobs Hartford Consensus
TXA – Why Wait 60 to 180 Minutes to Give It?

- CRASH-2 showed that giving TXA earlier than one hour is better than giving it later, but was not designed to show whether giving it even sooner after injury might improve outcomes.
- In elective surgery, TXA is given pre-operatively, or in extremity orthopedic surgery, just before the tourniquet is released.
- The best way to prevent death from hemorrhage is to PREVENT the blood from being lost in the first place.
- Give TXA IMMEDIATELY for casualties with non-compressible hemorrhage!
Noncompressible Hemorrhage in TCCC

Can Be Done **Now**

Minimize evacuation time to surgical capability
Pelvic Binders
Far-Forward Whole Blood
Optimize TXA use; administer it immediately when indicated

*Avoidance of platelet-impairing NSAIDs*
Triple-Option Analgesia
Hypothermia Prevention
Many Ibuprofen-Type Meds Can Help You Bleed to Death

- Aspirin, ibuprofen, ketorolac, and other nonsteroidal anti-inflammatory medicines (NSAIDS) other than meloxicam should be avoided while in a combat zone because they interfere with blood clotting.
- Aspirin, ibuprofen, and similar drugs may inhibit platelet function for approximately 7-10 days after the last dose.
- You **definitely** want to have your platelets working normally if you get shot.
- Acetaminophen (Tylenol) and meloxicam (Mobic) **DO NOT** interfere with platelet function – this is the primary feature that makes them the non-narcotic pain medications of choice.

*Text from TCCC Curriculum*
NSAID Use in Deployed US Forces

- Forward Operating Base in Afghanistan
- Soldiers surveyed about over-the-counter or prescription NSAID use

Self-Induced Bleeding Diathesis in Soldiers at a FOB in South Eastern Afghanistan

COL Melvyn Harris, MC USAR; MAJ Robert Baba, MS USAR; LTC Richard Nahouraii, MC USAR; COL Peter Gould, AN USAR

ABSTRACT Modern warfare necessitates that the physician recognize risk factors and clinical scenarios that contribute to the development of acute coagulopathy of trauma and the need for massive transfusion. To date, this is the only prospective study done in an active war zone that specifically looks at a self-induced bleeding diathesis problem among soldiers. If correct, then large numbers of soldiers are exposed to bleeding abnormalities well before sustaining injury.
“NSAIDs induce platelet dysfunction, disrupting the primary pathway in hemostasis..... a self-induced functional platelet disorder among significant numbers of soldiers located in hostile zones of imminent danger.”
NSAID Use in Deployed US Forces

**TABLE I.** Frequency of NSAID use among soldiers

<table>
<thead>
<tr>
<th>NSAID Use</th>
<th>Number of Soldiers $N = 175$</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily</td>
<td>91</td>
<td>52</td>
</tr>
<tr>
<td>2 + times weekly</td>
<td>40</td>
<td>23</td>
</tr>
<tr>
<td>Weekly</td>
<td>30</td>
<td>17</td>
</tr>
<tr>
<td>None</td>
<td>14</td>
<td>8</td>
</tr>
</tbody>
</table>

- 175 soldiers surveyed - **75% reported using NSAIDs more than twice a week**
- **TCCC**: Use acetaminophen and meloxicam for minor pain at your forward location!
Noncompressible Hemorrhage in TCCC

Can Be Done **Now**

Minimize evacuation time to surgical capability

Pelvic Binders

Far-Forward Whole Blood

Optimize TXA use; administer it immediately when indicated

Avoidance of platelet-impairing NSAIDs

**Triple-Option Analgesia**

Hypothermia Prevention
Warning: Morphine and Fentanyl Contraindications

- Hypovolemic shock – opioids may cause a further decrease in blood pressure
- Respiratory distress
- Unconsciousness
- Severe head injury
- **DO NOT** give morphine or fentanyl to casualties with these contraindications.

TCCC Curriculum
3. Moderate to Severe Pain
Casualty IS in hemorrhagic shock or respiratory distress

OR

Casualty IS at significant risk of developing either condition

- **Ketamine** 50 mg IM or IN
  Or

- **Ketamine** 20 mg slow IV or IO
Noncompressible Hemorrhage in TCCC

Can Be Done Now

Minimize evacuation time to surgical capability
Pelvic Binders
Far-Forward Whole Blood
Optimize TXA use; administer it immediately when indicated
Avoidance of platelet-impairing NSAIDs
Triple-Option Analgesia
Hypothermia Prevention
Hypothermia Prevention and Coagulation

• Even a small decrease in body temperature can interfere with blood clotting and increase the risk of bleeding to death.

• Casualties in shock are unable to generate body heat effectively.

• Wet clothes and helicopter evacuations increase body heat loss.

• Remove wet clothes and cover casualty with hypothermia prevention gear.

• Hypothermia is much easier to prevent than to treat!

Text from TCCC Curriculum
Use the HPMK to prevent hypothermia in casualties
Noncompressible Hemorrhage in TCCC

What is the impact of these interventions?
Reducing Deaths from Bleeding: Memorial Hermann 2017

Trends in 1029 trauma deaths at a level 1 trauma center: Impact of a bleeding control bundle of care

Blessing T. Oyeniyi, Erin E. Fox, Michelle Scerbo, Jeffrey S. Tomasek, Charles E. Wade, John B. Holcomb

Center for Translational Injury Research, Division of Acute Care Surgery, Department of Surgery, Medical School, The University of Texas Health Science Center at Houston, Houston, TX, USA

TCCC bleeding interventions as used in the civilian sector
Reducing Deaths from Bleeding: Memorial Hermann 2017

- Identify the bleeding patient
- Prehospital and hospital DCR
- Prehospital and hospital extremity and junctional tourniquets
- Prehospital and hospital pelvic binders
- Prehospital and hospital hemostatic dressings
- REBOA
- Coagulation monitoring with thromboelastography
- TXA for patients with significant fibrinolysis
- Decreased time to operating room
- Decreased time to interventional radiology
- Goal directed resuscitation with blood products as bleeding slows
“Concentrating on the first hour post injury, the primary cause of death changed from hemorrhage (60.3%) followed by head injury (37.5%) in 2005–2006 to mostly head injuries (52.7%) followed by hemorrhage (38%) in 2012–2013.”

- 37% reduction in bleeding deaths in the first hour
Reducing Deaths from Bleeding: Memorial Hermann 2017

- 11% absolute reduction in deaths from bleeding

![Bar chart showing reduction in deaths from bleeding]
On the Horizon

Options for the management of noncompressible hemorrhage in TCCC currently being evaluated
Noncompressible Hemorrhage: Future Treatment Options?

More Research and/or FDA Approval Needed

Dried Plasma - if no whole blood or 1:1
Compensatory Reserve Index Monitor
ResQFoam
REBOA
Re-Look at AAJT?
Pelvic Hemostatic belt
Dried Plasma Rather Than Hextend or Crystalloids When Whole Blood and RBCs Are Not Feasible
Explore all options to make an FDA-approved dried plasma product available for all U.S. military combat medical providers. This product should be able to be transfused to casualties of any blood type; should be able to withstand the temperatures encountered in military prehospital settings; should have a long shelf life, and should not be packaged in breakable containers.
FDA-Approved Dried Plasma Product

- Colloids and crystalloids are the LEAST desirable of the options for fluid resuscitation of hemorrhagic shock
- Dried plasma is a much better option
- FDP products are available in the near term

Photo – SGM F Bowling
Prehospital Plasma

- Liquid or thawed plasma is not an option for most ground troops
- Dried plasma (freeze-dried or spray-dried) is currently the best option for units not able to utilize liquid plasma
- Dried plasma contain approximately the same levels of clotting proteins as liquid plasma
- Most coalition partners are using freeze-dried plasma at present
- Outcomes data pending
- No FDA-approved dried plasma product at present – some SOF units have FDP under a treatment protocol
- Plasma should be available across the battlefield
Noncompressible Hemorrhage

More Research and/or FDA Approval Needed

Dried Plasma - if no whole blood or 1:1

Compensatory Reserve Index Monitor
ResQFoam
REBOA
Re-Look at AAJT?
Pelvic Hemostatic belt
Compensatory Reserve
Index Monitor

- Impending hemodynamic decompensation alert
- BEFORE blood pressure drops
- How much fluid is enough?
- Think of a blood volume “gas gauge”
Compensatory Reserve Index Monitor
Compensatory Reserve Index Monitor

“The CRI algorithm trends a patient’s intravascular volume, relative to the individual patient’s response to hypovolemia. Flashback’s CRI monitors estimate compensatory reserve values based on non-invasive arterial waveforms such as the photoplethysmogram (PPG) signal used by pulse-oximeters. The CRI algorithm continuously analyzes and compares the entirety of each PPG waveform in a window of time to trend Waveform features that are indicative of intravascular volume loss. Early identification of aberrant physiology would allow healthcare providers to intervene when the physiology is less complex and more likely to respond to therapy.”
Compensatory Reserve Index Monitor

Now FDA-approved
After review of the information submitted in the *de novo* request, FDA has determined that the CipherOx CRI™ Tablet indicated for the following:

*The CipherOx CRI Tablet is indicated for continuous noninvasive monitoring of functional oxygen saturation of arterial hemoglobin (SpO2), pulse rate (measured by an SpO2 sensor), and the Compensatory Reserve Index (CRI), which trends changes in intravascular volume relative to the individual patient’s response to hypovolemia.*

For patients with a finger thickness of 0.3” to 1” in hospital and pre-hospital settings.

*CRI trends with changes in intravascular volume relative to the individual patient’s response to hypovolemia, and should only be used by qualified medical providers as an adjunct to rather than as a replacement for traditional hemodynamic measures. CRI is indicated for adults (19-36 years old) in the supine position under non-motion conditions and without cardiovascular disease. CRI has not been studied in trauma patients.*

can be classified in class II with the establishment of special controls for class II. FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks and mitigation measures associated with the device type are summarized in Table 1.
If you have any questions concerning this classification order, please contact Nathalie Yarkony at 301-796-1235.

Sincerely,

Jonette R. Foy -S

Jonette Foy, Ph.D.
Deputy Director
for Engineering and Science Review
Office of Device Evaluation
Center for Devices and
Radiological Health
Research questions:
• Studies showing survival benefit in trauma?
• How does it account for:
  - A potential unrepaired vascular injury?
  - Moderate/severe TBI?
  - Effects of different resuscitation fluids?
• Needs to be optimized for combat medics
• Cost and durability?
Noncompressible Hemorrhage

More Research and/or FDA Approval Needed

Dried Plasma - if no whole blood or 1:1
Compensatory Reserve Index Monitor
ResQFoam
REBOA
Re-Look at AAJT?
Pelvic Hemostatic belt
Prehospital Control of Abdominal/Pelvic Hemorrhage

• REBOA? AAJT? ResQFoam? All 3?
ResQFoam

Self-Expanding Polyurethane Foam
ResQFoam

- Left figure - liver injury
- Right figure – iliac artery injury
ResQFoam
Way Ahead

• FDA approval to begin clinical trials obtained
• WHO is going to Use It? And where?
• Contraindicated in thoracic vascular injuries? (Holcomb, Rhee, etc)
• Indications for use?
• Unit cost?
• Initial training? Skills sustainment?
• TCCC Equipment Rapid Fielding Initiative?
Noncompressible Hemorrhage

More Research and/or FDA Approval Needed

Dried Plasma - if no whole blood or 1:1
Compensatory Reserve Index Monitor
ResQFoam
REBOA
Re-Look at AAJT?
Pelvic Hemostatic belt
# 9 (Tie)

- Perform comparative studies of resuscitative endovascular balloon occlusion of the aorta (REBOA) vs the Abdominal Aortic Junctional Tourniquet vs Polyurethane Self-Expanding Foam with an evaluation of the advantages and disadvantages of each option.
• Balloon occlusion of the aorta at a specified level
REBOA Times

• Zone 1 REBOA only tolerated for 30-45 minutes *(Holcomb – 2017)*

• Zone 3 REBOA – tolerated for approximately 120 minutes *(Holcomb 2017)*

• Not good evidence to date that this procedure can be reliably performed by non-surgeons – but *procedural fluency* is the key

• With significant training REBOA, could likely be performed with good success by non-surgeons
We Don’t Need REBOA to Occlude the Aorta in Zone 3

The AAJT will do that – but may have other adverse effects.
The Defense Health Board (DHB) recommended inclusion of the Combat Ready Clamp™ (CRoC) to the Tactical Combat Casualty Care Guidelines. I support the DHB recommendation.

However, since the release of the DHB recommendation, several more U.S. Food and Drug Administration-approved medical devices can control hemorrhage that is not amenable to the application of a tourniquet. In order to incorporate the new hemorrhage control capability throughout the Department, please remove the specific reference, "CRoC," from the Tactical Combat Casualty Care Guidelines and replace the reference with the more generic nomenclature, "CoTCCC recommended junctional tourniquet." This will better facilitate Service-level flexibility for acquisition, distribution, and training, yet preserve the intent of the DHB recommendation.

Dr. Jonathan Woodson
“The three CoTCCC-recommended junctional tourniquets are:
- The Combat Ready Clamp
- The Junctional Emergency Treatment Tool
- The SAM Junctional Tourniquet

“The Abdominal Aortic Tourniquet (a truncal tourniquet) is another option for junctional hemorrhage control, but has a shorter maximum length of application than the 3 junctional tourniquets listed above. The AAT is also relatively contraindicated in the presence of penetrating abdominal injuries, which often occur in association with junctional bleeding in casualties injured by the dismounted IED attacks currently prevalent in Afghanistan.”

Dr. Frank Butler/Col Jeff Bailey
After the publication of the TCCC Guidelines related to junctional hemorrhage management, the manufacturer of the AAT sought U.S. Food and Drug Administration (FDA) approval to change the device’s name, remove the contraindication for penetrating abdominal trauma, and increase the approved duration of application. The device was renamed the "Abdominal Aortic and Junctional Tourniquet" (AAJT) and received clearance by the FDA for the changes noted above.
The attached product information sheet (July 2015) for the AAJT now states:

1. "Indication for use: Control of Difficult Bleeding in the Pelvis, Inguinal Area and Axilla”

2. "Contraindications for use in abdominal placement
   - Known abdominal aortic aneurysm
   - Pregnancy”

3. "Recommended application time for placement: up to four hours”

4. "Do not remove until directed to do so by a physician“ (and how do THEY know???)

   * No animal or human data for 4-hour applications
The third arm of the study was designed to explore long-term effects of a 2-hour application of CRoC on the lower abdomen (umbilicus) to occlude the abdominal aorta at the bifurcation site and stop blood flow in both lower extremities. This was consistent with a new FDA-approved indication of CRoC for the control of bilateral hemorrhage in casualties with double amputees.

*Kheirabadi et al
J Trauma 2014*
AAJT Update
ISR Study #1

- Three animals in which blood flow was successfully blocked by CRoC for 2 hours developed significantly more disabilities than seen in the inguinal CRoC group. One animal showed no mobility improvement 3 days after surgery (scored 1) and had to be euthanized. This pig was also unable to void and had excessively full bladder during this period. When this animal and another pig that did not fully recover in 2 weeks underwent necropsy, deep and widespread necroses were found on their lumbar muscles, which could only be explained by total and permanent ischemia (Fig. 6). Further experimentation of this group was therefore halted.
AAJT Update
JTS Note

• No human or animal data have been found to date that document the safety and efficacy of the AAJT when it is applied to the abdomen in the presence of an unrepaired vascular injury proximal to the site of aortic occlusion.

• Surface wound anatomy does NOT necessarily correlate well with internal bleeding sites.
“In light of the above and after discussion with the JTS leadership, further evaluation of the AAJT for use in TCCC will be suspended. This decision is subject to change as new data become available or if the recommendations for use of this device are modified by its manufacturer.”
Physiological Consequences of Abdominal Aortic and Junctional Tourniquet (AAJT) Application to Control Hemorrhage in a Swine Model.

Kheirabadi BS¹, Terrazas IB, Miranda N, Voelker AN, Grimm R, Kragh JF Jr, Dubick MA.

**Abstract**

**INTRODUCTION:** Specialized tourniquets such as Abdominal Aortic and Junctional Tourniquet (AAJT) have been deployed for control of junctional hemorrhage with limited information concerning their efficacy and safety. We examined physiological effects of a 2-h abdominal application of AAJT to control groin hemorrhage in a swine model.

**CONCLUSION:** The ischemia-induced hyperkalemia and metabolic acidosis associated with AAJT application are life-threatening in spontaneously breathing subjects. Cardiopulmonary resuscitation appears necessary when AAJT is released to prevent life-threatening consequences.

- So - two hours of AAJT is a No-Go
- And the FDA-approved time is 4 hours
USAISR Study #3
Kheirabadi 1-2 Hour AAJT

Long-term Effects of Abdominal Aortic & Junctional Tourniquet (AAJT) Application to Control Junctional Hemorrhage in Swine

U.S. Army Institute of Surgical Research

Bijan S. Kheirabadi, PhD, Irasema B. Terrazas, MS, Nahir Miranda, MS, SPC Amber N. Voelker, BS, LTC Ammon W. Brown, DVM, and Michael A. Dubick, PhD

Military Health System Research Symposium
Kissimmee, FL
Aug 15-18, 2016
Results

Hind Leg Motor Function Assessment
(Tarlov Score)

- Stand and walk normally
- Stand and limping
- Can stand briefly
- Paraplegic

Post-op Days

Recovery rate:
- 1 hr: 6/6
- 1.5 hr: 3/6
- 2 hr: 0/3
- Control: 2/2
Results

Liver/muscle damage indicator enzymes

**AST**

- 2 hr
- 1.5 hr
- 1 hr
- Control

**ALT**

- 2 hr
- 1.5 hr
- 1 hr
- Control
Summary

- 1-hr occlusion of blood flow to lower extremities by AAJT was tolerated and did not cause irreversible neuromuscular damage in pigs.

- 2-hr lower body ischemia by AAJT application, however, persistently caused irreversible neural and muscular damages (paraplegia).

- The effects of 1.5-hr use of AAJT varied among individual animals, while some (60%) tolerated and eventually recovered neuromuscular function, others developed permanent paralysis.
Conclusions

- Ischemic reperfusion injuries associated with abdominal application of AAJT appear to be time dependent in swine.

- Application of AAJT to control lower body hemorrhage and to improve upper body circulation should not exceed one hour.

- Fluid administration and respiratory support at the time of release of AAJT also appear necessary to treat acute metabolic derangement (hyperkalemia and acidosis).
1. Animal study showing that mortality is not increased in presence of unrepaired vascular injury above the AAJT or Zone 3 REBOA? That could increase bleeding.

– John Holcomb comments– Not worth doing; will show increased mortality.
“Doing the animal study you describe would be like doing an animal study of extremity tourniquet application distal to an injury. The concept of proximal control on an injured vessel to decrease bleeding is central to vascular surgery. Kind of like asking if you should jump with a parachute. In my opinion.”
2. Identify an injury pattern that provides assurance that there is NOT a proximal vascular injury?
   – Case series of DCBI amputation injuries/fatalities?
   – How many had vascular injuries proximal to the aortic bifurcation?
   – What if 1 in 20 has a proximal vascular injury?
Dr. John Holcomb
500 Trauma Laparotomies

- 402 consecutive trauma patients who required trauma laparotomy.
- 42% penetrating trauma
- Research Question: Would Zone 3 REBOA (or AAJT) have helped them?

- Preliminary Answer: Aortic occlusion in Zone 3 would have harmed 90% of these patients.
- Need final results
- Need to do this with JTS/AFMES cases as well.
- Note: Zone 1 REBOA (and probably ResQFoam) would have helped 90%.
Noncompressible Hemorrhage

More Research and/or FDA Approval Needed

Dried Plasma - if no whole blood or 1:1
Compensatory Reserve Index Monitor
ResQFoam
REBOA
Re-Look at AAJT?
Pelvic Hemostatic belt
Pelvic Hemostatic Belt

Use of pelvic hemostasis belt to control lethal pelvic arterial hemorrhage in a swine model


• Swine model of uncontrolled hemorrhage
• Iliac artery injury
• PHB vs PASG (pelvic compartment) vs controls
• N = 6/6/5
• Hextend infusion 60 mL/min
• 60-minute study period
Pelvic Hemostatic Belt

- Not yet FDA-approved
Pelvic Hemostatic Belt

- Intra-pelvic pressure not measured
Survival

- PHB 6/6
- PASG 2/6
- Controls 0/5
Questions?