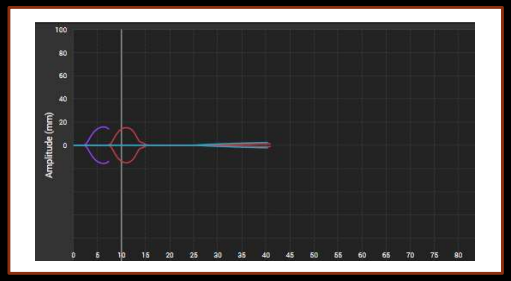
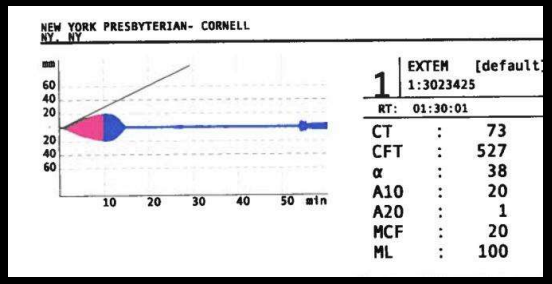




# Viscoelastic Testing is Superior to Conventional Lab based Coagulation Testing for Hemostatic Monitoring during Traumatic Hemorrhage: PRO!

**Melissa Cushing, MD**

**Professor of Pathology and Laboratory Medicine**
**Division Director of Transfusion Medicine and Cellular Therapy**
**Executive Vice Chair for Clinical Affairs, Dept of Pathology and Laboratory Medicine**

Weill Cornell Medicine

NewYork-Presbyterian
The University Hospital of Columbia and Cornell

# disclosures

- I am on the Scientific Advisory Board for Cerus and Haemonetics
- I have served as a consultant for Octapharma


143.
CTH
146.
CT
1.0
CTR
18.8
CS
17.2
PCS
1.6
FCS
Constantly think about how you could be doing things better and keep questioning yourself
- Elon Musk

# Limitations of Conventional Coagulation Testing

- Poorly reflect in vivo coagulation
  - PT/PTT
    - Tests run on plasma samples, removes interaction of platelets, red cells, WBC
    - Do not estimate overall clot strength – test read at the initiation of fibrin polymerization when less than 5% of total thrombin generated
  - Platelet counts give no information about underlying platelet function
- Lack sensitivity and specificity in acute bleeding (PT and PTT designed for drug monitoring)
- Significant time delay in getting results (45 minutes-1 hour in most hospitals)
- Conventional coagulation tests cannot evaluate fibrinolysis

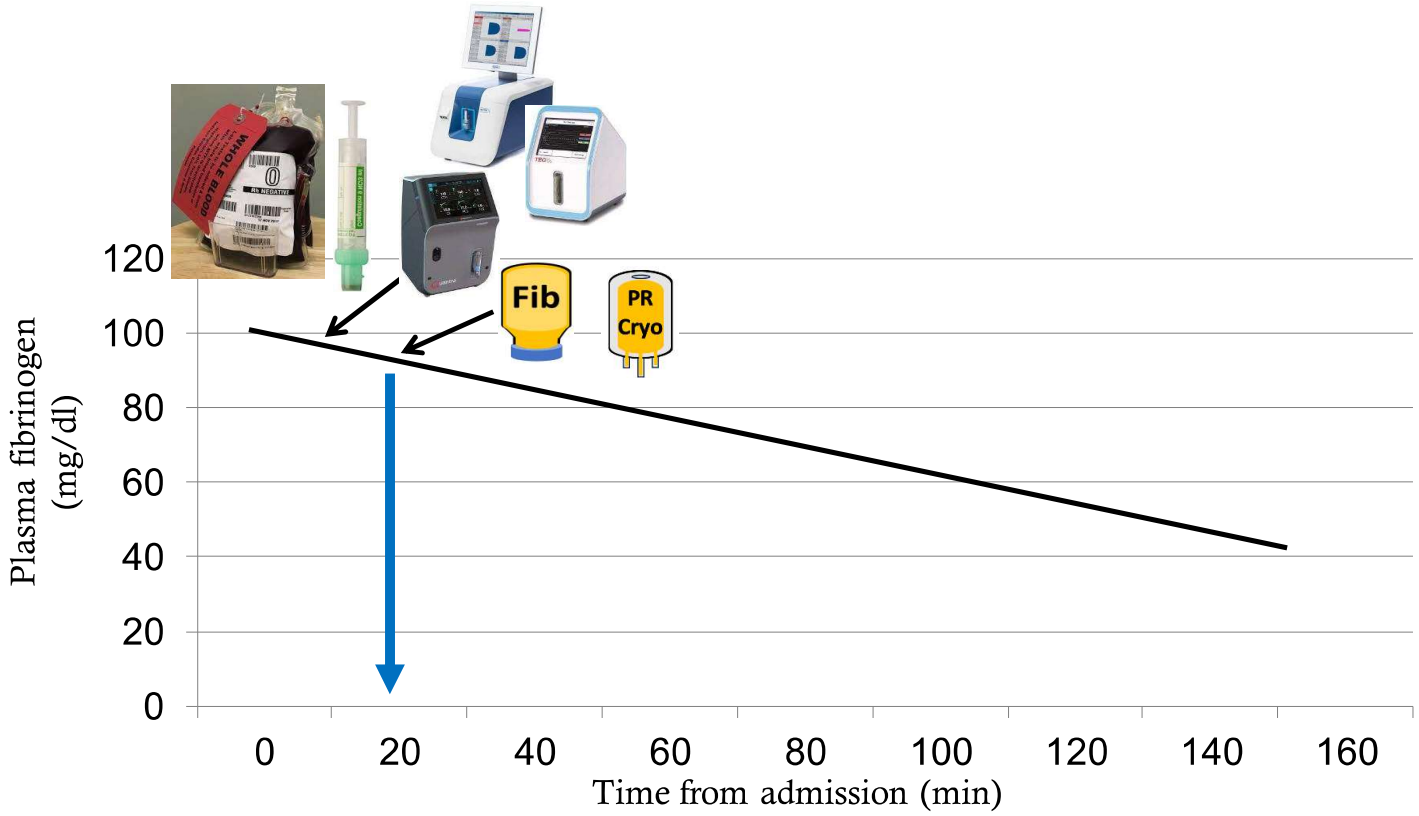
## precision medicine = rapid, goal directed therapy

- VET analyzes all components of the clot (except the endothelium and VWF) and directs therapy to a specific deficiency
- VET can provide simple, rapid evaluation for hyperfibrinolysis
- VET can be rapidly available in 5-10 minutes at the patient's bedside for immediate decision-making

# *time matters in trauma*

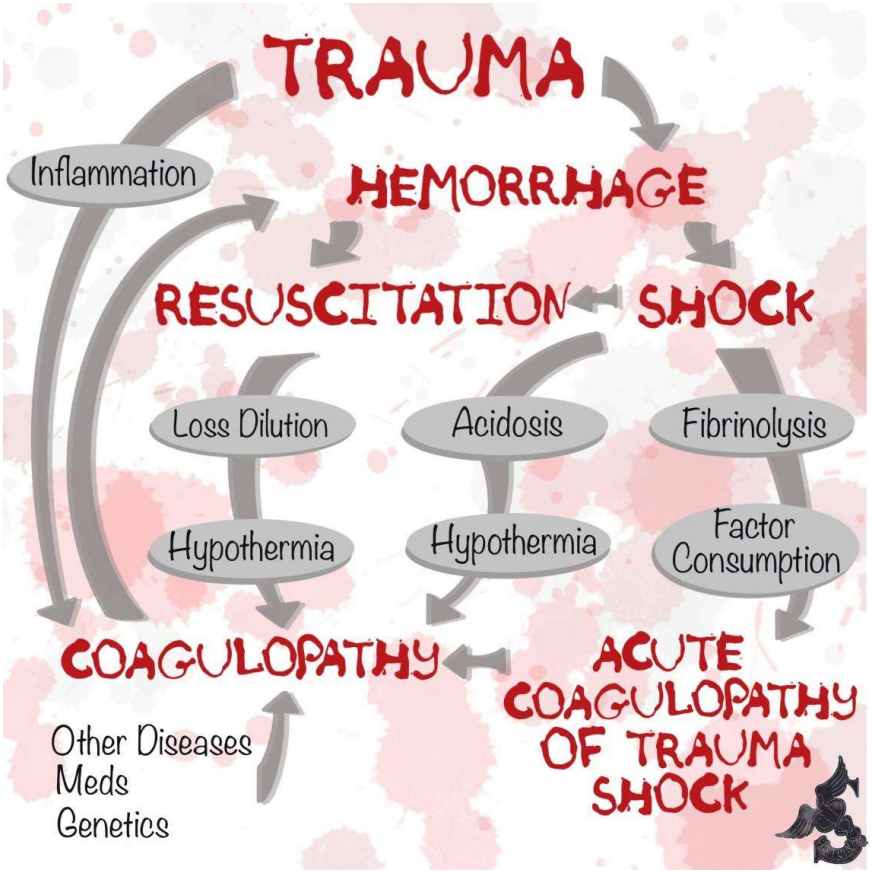

WARNING! NO BROWN BAGS IN THE COOLER
Plateletes/Cryo Placed in Coolers will be Wasted

2022 Approach in trauma: **Bleeding 300 mL per 30 min**




Rapid goal-directed therapy with POC testing in <u>20</u> minutes

**= 250 mL blood loss before definitive treatment**



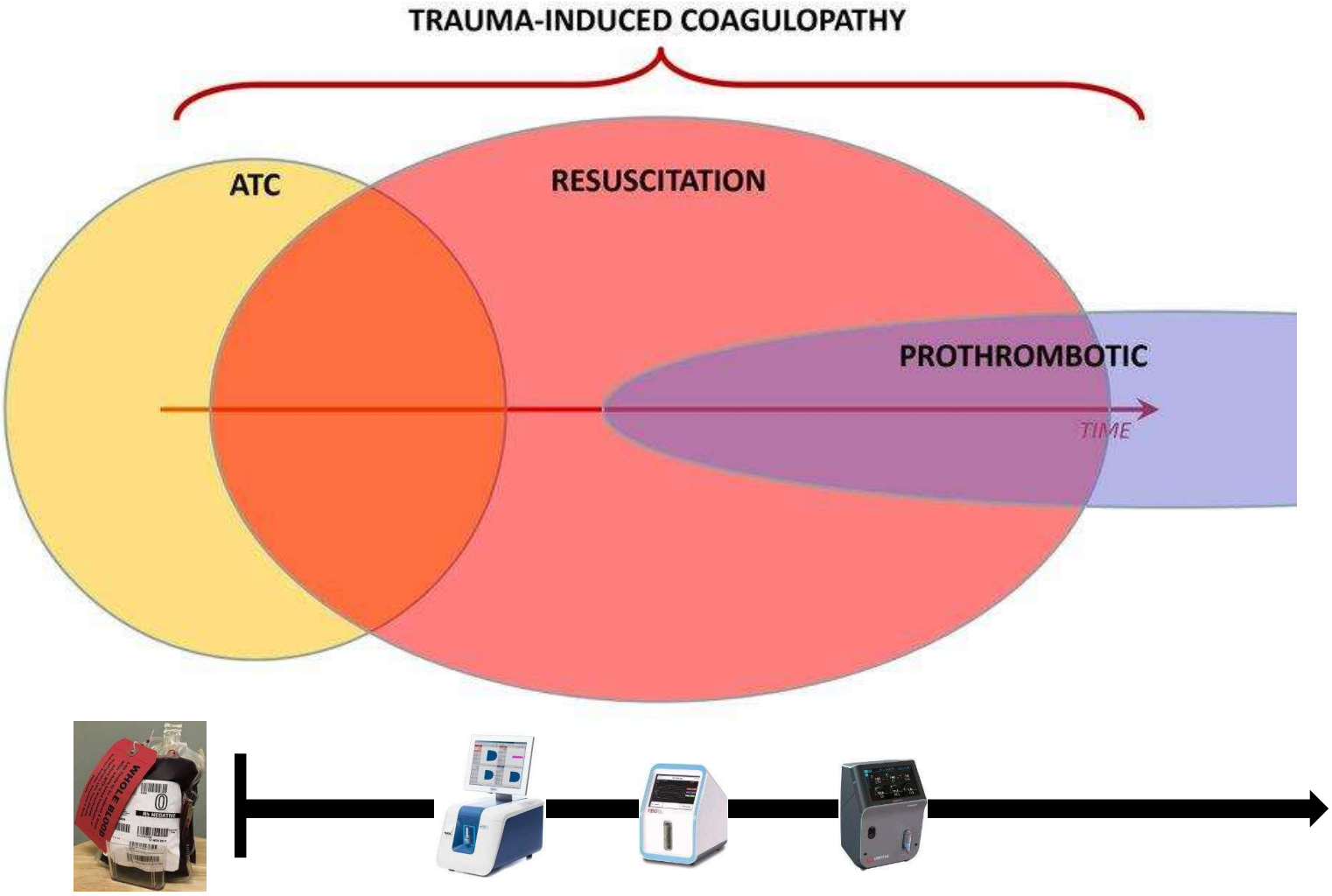

https://criticalcarenow.com/

-Trauma-induced coagulopathy is an umbrella term that includes multiple mechanisms of hemostasis derangement, as well as later thrombotic complications.

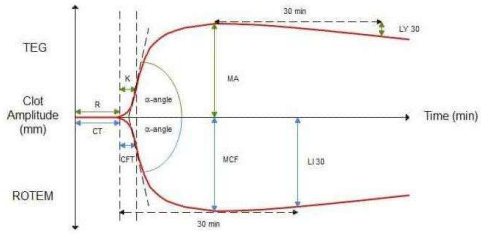
-Coagulopathy dependent on mechanism of injury, time from injury to admission, volume of fluids given, and other factors

-***One size does not fit all***. Tailored therapy is necessary.

Slide adapted from Karim Brohi



# Supportive Literature – Level of the evidence?



# Meta-analysis

# VET reduces mortality and numbers of transfused blood products

Meta-analysis – Grade IA

**Thromboelastography (TEG) or rotational thromboelastometry (ROTEM) to monitor haemostatic treatment in bleeding patients: a systematic review with meta-analysis and trial sequential analysis**

A. Wikkelsø, J. Wetterslev, A. M. Møller, A. Afshari

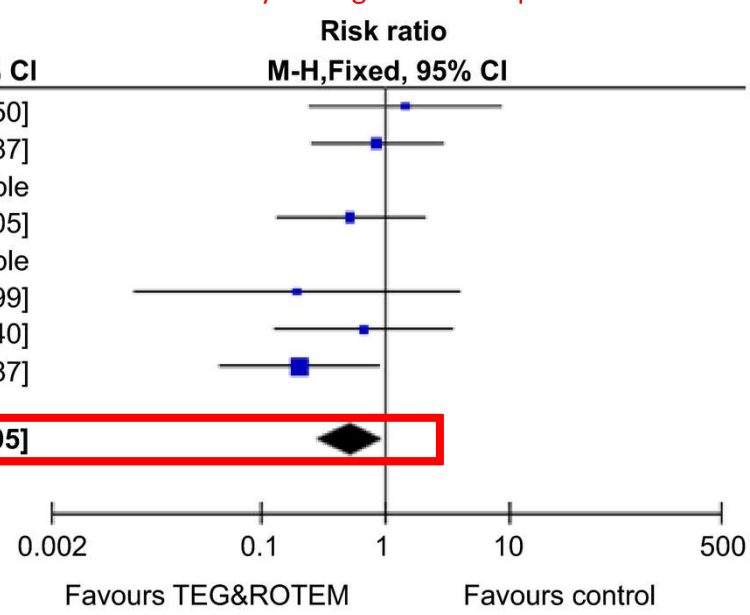
First published: 04 January 2017 | https://doi.org/10.1111/anae.13765 | Cited by: 36

Forrest plot of primary outcome: mortality at longest follow-up

| Study or subgroup | TEG or ROTEM Events | Total | Control Events | Total | Weight | Risk ratio M-H,Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Ak 2009 | 3 | 114 | 2 | 119 | 7.5% | 1.45 [0.25, 8.50] |
| Girdauskas 2010 | 4 | 27 | 5 | 29 | 17.8% | 0.86 [0.26, 2.87] |
| Nakayama 2015 | 0 | 50 | 0 | 50 | | Not estimable |
| Paniagua 2011 | 3 | 26 | 4 | 18 | 17.4% | 0.52 [0.13, 2.05] |
| Royston 2001 | 0 | 30 | 0 | 30 | | Not estimable |
| Shore-Lesserson 1999 | 0 | 53 | 2 | 52 | 9.3% | 0.20 [0.01, 3.99] |
| Wang 2010 | 2 | 14 | 3 | 14 | 11.1% | 0.67 [0.13, 3.40] |
| Weber 2012 | 2 | 50 | 10 | 50 | 36.9% | 0.20 [0.05, 0.87] |
| **Total (95% CI)** | | **364** | | **353** | **100.0%** | **0.52 [0.28, 0.95]** |
| Total events | 14 | | 26 | | | |

Heterogeneity $\chi^2 = 4.08$, d.f. = 5 ($p = 0.54$): $I^2 = 0\%$

Test for overall effect: $Z = 2.13$ ($p = 0.03$)




Wikkelso et al. Anaesthesia 2017, 72, 519–531

# The use of viscoelastic haemostatic assays in goal-directing treatment with allogeneic blood products – A systematic review and meta-analysis

Mathilde Fahrendorff[1*], Roberto S. Oliveri[1] and Pär I. Johansson[1,2,3]

Meta-analysis- Grade IA

**Results:** Fifteen RCTs ($n = 1238$ patients) were included. Nine trials referred to cardiothoracic patients, one to liver transplantation, one to surgical excision of burn wounds and one to trauma. One trial was conducted with cirrhotic patients, one with patients undergoing scoliosis surgery while one trial randomised treatment in post-partum females presenting with bleeding. The amount of transfused red blood cells (RBCs), fresh frozen plasma (FFP) and bleeding volume was found to be significantly reduced in the VHA-guided groups, whereas no significant difference was found for platelet transfusion requirements or mortality.

Fahrendorff *et al. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine* (2017) 25:39
DOI 10.1186/s13049-017-0378-9

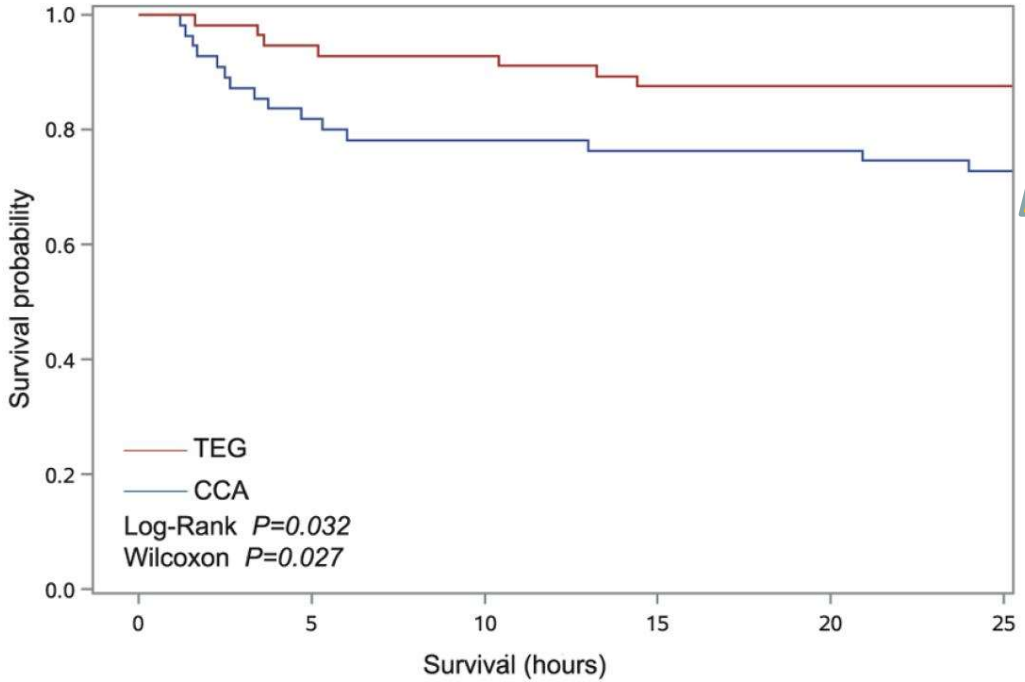
# Clinical trials

## Goal-directed Hemostatic Resuscitation of Trauma-induced Coagulopathy:

### A Pragmatic Randomized Clinical Trial Comparing a Viscoelastic Assay to Conventional Coagulation Assays

cbslocal.com

Clinical Trials –Grade IB




**Conclusions—**Utilization of a goal-directed, TEG-guided MTP to resuscitate severely injured patients improves survival compared with an MTP guided by CCA and utilizes less plasma and platelet transfusions during the early phase of resuscitation.

*Ann Surg.* 2016 June ; 263(6): 1051–1059.

**iTACTIC Subgroup Analysis**

- 28-day mortality In coagulopathic group (PTr> 1.2) :
  - CCT: 55%
  - TEG/ROTEM: 41%

  28-day mortality in patients who required massive transfusion (>10 RBCs)
  - CCT: 47%
  - TEG/ROTEM: 38%

## iTACTIC Subgroup Analysis – Severe Brain Injury Group

- 19% of major hemorrhage patients also had severe traumatic brain injury:
  - 28 day mortality:
    - CCT: 74%
    - ROTEM/TEG: 44%

**iTACTIC**

- 10% lower rate of thrombotic events in VET vs CCT.

# Caveats for interpreting iTACTIC results

- Most of the participating centers didn't use VET augmented MHP in their clinical trauma protocols routinely before iTACTIC (did they follow protocols?)
- Assumption that VET could reduce mortality or massive transfusion from 28% to 15% is very ambitious, especially since only 29% were even mildly coagulopathic (PTr > 1.2) and in the study overall mortality was only 16% for the entire cohort and massive transfusion was only seen in 27% of patients.
- Inaccurate to use CCT to define coagulopathy (PTr > 1.2 is close to reference range)
- Patients who are not coagulopathic are unlikely to see benefit from any type of coag testing
  - Very likely study is underpowered because of lower than expected incidence of TIC
- All patients may not benefit from a VET guided protocol (especially if they aren't coagulopathic)
- Took 1 hour from the first guided VET intervention to get products (products all frozen in the lab)

# Retrospective Studies

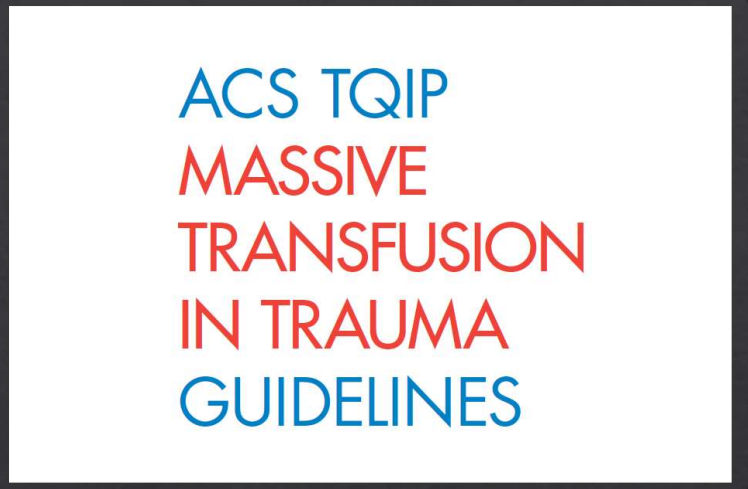
# Retrospective trials evaluating utility of VET in trauma

| Date | Study | Patient Population | Findings | VET |
|---|---|---|---|---|
| 2012 | Tapia N et al<br>VET vs MTP<br>Before/after MTP implemented | Massively transfused penetrating trauma at a single urban trauma center in U.S.<br>N=289 | MTP equivalent for patients receiving 6U or more RBC or blunt trauma; MTP worsened mortality in 10 or more units penetrating vs. VET | TEG |
| 2018 | Deng Q et al<br>Propensity score matched | Pediatric Trauma at 6 institutes in China<br>N=332 | Earlier treatment, less plasma tx, decreased LOS for VET protocol | ROTEM |
| 2019 | Guth C. et al<br>Before/after (VET + DCR + TXA) | Single center in France<br>Blunt and penetrating N=380 | VET decreased use of blood products, need for massive transfusion, and improved survival | |
| 2019 | Cohen J et al<br>Predict MTP and identify ACT | Military trauma in Afghanistan<br>N=40 | Integrating ROTEM into early identification of ATC increases detection | ROTEM |
| 2020 | Lammers DT et al<br>VET vs CCT<br>Trauma Registry | Dept of Defense<br>N=3320 | VET associated with decreased mortality | ROTEM |

RESEARCH Open Access

The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition

Donat R. Spahn[1], Bertil Bouillon[2], Vladimir Cerny[3,4,5,6], Jacques Duranteau[7], Daniela Filipescu[8], Beverley J. Hunt[9], Radko Komadina[10], Marc Maegele[11], Giuseppe Nardi[12], Louis Riddez[13], Charles-Marc Samama[14], Jean-Louis Vincent[15] and Rolf Rossaint[16*]



ACS TQIP
MASSIVE
TRANSFUSION
IN TRAUMA
GUIDELINES

# Guidelines

# What does Dr. Callum recommend?

Randomized Controlled Trial > Clin Chim Acta. 2019 Aug;495:253-262.
doi: 10.1016/j.cca.2019.04.066. Epub 2019 Apr 17.

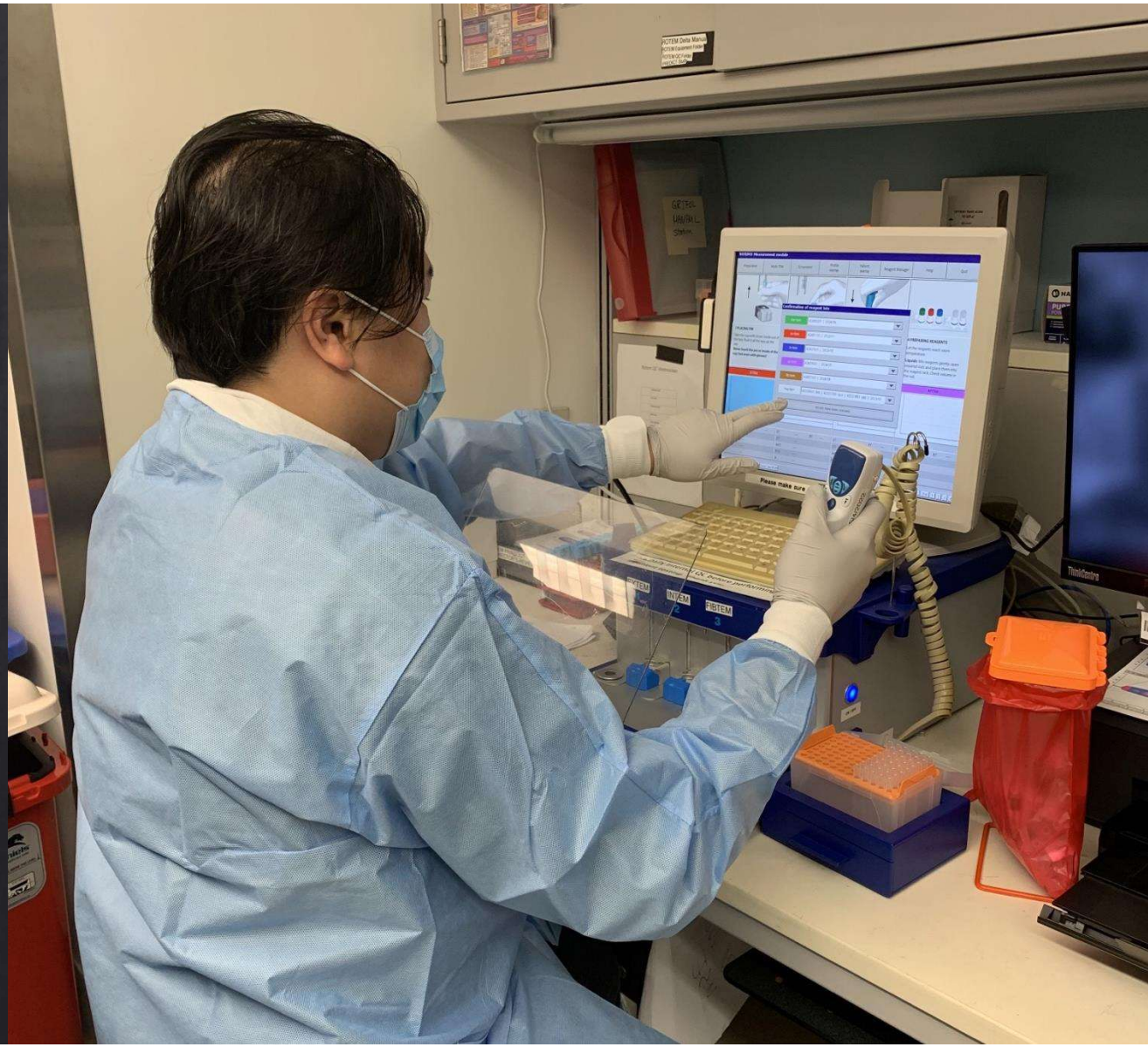
## A comparative study of viscoelastic hemostatic assays and conventional coagulation tests in trauma patients receiving fibrinogen concentrate

Henry T Peng [1], Bartolomeu Nascimento [2], Homer Tien [2], Jeannie Callum [2], Sandro Rizoli [3], Shawn G Rhind [4], Andrew Beckett [5]

**Conclusions:** TEG and ROTEM detected increases in clot strength following early use of fibrinogen. ROTEM also detected changes in coagulation time and clot lysis. Both were better than CCTs for monitoring coagulation profiles and predicting transfusion requirements.

VET are performed by professionals

But… we have choices



# Turnaround time is critical for traumatic hemorrhage

> Transfusion. 2010 Dec;50(12):2547-52. d

## Development of a rapid … age panel

Wayne L Chandler [1], Chris Ferrell, Sara Trin

**Jeannie L. Callum, BA, MD, FRCPC, CTBS**
*Clinical Pathology*
*e-mail: jeannie.callum@sunnybrook.ca*
**Sandro Rizoli, MD, PhD, FRCSC, FACS**
*Department of Surgery*
*Sunnybrook Health Sciences Centre*
*Toronto*
**Jacob Pendergrast, MD, FRCPC**
*University Health Network*
*Toronto, Ontario, Canada*

The 10 modifications made to standard practice were as follows:

1. Emergency hemorrhage panels prioritized over all other STAT and routine samples.
2. PTT removed from their hemorrhage panel.
3. Thrombin time (TT) removed from the hemorrhage panel.
4. Samples moved directly to testing area upon arrival to the laboratory, with computer entry and accessioning labels performed while the sample was commencing centrifugation.
5. Centrifugation time shortened from 8 minutes at 2000 × *g* to 2 minutes at 4440 × *g*.
6. Checks for clots eliminated after determining that clots in samples did not cause a clinically significant impact on the PT result and would only result in one erroneous fibrinogen result (normal to falsely low reading) in 2300 samples.
7. Checks for hemolysis eliminated after determining that no clinically significant impact on the PT or the fibrinogen result was noted.
8. Critical results not repeated before release.
9. All results, critical or not, called to the clinical team immediately.
10. Calibration curve for fibrinogen extended down to 53 mg/dL. If the result fell below this level, the result was reported as less than 53 mg/dL instead of doing the standard dilutions and repeat testing to get an "exact" result.

Too Complicated

And sample must still be delivered to a Central Lab

# So how do we successfully deploy VET in trauma?

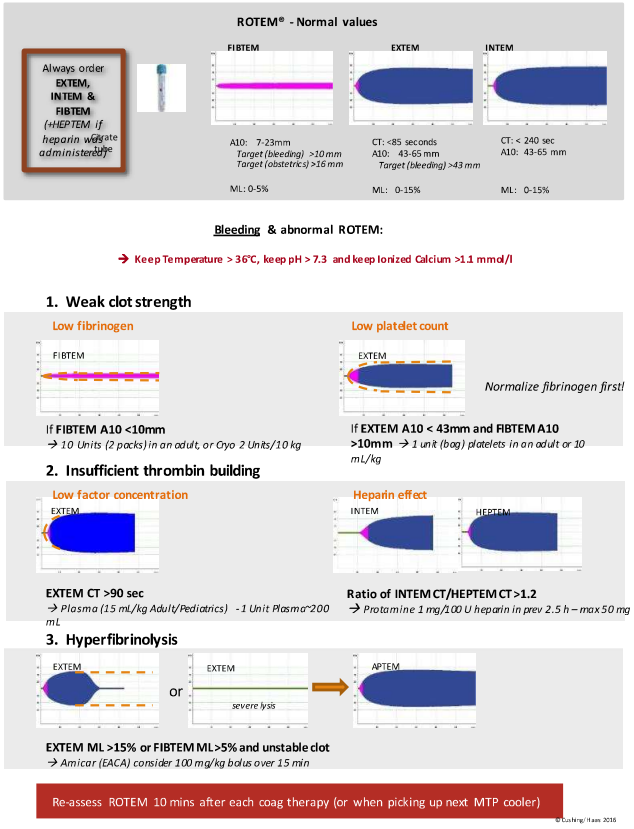
1) Ensure accurate testing
   a. Proper sample collection (fill the citrate tube correctly)
   b. Proper transport (pneumatic tube may affect results)
   c. Proper test performance with trained operators, proper QC and calibration of instrument
2) Integrate VET results with clinical decision-making (algorithm-based approach), also taking in account clinical factors
3) Use data driven thresholds/triggers for transfusions

# 4) Utilize algorithms

Trauma Bleeding Algorithm

Weill Cornell Medicine

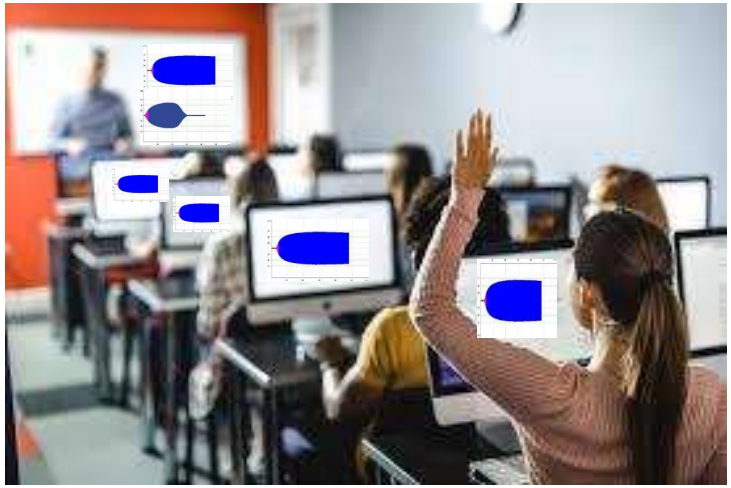
## ROTEM *Bleeding* management



# So how do we successfully deploy VET in trauma?

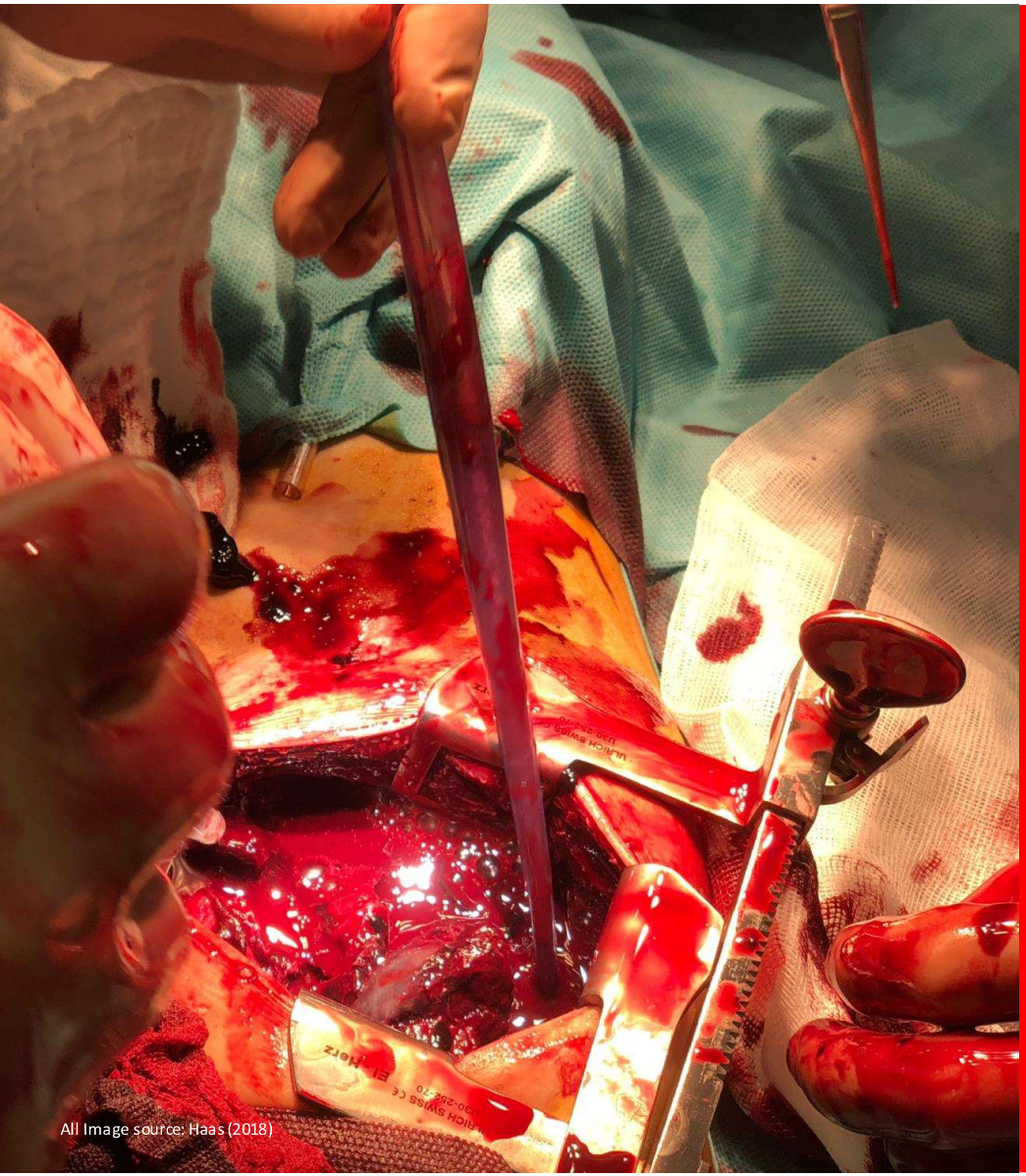
5) Ensure an iterative testing algorithm, fix problem and reassess to ensure coagulopathy is resolved
6) Provide immediate access to results (remote viewing capability from anywhere)
7) Remind physicians that VET is conducted under ideal lab settings (enough ionized Ca, normothermia, normal pH), patient may not be in this condition.
8) Educate anesthesiologists trauma surgeons, and other team members in VET interpretation

Ongoing education and algorithm reinforcement are important!



# If you build it, they will come?


143.
CTH
146.
CT
1.0
CTR
18.8
CS
17.2
PCS
1.6
FCS
Constantly think about how you could be doing things better and keep questioning yourself
- Elon Musk



All Image source: Haas (2018)

# I know how I want to treat my patient.


Image source: https://pixabay.com/photos/thinking-thinking-work-man-face-272677/
License: CC Public Domain.

Slide courtesy of Thorsten Haas


normal


THANK
YOU