# The Staging of Trauma-Induced Coagulopathy: *Monitoring & Therapeutic Implications*

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# Disclosures

*The opinions or assertions contained herein are the private views of the author and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.*

# More Important Disclosure

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*revie* *in Dr.*
*Mo* *ced*
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*consult* *, I must*
*disclos* ***fied by***

***I am s*** ***rauma***

# Overview

**Staging TIC?:** ATC, hyperfibrinolysis vs. “shutdown,” hypercoagulability, DIC, “bloody vicious circle,” clinical staging?

**Limitations of monitoring:** no good answers, not sure what any of the results really mean

**Therapeutic implications:** goal-directed therapy? Empiric therapy? No therapy? **First, do no harm: don’t overdo it.**

**RDCR considerations:** pre-hospital/POI care, prolonged field care

# Terminology & Up Front Issues

**ATC:** acute traumatic coagulopathy

-- pre-intervention, early coagulation disturbance (PT, INR, aPTT)

**TIC:** trauma-induced coagulopathy

-- broadly, the coagulation changes including ATC and continuing through first few days post-trauma

**Problems:** no baseline, admission studies, missing data over time, plasma samples, dilution effects ignored, clot-based assays → **WE'RE GOING TO GET THIS WRONG!**

# Why we care about TIC

**Having TIC, as defined by admission INR >1.5, is associated with bad outcomes (US combat trauma patients). Mean INR was 1.5 in transfused patients.**

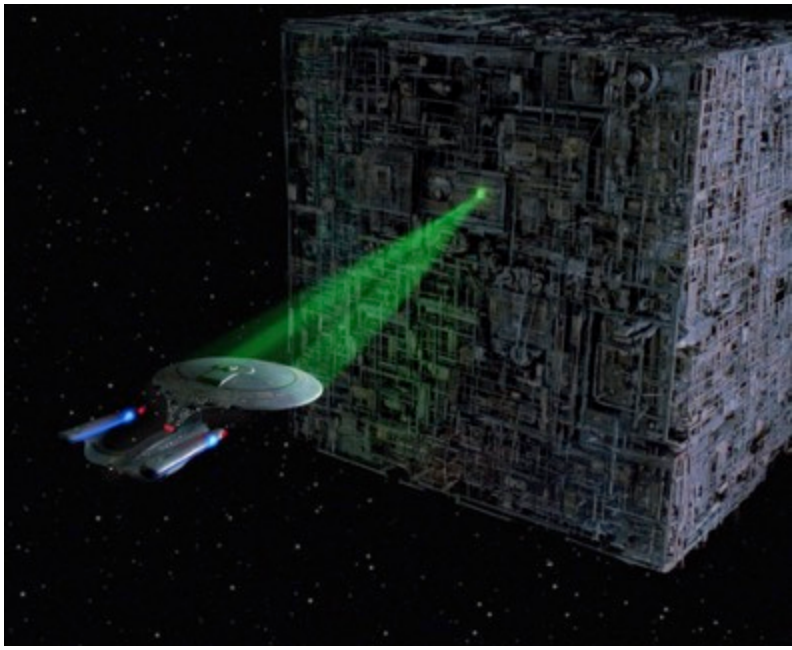
**TABLE 3.** Factors Associated with Survival Outcomes: Survivor Status and Blood Use Versus Coagulopathy

| Parameter | INR < 1.5 | INR > 1.5 | *p* |
|---|---|---|---|
| n | 1,224 | 592 | <0.001 |
| INR, mean (SD) | 1.2 (0.2) | 2.2 (1.0) | <0.001 |
| Nonsurvivors, % | 6 | 30 | <0.001 |
| Blood use, U per patient | 6 | 10 | <0.001 |
| IQR | 2–12 | 4–23 | |

(*J Trauma Acute Care Surg*. 2012;73: S445–S452.

# TIC Schools of Thought

- You are anticoagulated!
  - Protein C as the driver
- Fibrinolysis is THE problem!
  - Followers of CRASH
- CRASH is EVIL!
  - TEG says, “No TXA for you!”
  - Shutdown vs. lysis vs. normal
- All you need is love… er, I mean *FIBRINOGEN*!
  - And maybe PCCs
- It’s really all just DIC of either thrombotic or fibrinolytic phenotype…
  - Just have some sake and thrombomodulin, ATIII, TXA…relax



**Resistance is futile…**

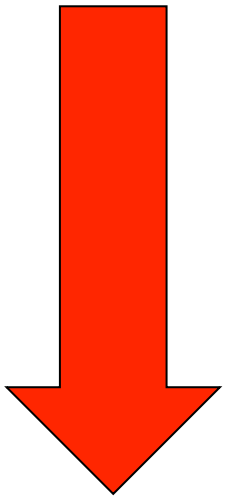
**You will be assimilated!**

# Lighting the fire…

# Stage 1: normal early response

- Hemorrhage causes: Shock & Coagulopathy
  - Decreased perfusion → **hypoxia**, **cell injury**, ↓metabolism → **hypothermia**
  - **Release reactions**: Catecholamines, tPA, vWF, TF/PDI, DAMPs, PAMPs, PS/MPs, cytokines, ROS/RNS, EC glycocalyx
  - **Protease activation**: coagulation & complement proteases
  - **Cellular activation**: platelets, neutrophils, endothelium, etc. → proteins & cells stick
  - **Low BP → movement of interstitial fluid into vascular compartment (dilution: by 1/3 if HCT 45→30)**

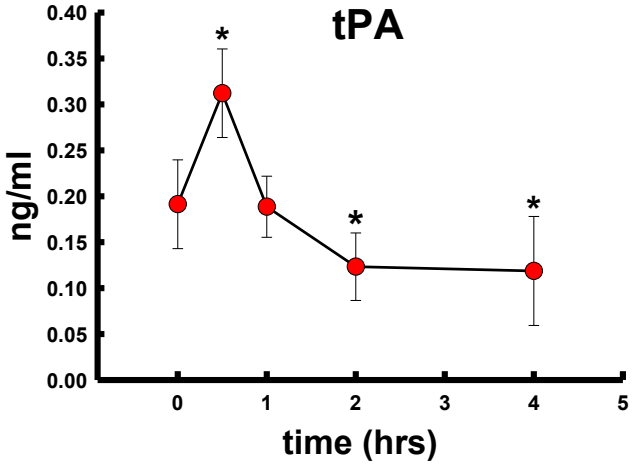
***Normal response***

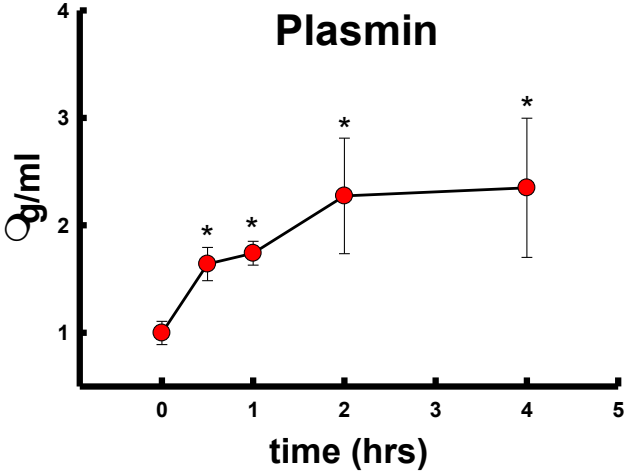


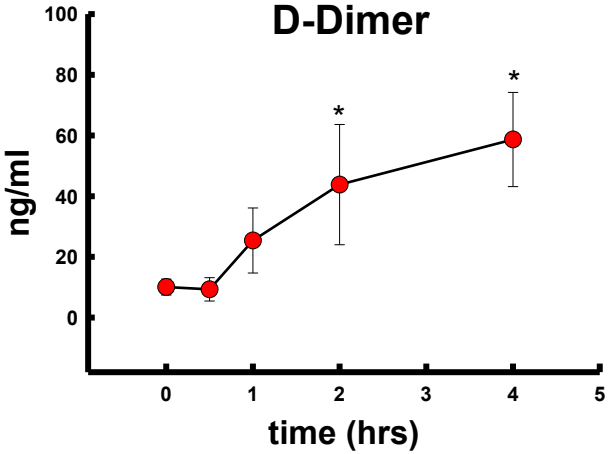
***Loss of auto-regulation?***

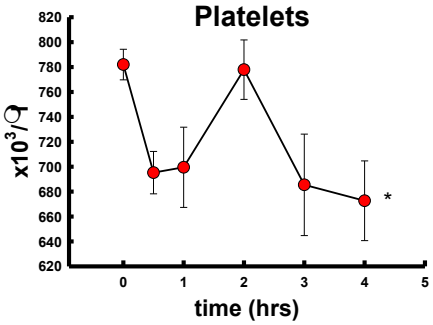
**Net effect: thrombin↑, fibrinogen↓, DDimers ↑, cells & proteases activated, blood diluted**

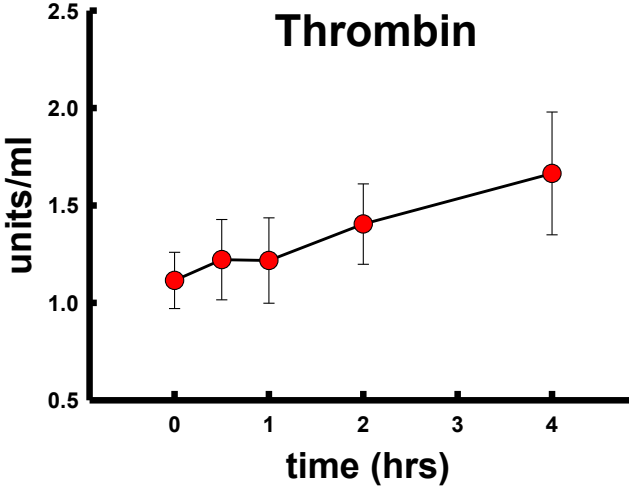
# Acute Traumatic Coagulopathy? Animal Models

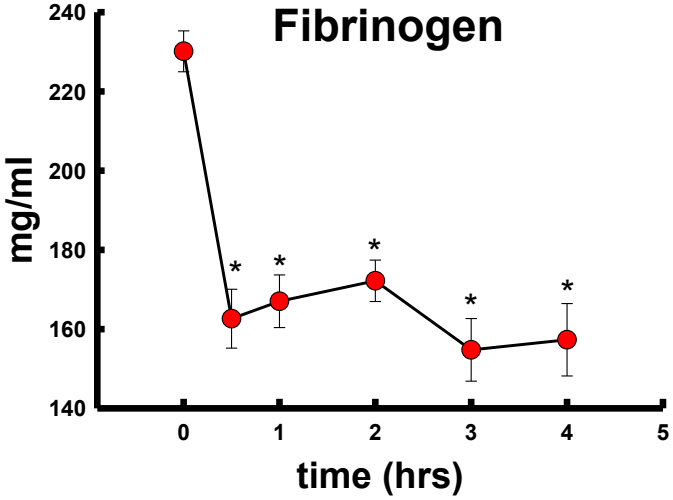


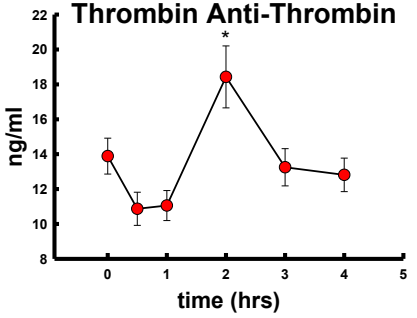



# What about Protein C anticoagulation?

**"xigris" dose**

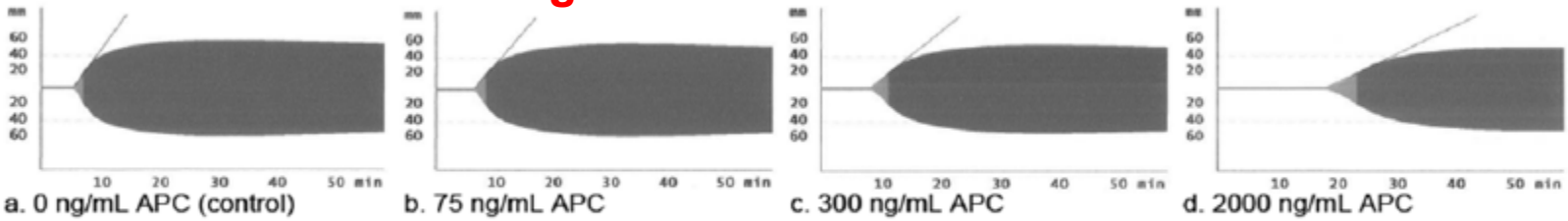



**Fig 1. Characteristic ROTEM EXTEM tracings from a study subject.** In every single one of the 20 subjects, as depicted here, increasing concentration of aPC produced ROTEM tracings consistent with worsening acute traumatic coagulopathy.

doi:10.1371/journal.pone.0150930.g001

| Reported doses in Howard et al. (ng/ml) | Converted doses in Howard et al. (nM) | Potential doses* in Howard et al. (nM) | Reported doses in Campbell et al. (nM) |
|---|---|---|---|
| **0** | 0 | 0 | 0.001 |
| | | | 0.01 |
| | | | 0.10 |
| **75** | **1.33** | | **1.00** |
| **300** | 5.34 | 2.67 | 3.30 |
| | | 10.68 | 10.00 |
| **2000** | 35.59 | | 33.00 |
| | | 71.18 | 100.00 |

# What about Protein C anticoagulation?

**1245 patients, 10 trauma centers (PROMMTT)**
**In 69 patients, PC *activity* drops 30%**
**aPC 37ng/ml**

TABLE 4. Factor Levels by INR and PTT-Based Coagulopathy

| | INR-Based | | | PTT-Based | | |
|---|---|---|---|---|---|---|
| | Coagulopathic (n = 69) | Noncoagulopathic (n = 87) | *p* | Coagulopathic (n = 32) | Noncoagulopathic (n = 123) | *p* |
| PT | 18.5 (16.5–24.0) | 14.9 (13.8–16.6) | <0.001 | 21.0 (16.8–28.9) | 15.6 (14.2–18.0) | <0.001 |
| PTT | 32.6 (27.5–38.0) | 26.9 (23.4–30.5) | <0.001 | 38.2 (32.9–48.6) | 27.2 (23.9–31.6) | <0.001 |
| Fibrinogen | 279 ± 34 | 209 ± 11 | <0.001 | 213 ± 18 | 271 ± 30 | <0.001 |
| Factor II | 61.9 ± 24.0 | 74.5 ± 26.1 | 0.01 | 52.3 ± 26.0 | 72.9 ± 24.1 | 0.001 |
| Factor V | 35.1 ± 23.0 | 57.6 ± 30.4 | <0.001 | 24.8 ± 20.0 | 54.2 ± 28.7 | <0.001 |
| Factor VII | 74.0 ± 29.9 | 91.5 ± 37.6 | 0.01 | 67.7 ± 26.8 | 87.4 ± 36.0 | 0.01 |
| Factor VIII | 302.0 ± 237.4 | 405.6 ± 237.4 | 0.01 | 180.2 ± 143.7 | 407.2 ± 240.7 | <0.001 |
| Factor IX | 108.4 ± 78.1 | 125.4 ± 102.2 | 0.27 | 91.9 ± 48.6 | 124.6 ± 99.1 | 0.02 |
| Factor X | 60.3 ± 25.0 | 72.5 ± 32.6 | 0.02 | 57.0 ± 27.6 | 69.2 ± 29.9 | 0.07 |
| Antithrombin III | 70.7 ± 24.8 | 80.6 ± 27.0 | 0.01 | 68.6 ± 25.5 | 78.4 ± 26.3 | 0.06 |
| D-dimer | 4.0 (1.4–20.0) | 3.8 (0.0–14.8) | 0.25 | 12.8 (4.0–20.0) | 3.0 (0.0–15.5) | 0.02 |
| Protein C | 71.3 ± 24.9 | 87.9 ± 32.2 | <0.001 | 66.5 ± 28.6 | 84.3 ± 29.7 | 0.003 |
| aPC | 37.2 (13.5–64.6) | 8.1 (1.1–16.5) | <0.001 | 37.2 (17.5–64.6) | 6.9 (1.9–12.8) | 0.001 |

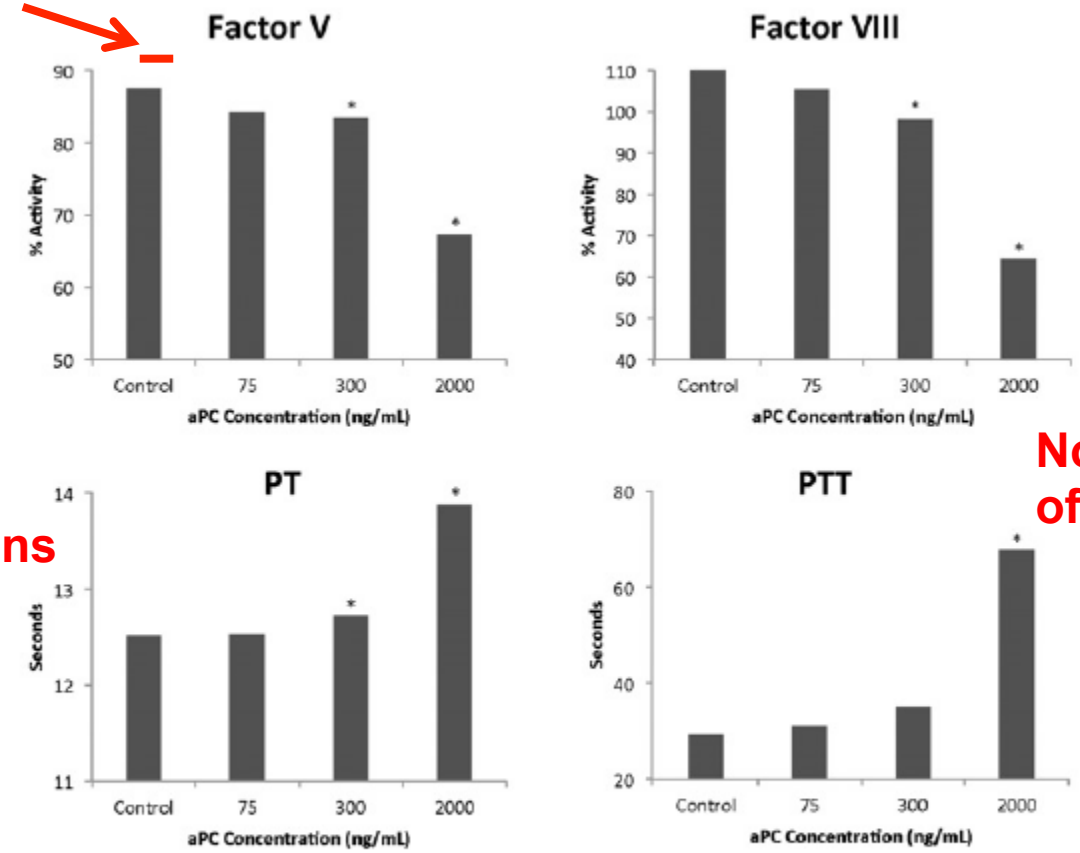
*J Trauma Acute Care Surg*. 2013;75:S40–S47.

# What about Protein C?

**Reported clinical aPC range**

**"xigris" dose is 75ng/ml**

**Total PC in humans 4000ng/ml**




**No "de-repression" of lysis**

**Fig 3. Changes in standard coagulation measures and factor activity assays by aPC concentration.** Findings were confirmed in conventional plasma tests, with significantly increased PT and PTT at higher levels of APC. Corresponding decreases in Factors V and VIII are consistent with the primary anticoagulant mechanism of APC. * indicates $p$-value < 0.05 by mixed effects model by-group analysis, compared to control. PT, prothrombin time, PTT partial thromboplastin time.

PLOS ONE | DOI:10.1371/journal.pone.0150930 March 23, 2016

# Is thrombin really a limiting factor?

**TABLE 4.** Patient Demographics, Injury, Resuscitation Volumes, and Outcomes in Hypocoagulable Patients

| | Nonhypocoagulable Peak ≥ 250 (n = 285) | Hypocoagulable Peak < 250 (n = 58) | *p* |
|---|---|---|---|
| Demographics | | | |
| Age | 37 (28 to 52) | 44 (28 to 54) | 0.4282 |
| Male | 237 (79%) | 52 (88%) | 0.0976 |
| Injury | | | |
| Penetrating | 87 (30%) | 8 (14%) | 0.0717 |
| GCS score | 14 (3 to 15) | 11 (3 to 15) | 0.0710 |
| w-RTS | 7 (4.1 to 7.8) | 6.4 (4.1 to 7.84) | 0.8448 |
| Head AIS score | 0 (0 to 3) | 3 (0 to 4)* | 0.0083 |
| ISS | 16 (9 to 25) | 25 (13 to 30)* | 0.0031 |
| Base excess | −2 (−5 to 1) | −3 (−8 to −1)* | 0.0159 |
| Resuscitation volumes | | | |
| Prehospital crystalloid | 100 (0 to 400) | 150 (0 to 500) | 0.5224 |
| Transfused, % | 54.8 | 68.9 | 0.0807 |
| MT, % | 6.3 | 22.2 | 0.0007 |
| 24-h RBC | 0 (0 to 3) | 2 (0 to 8)* | 0.0216 |
| 24-h plasma | 1 (0 to 4) | 3 (0 to 8)* | 0.0035 |
| 24-h platelets | 0 (0 to 0) | 0 (0 to 12)* | 0.0055 |
| 24-h crystalloid | 1,050 (0 to 3,000) | 0 (0 to 2,125) | 0.1163 |
| Outcomes | | | |
| Vent-free days | 29 (24 to 30) | 28 (0 to 30)* | 0.0159 |
| ICU-free days | 28 (22 to 30) | 25 (0 to 30)* | 0.0244 |
| Hospital-free days | 24 (12 to 29) | 15 (0 to 27)* | 0.0009 |
| 24-h mortality, n (%) | 8 (3) | 6 (10)* | 0.0064 |
| 30-d mortality, n (%) | 34 (11) | 17 (29)* | 0.0004 |

Median and IQR values are reported. Mann-Whitney U-tests were performed to determine statistical significance between groups.
GCS, Glasgow Coma Scale.
*Indicates statistical significance.

**Healthy Control Peak**

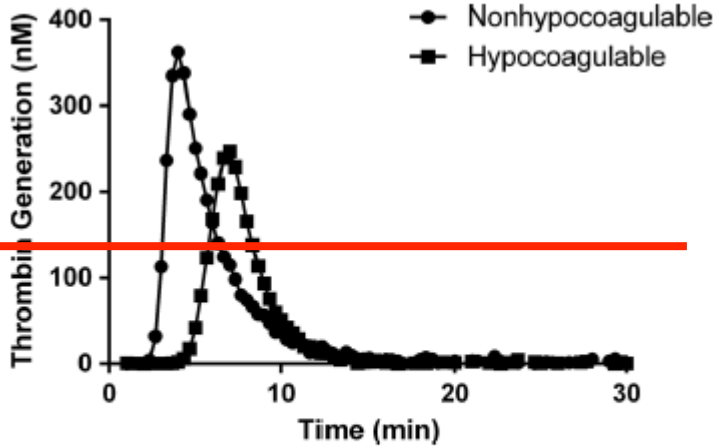



**Figure 1.** Representative thrombogram from nonhypocoagulable and hypocoagulable patients. One representative thrombogram was selected from each subgroup, with ● representing nonhypocoagulable and ■ representing hypocoagulable.

**TABLE 2.** TG in Healthy Controls Versus Trauma Patients

| | Healthy Controls (n = 29) | Trauma Patients (n = 406) | *p* |
|---|---|---|---|
| Lag time | 3.5 (3.3–4.1) | 4.0 (3.3–4.7)* | 0.01 |
| ETP | 1,299 (1,237–1,540) | 1,290 (1,088–1,518) | 0.17 |
| Peak | 124.6 (91.1–156.2) | 316.2 (270.1–355.5)* | <0.001 |
| ttPeak | 9.9 (8.5–10.7) | 6.0 (5.3–6.8)* | <0.001 |
| Rate | 20.9 (14.3–28.4) | 165.8 (132.5–199.2)* | <0.001 |

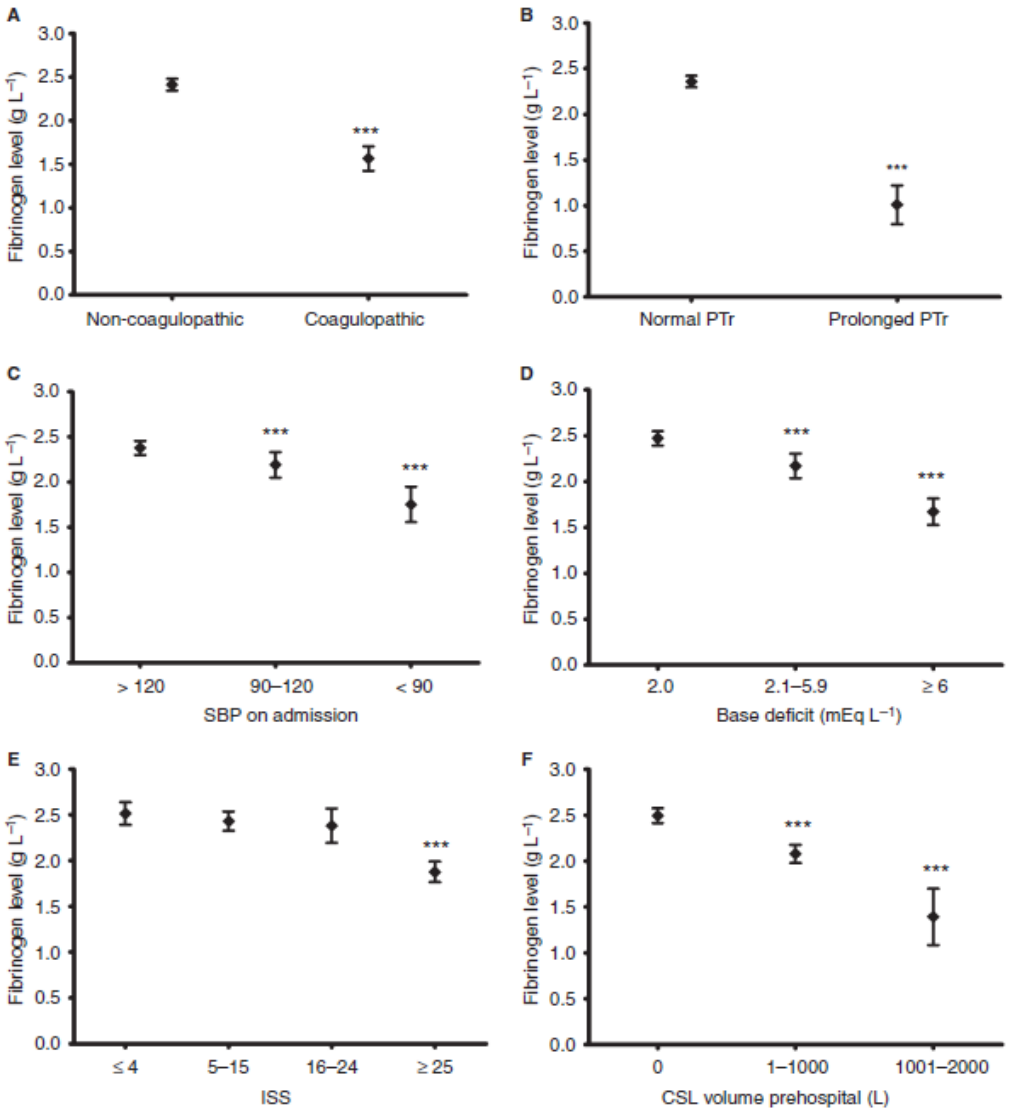
Median and IQR values are reported. The Mann-Whitney U-test indicates significant difference between groups.
*Indicates statistical significance.

(*J Trauma Acute Care Surg*. 2014;00: 00–00.

# Is it all about the fibrinogen?

**The sicker you are, the lower your fibrinogen…**

***So give fibrinogen?***

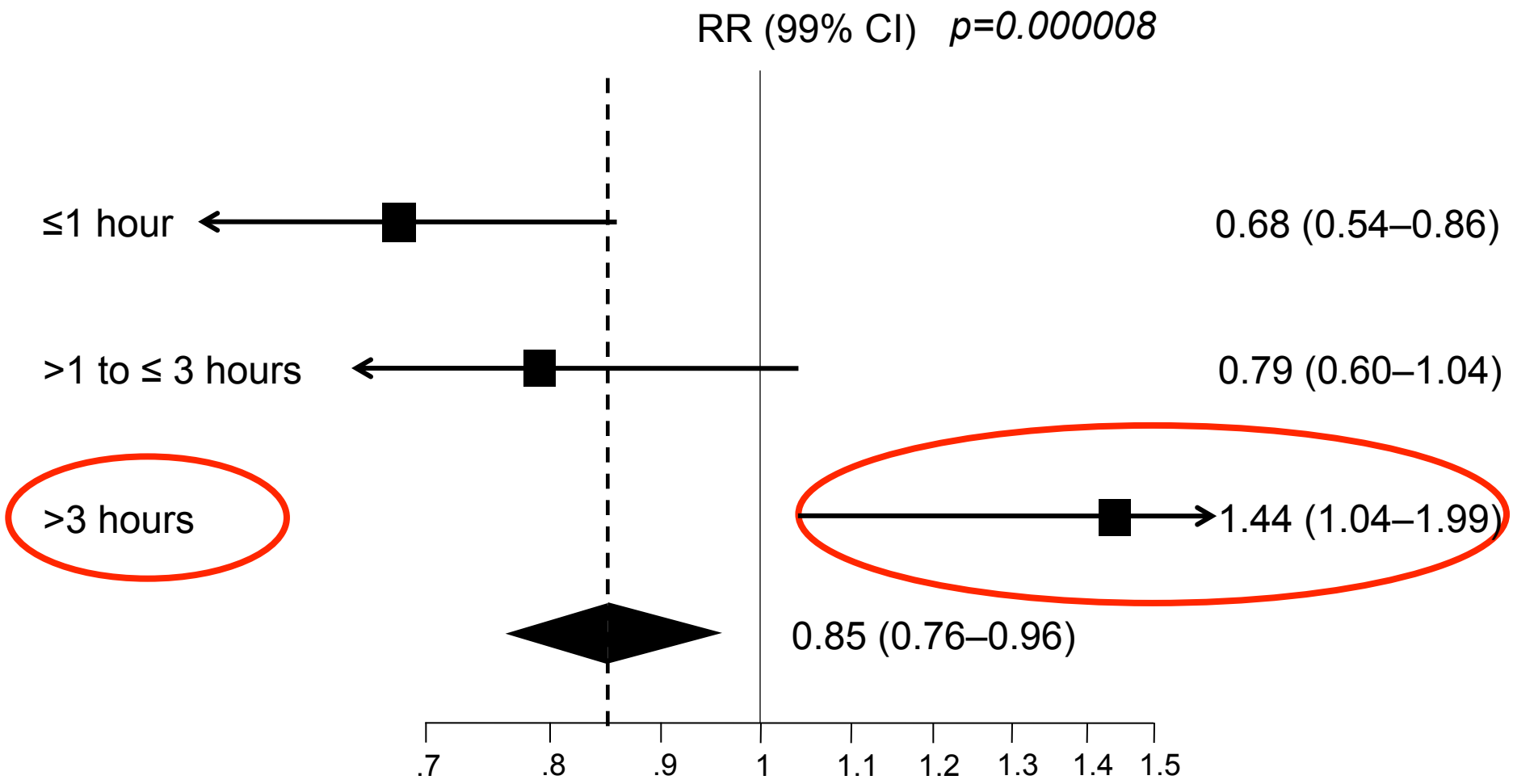



*Journal of Thrombosis and Haemostasis*, **10**: 1342–1351

# CRASH-2 Summary

| Cause of death | TXA<br>10,060 | Placebo<br>10,067 | Risk of death | P value |
|---|---|---|---|---|
| **Bleeding** | **489** | **574** | **0·85 (0·76–0·96)** | **0·0077** |
| Vascular occlusion | 33 | 48 | 0·69 (0·44–1·07) | 0·096 |
| Multi-organ failure | 209 | 233 | 0·90 (0·75–1·08) | 0·25 |
| Head injury | 603 | 621 | 0·97 (0·87–1·08) | 0·60 |
| Other | 129 | 137 | 0·94 (0·74–1·20) | 0·63 |
| **Any death** | **1463** | **1613** | **0·91 (0·85–0·97)** | **0·0035** |

# Give TXA EARLY!

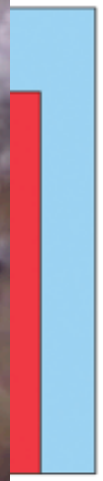


# No TXA for you! (haters of CRASH-2)

**Fibrinolys**
**also a nor**

**Use TEG t**

Moore

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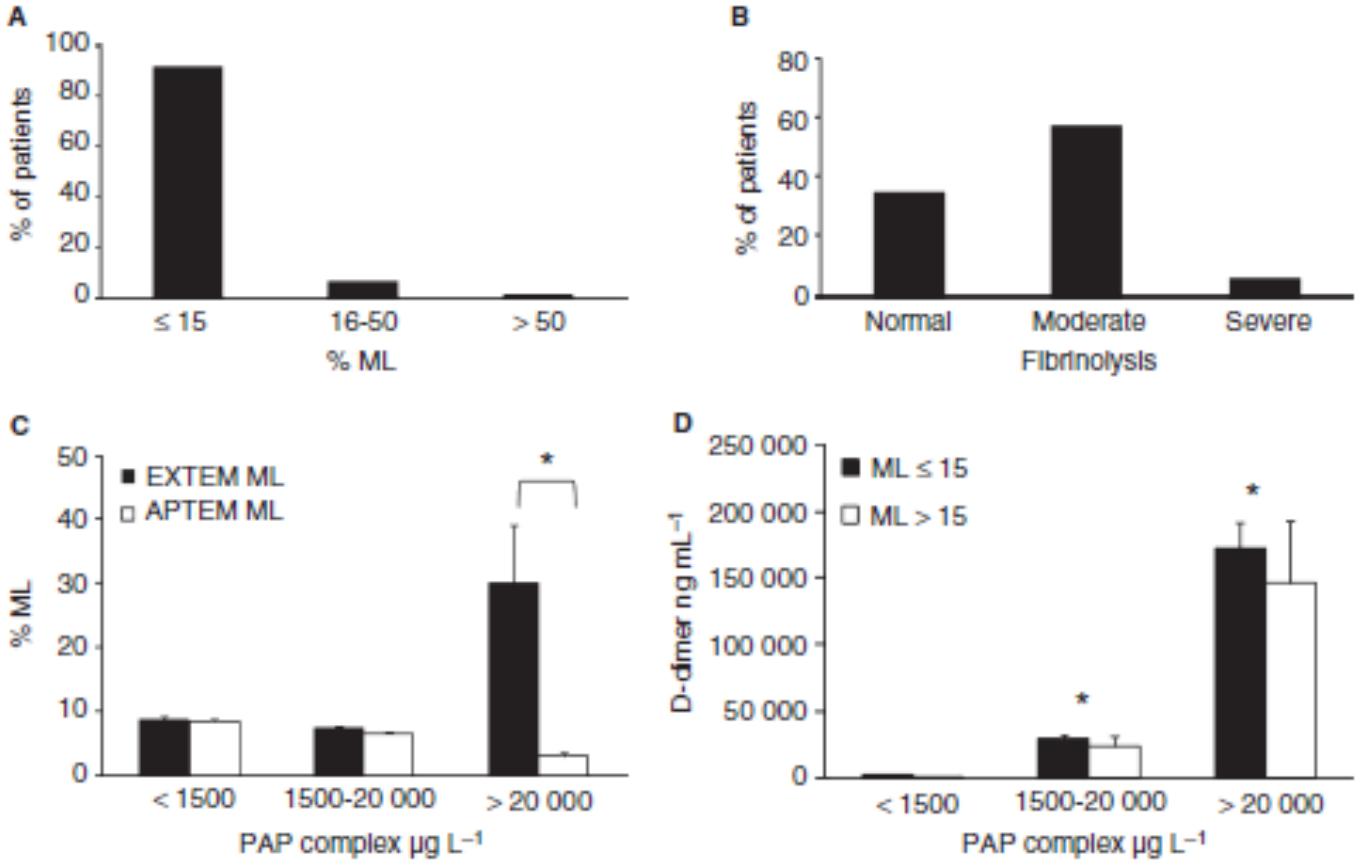
# Thromboelastometry underestimates fibrinolysis

**All about lysis?**




*Journal of Thrombosis and Haemostasis*, **11**: 307–314

# Patients with fibrinolysis also had high thrombin activation

**Table 2** TEM and coagulation factor assays

| | All patients | Normal | Moderate | Severe | TEM lysis only |
|---|---|---|---|---|---|
| ML | 9.4 (8.0–10.8) | 8.1 (7.4–8.7) | 6.6 (6.0–7.1)* | 45.5 (28.0–63.0)*† | 18.4 (16.5–20.3)* |
| PAP complex (μg $L^{-1}$) | 4690 (3887–5494) | 928 (862–993) | 5844 (4835–6854)* | 17 503 (10 502–24 503)*† | 1011 (794–1227) |
| t-PA (ng $mL^{-1}$) | 11.8 (10.2–13.5) | 8.0 (6.8–9.1) | 12.4 (10.8–14.0)* | 39.1 (14.5–63.7)* | 8.3 (3.8–12.7) |
| D-dimer (ng $mL^{-1}$) | 30 544 (22 822–38 266) | 2576 (1727–3426) | 38 687 (30 502–46 872)* | 88 831 (31 348–146 315)* | 865 (488–1243)* |
| Antiplasmin (IU $dL^{-1}$) | 122.8 (119.6–126.1) | 131.4 (127.6–135.2) | 120.4 (116.0–125.0)* | 86.7 (66.0–107.3)*† | 130.4 (119.9–141.0) |
| PAI-1 (pmol $L^{-1}$) | 32.7 (28.0–37.4) | 38.3 (27.7–48.9) | 29.6 (24.6–34.6) | 28.6 (21.4–35.8) | 43.7 (0.1–87.4) |
| $PF_{1+2}$ (pmol $L^{-1}$) | 1865 (1562–2168) | 596 (489–703) | 2314 (1911–2716)* | 5062 (2546–7577)* | 316 (234–399)* |
| Fibrinogen (g $L^{-1}$) | 2.1 (2.0–2.1) | 2.2 (2.1–2.3) | 2.1 (1.9–2.1)* | 1.5 (1.1–1.9)*† | 2.1 (1.7–2.4) |
| TAFI (μg $mL^{-1}$) | 12.6 (12.2–13.0) | 13.5 (12.9–14.1) | 12.0 (11.5–12.5)* | 10.6 (9.0–12.4)* | 13.3 (11.1–15.3) |
| TAFIa (ng $mL^{-1}$) | 132 (117–147) | 84 (66–103) | 153 (133–173)* | 303 (179–427)*† | 66.9 (58.2–75.5) |

ML, ROTEM maximum clot lysis; PAI-1, plasminogen activator inhibitor-1; PAP complex, plasmin–antiplasmin complex; $PF_{1+2}$, prothrombin fragments 1+2; TAFI, thrombin-activatable fibrinolysis inhibitor; TAFIa, activated thrombin-activatable fibrinolysis inhibitor; t-PA, tissue plasminogen activator. Values are means (confidence intervals). $\alpha_2$-Antiplasmin: normal range, 76–126 IU $dL^{-1}$; intra-assay and inter-assay variability, 0.5% and 3.2%. D-dimer: normal range, < 550 ng $mL^{-1}$; intra-assay and inter-assay variability, 4.1% and 4.3%. PAI-1: normal range, 4–43 ng $mL^{-1}$; intra-assay and inter-assay variability, 6.0% and 5.6%. PAP complex: normal range, 120–700 μg $L^{-1}$; intra-assay and inter-assay variability, 4.2% and 7.3%. $PF_{1+2}$: normal range, 69–229 pmol $L^{-1}$; intra-assay and inter-assay variability, 4.5% and 7.65%. TAFI: normal range, 7.6–10.6 μg $mL^{-1}$; intra-assay and inter-assay variability, 4.3% and 6.9%. TAFIa: normal range, 8.53–22.07 ng $mL^{-1}$; intra-assay and inter-assay variability, 3.4% and 3.15%. t-PA: normal range, 2–12 ng $mL^{-1}$; intra-assay and inter-assay variability, 4.5% and 6.4%. *$P < 0.05$ vs. no lysis; †$P < 0.05$ for moderate vs. severe lysis.

***This is looking like loss of autoregulation: the sicker you are the more everything is activated/consumed…***

*Journal of Thrombosis and Haemostasis*, **11**: 307–314

# Stage 2: ATC, 20-120 min?

- Overwhelming shock/coagulopathy → loss of autore
  - E
  - A
  - D
  - A
    gl
  - H
    D
  - D


**Net effe** **but…**

**IS THERE COAGULOPATHIC or ANATOMIC BLEEDING??**

# So what's really happening?

- First response: **STOP THE BLEED!**

- Last line of defense: **REVERSE GEARS; KEEP THE PIPES OPEN?** ("Hail Mary pass")
  - Fibrinolysis
  - Protein C pathway?
  - Platelet inhibition

***(i.e., ATC is the last ditch attempt to maintain perfusion.)***

- **OR**, does maximum effort to stop the bleed led to consumption, dilution, loss of autoregulation → ***ATC is BLOOD FAILURE?***

# Nature's response vs. organ failure

- When we say "coagulopathy," are we referring to PATHOLOGY or ADAPTIVE RESPONSE?

- We know that ATC means worse outcomes, but…
- Is the patient bleeding because of ATC or does the patient have ATC because of bleeding (shock)?
- Is a lytic response an attempt to avoid MOF?

**Lytics for ARDS?**

Treatment of severe acute respiratory distress syndrome: a final report on a phase I study.
Hardaway RM, Harke H, Tyroch AH, Williams CH, Vazquez Y, Krause GF.
Am Surg. 2001 Apr;67(4):377-82.
PMID:11308009

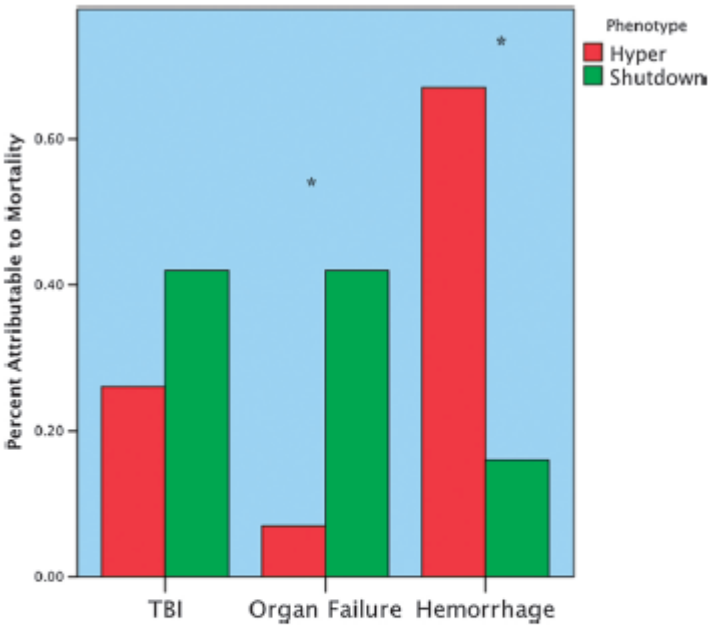


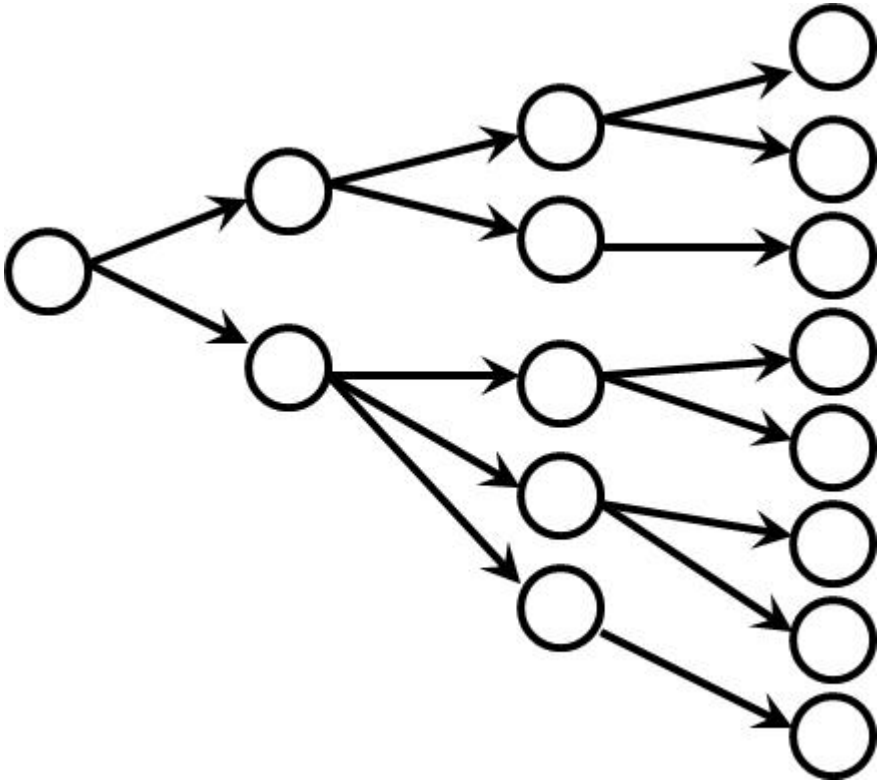

**Figure 3.** Distribution of mortality according to fibrinolytic phenotype. The *y* axis represents the percentage of total mortality per phenotype. The hyperfibrinolytic phenotype had a high frequency of mortality associated with hemorrhage. The shutdown phenotype has a high frequency of organ failure–related death. TBI did not reach statistical difference between phenotypes but was more common in the shutdown cohort. $*p < 0.05$. Hyper, hyperfibrinolysis; Shutdown, fibrinolysis shutdown; TBI, traumatic brain injury.

Moore et al. J Trauma 2014.

# Linear Evolution or Branching Path?

normal → ATC

or

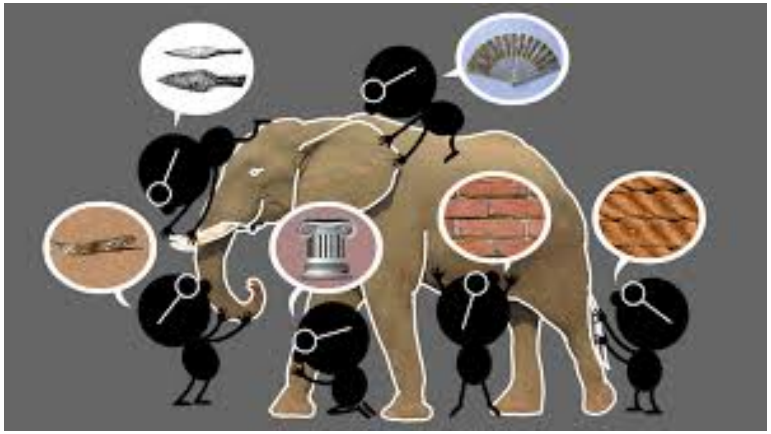


# Limitations of monitoring

- PT, aPTT: current standard but what do they mean?
  - Deficient thrombin?
  - Slow clot polymerization?
  - Plasma-based (lose RBC, PLT effects)

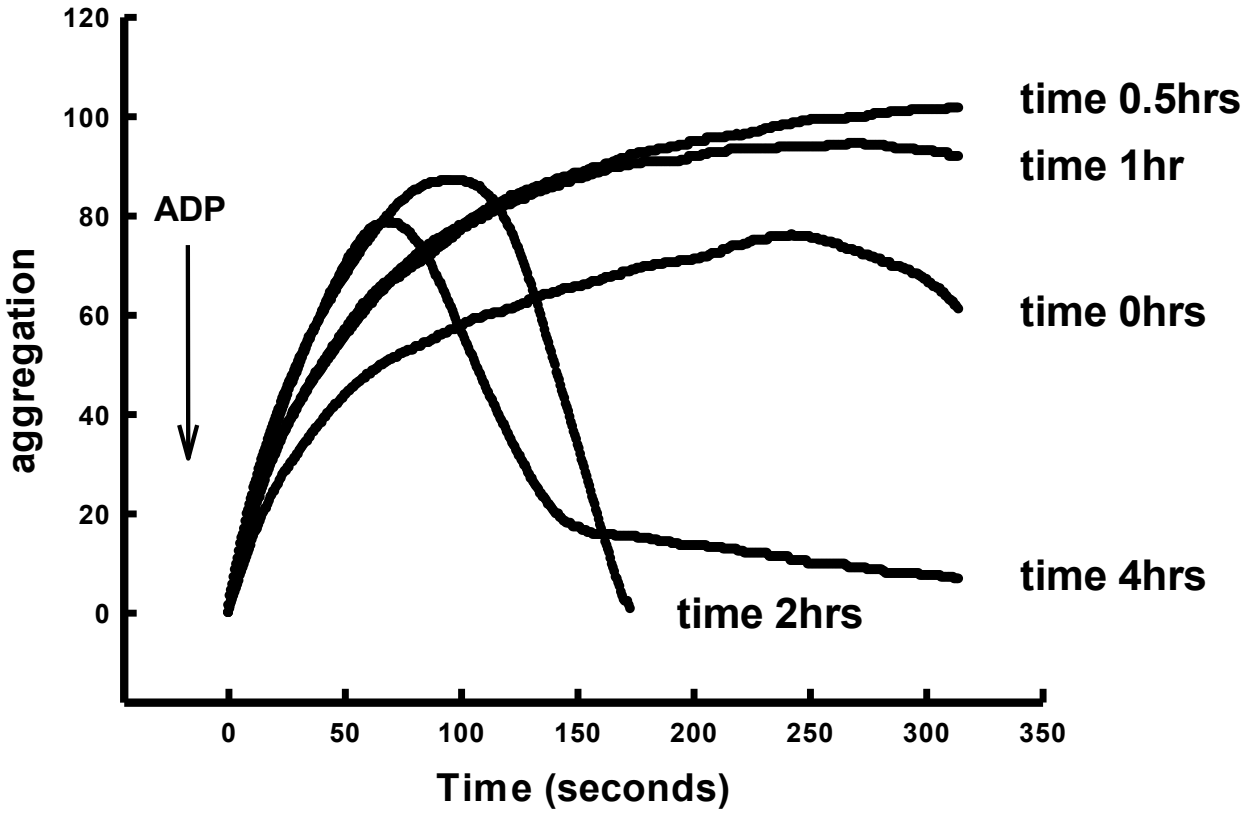
- ROTEM or TEG?
  - At least measuring whole blood!
  - Low shear
  - Insensitive to PLT defects and lysis

- PLT assays? Is this an elephant?
  - Aggregation
  - Adhesion
  - Release
  - catalysis



# Limitations of monitoring

- Speaking of platelet function in TIC… what do we do with this?



# Therapeutic targets?

- What the heck are we treating?

- Fix a dysfunctional coagulation system in order to decrease bleeding? (deliberate coagulation management)
  - Increase thrombin?
  - Increase fibrinogen?
  - Shut off fibrinolysis?
  - Shut off Protein C?

- Fix bleeding and resuscitate shock without making coagulopathy worse? (target overall homeostasis)
  - Repay oxygen debt
  - Rebalance plasma
  - Rescue endothelium
  - Reinforce platelets
  - Don’t dilute!

# Give blood, prevent TIC

**SHOCK,** Vol. 44, Supplement 1, pp. 138–148, 2015

OPEN

## EVALUATION OF PREHOSPITAL BLOOD PRODUCTS TO ATTENUATE ACUTE COAGULOPATHY OF TRAUMA IN A MODEL OF SEVERE INJURY AND SHOCK IN ANESTHETIZED PIGS

**Sarah Watts,* Giles Nordmann,* Karim Brohi,† Mark Midwinter,‡ Tom Woolley,* Robert Gwyther,* Callie Wilson,* Henrietta Poon,* and Emrys Kirkman***

**CBR Division, Defence Science and Technology Laboratory, Defence Science and Technology Laboratory, Porton Down, Salisbury; †Centre for Trauma Sciences, Blizard Institute, Queen Mary University of London, London; and ‡University of Birmingham, Birmingham, United Kingdom*

***CRYSTALLOID IS BAD!***

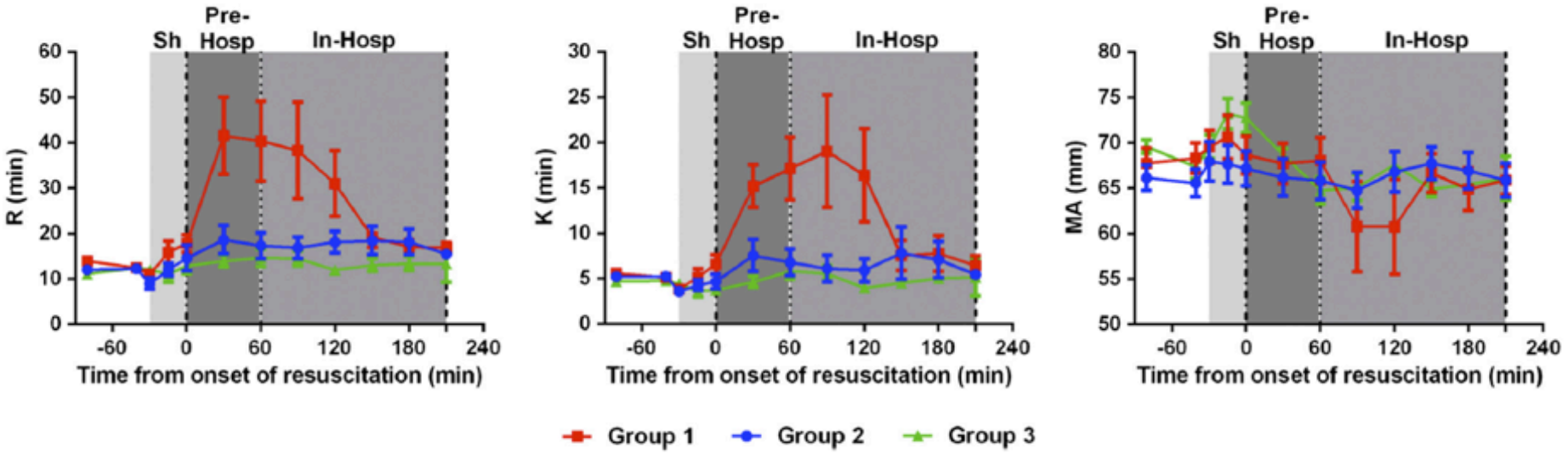



FIG. 3. **Effects of tissue injury, hemorrhagic shock, and resuscitation on TEG R time (clot initiation), K time (clot dynamics), and MA (clot strength) in three treatment groups.** For more details, see legend to Figures 1 and 2. Mean values ± SEM.

# Give plasma, prevent fibrinolysis

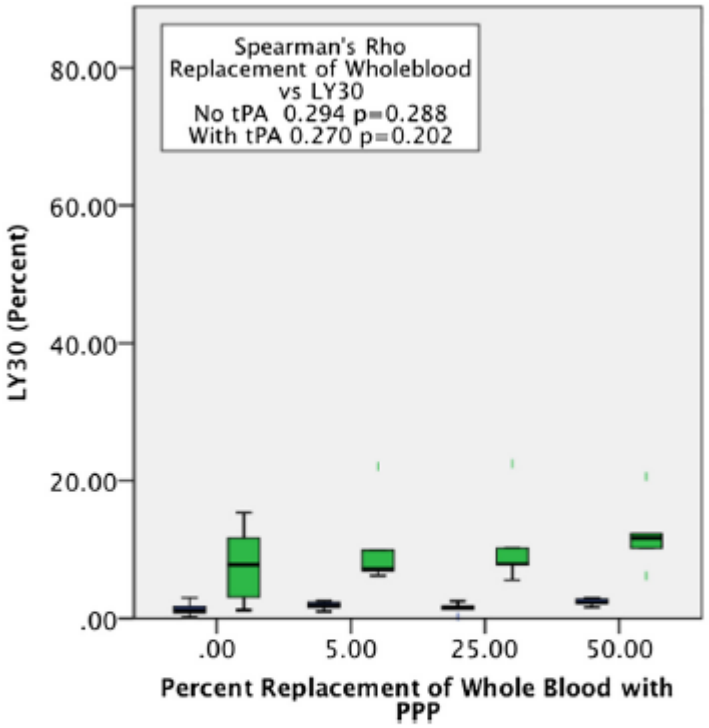



**Figure 2.** Plasma dilution of whole blood does not alter sensitivity to tissue plasminogen activator (tPA)-mediated fibrinolysis. The y axis represents the percent fibrinolysis quantified by LY30 (amount of blood clot lysed 30 minutes after reaching maximum amplitude). The x axis represents progressive dilution of whole blood with platelet poor, with largest dilution on the right. Blue bar, whole blood with no tPA added. Green bar, whole blood mixed with tPA. PPP, platelet poor plasma.

## Plasma Is the Physiologic Buffer of Tissue Plasminogen Activator-Mediated Fibrinolysis: Rationale for Plasma-First Resuscitation after Life-Threatening Hemorrhage

(J Am Coll Surg 2015;220:872–879.

Hunter B Moore, MD, Ernest E Moore, MD, FACS, Eduardo Gonzalez, MD, Gregory Wiener, BA, Michael P Chapman, MD, Monika Dzieciatkowska, PhD, Angela Sauaia, MD, Anirban Banerjee, PhD, Kirk C Hansen, PhD, Christopher Silliman, MD, PhD

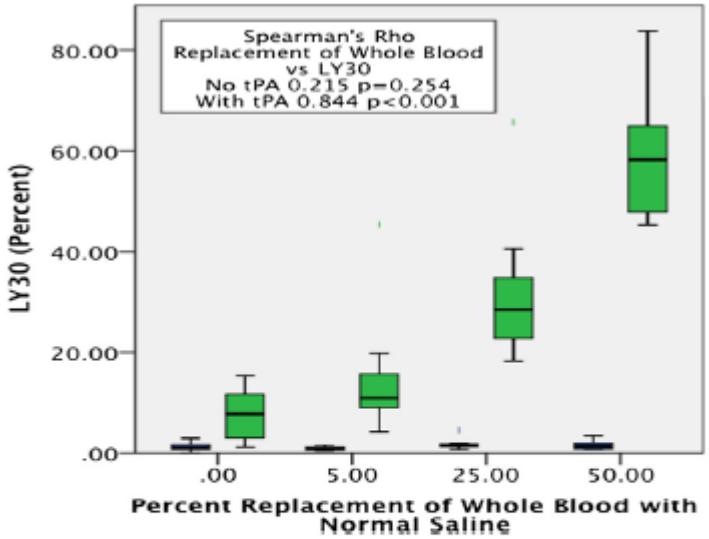
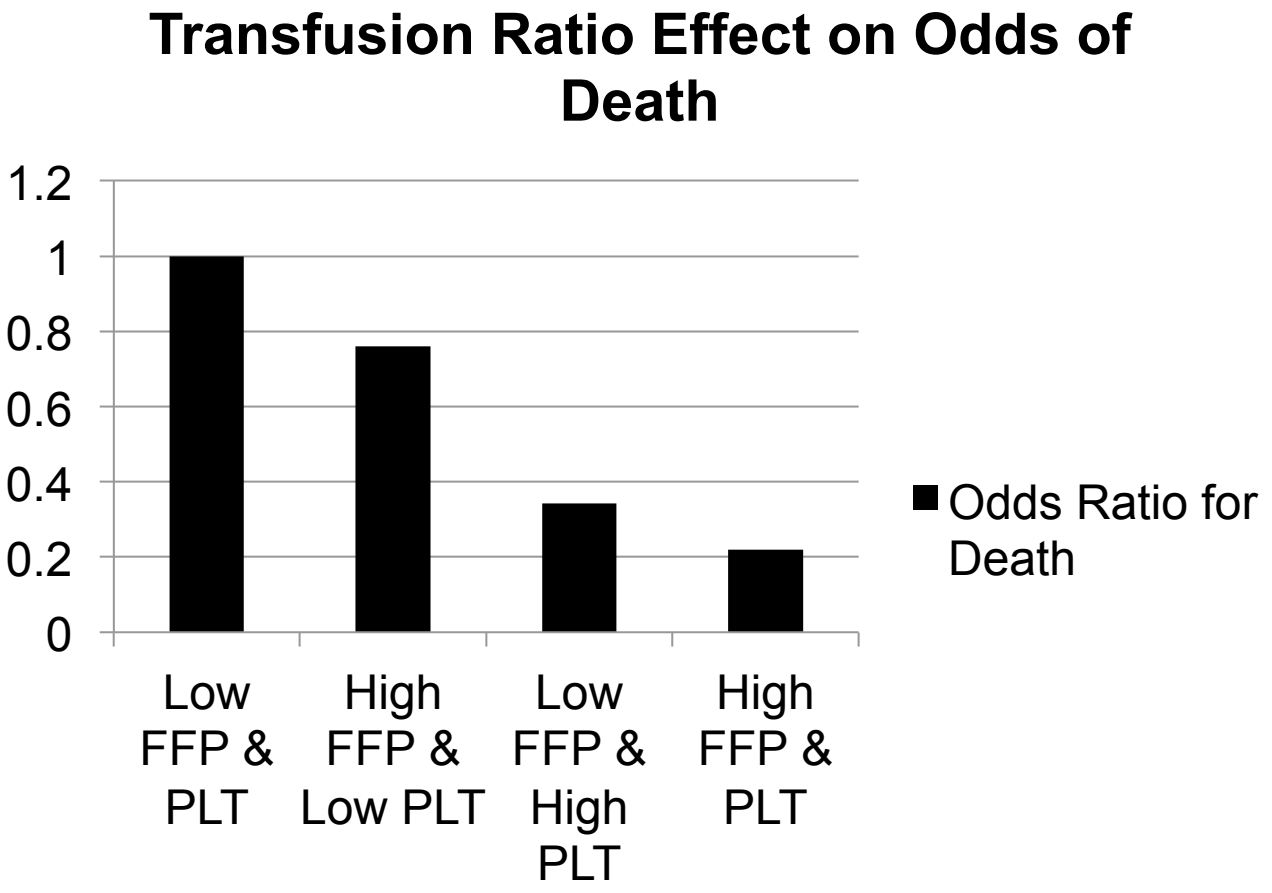



**Figure 1.** Normal saline (NS) dilution of whole blood increases sensitivity to tissue plasminogen activator (tPA)-mediated fibrinolysis. The y axis represents the percent fibrinolysis quantified by LY30 (amount of blood clot lysed 30 minutes after reaching maximum amplitude). The x axis represents progressive dilution of whole blood with saline, with largest dilution on the right. Blue bar, whole blood with no tPA added. Green bar, whole blood mixed with tPA.

# 10 year war transfusion study

***More plasma and platelets, more survival!***




Pidcoke HF, Aden JK, et al. J Trauma Acute Care Surg. 2012 Dec;73(6 Suppl 5):S445-52.

# Enlightened TIC Therapy?

- Goal-directed? We're not there yet…
  - How do you do this if you don't know what you're treating?
- First do no harm
  - When you're flying blind, use tools that are forgiving.
- Don't overdo it
  - Volume overload
  - Procoagulant overload
  - ***Remember acute phase response and hypercoagulable state w/in 48-72 hours***

# PCCs increase thrombin generation (not the problem)

**PCC in dark grey, note elevated ETP through day 4!**

**VTE risk!!!**

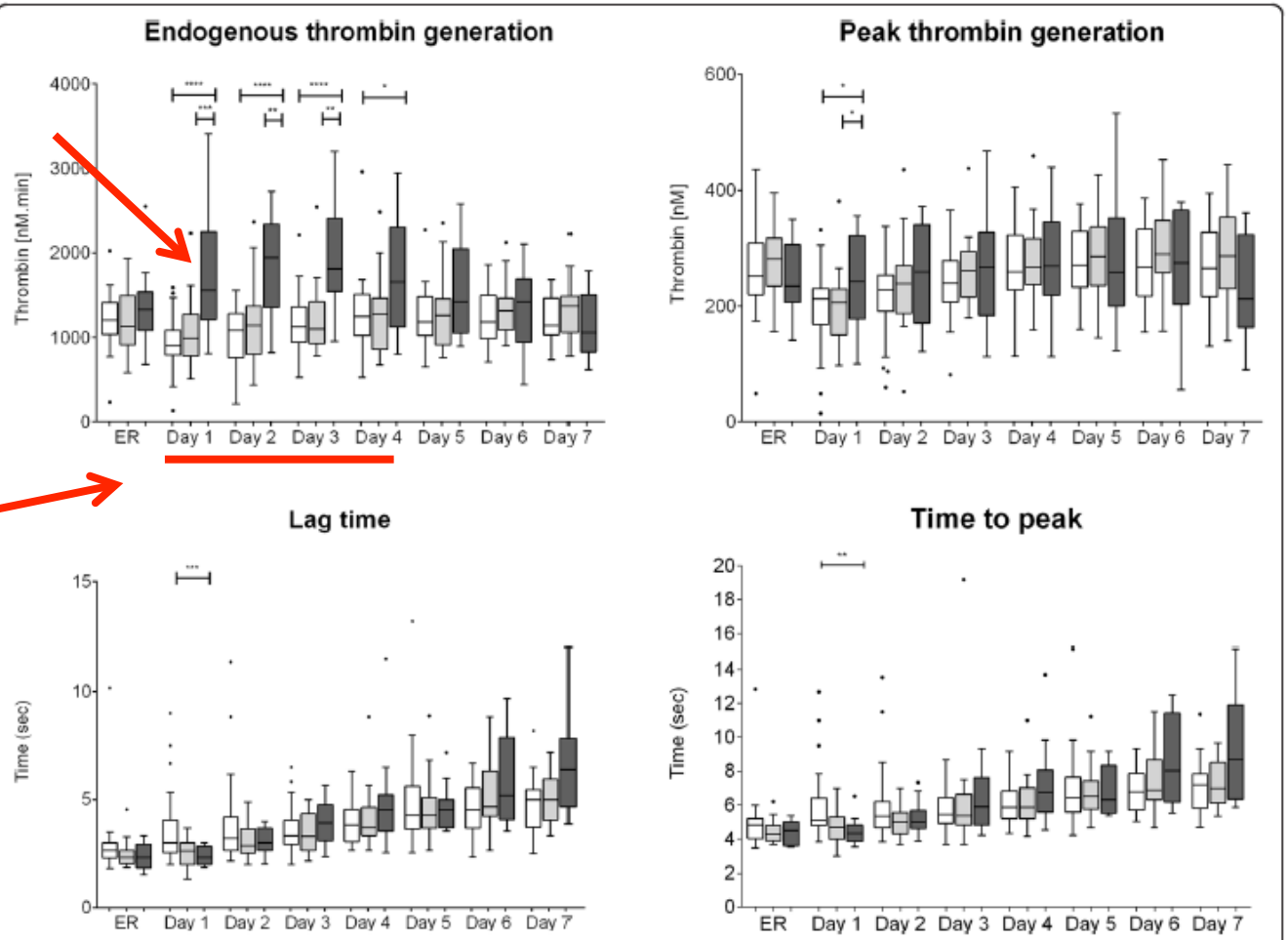



**Figure 1 Parameters relating to thrombin generation, from emergency room (ER) admission until day 7.** Endogenous thrombin potential was significantly higher over the first 3 to 4 days in the prothrombin complex concentrate-fibrinogen concentrate group (FC-PCC group) (dark gray) compared to the fibrinogen concentrate group (FC group) (light gray) and patients receiving no coagulation therapy (NCT group) (white). AUC, area under curve. *$P$ <0.05; **$P$ <0.01; ***$P$ <0.001; ****$P$ <0.0001; no indication = not significant. Data are presented as box and whisker plots (Tukey). Student $t$-test or Mann-Whitney rank sum test was used as appropriate for between-group comparisons.

Schöchl *et al. Critical Care* 2014, **18**:R147
http://ccforum.com/content/18/4/R147

# Give PCC, increase thrombogenicity

**PCC in dark grey; low AT means decreased autoregulation!**

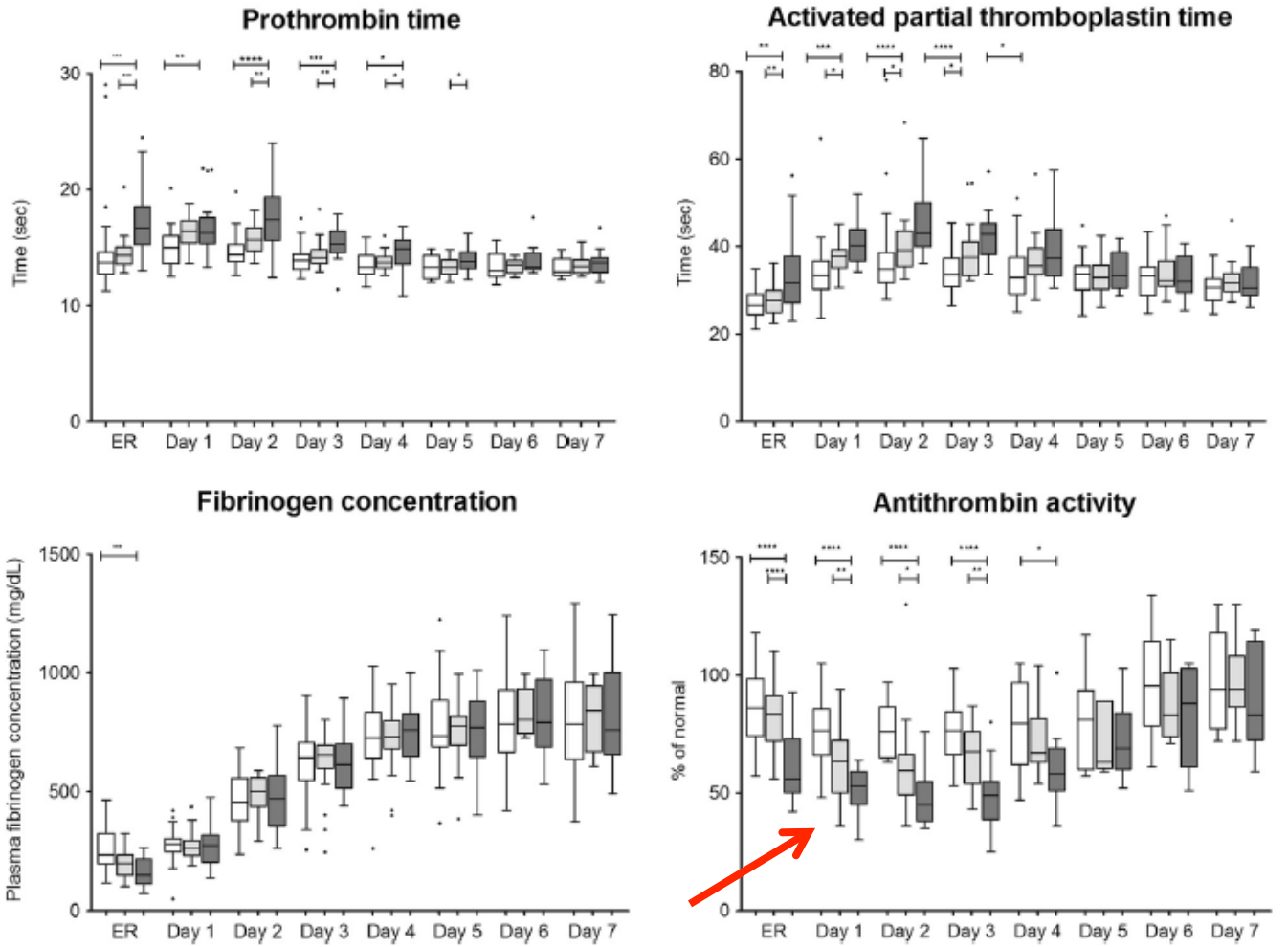



**Figure 2 Prothrombin time, activated partial thromboplastin time, fibrinogen concentration and antithrombin activity from emergency room (ER) admission until day 7.** The prothrombin complex concentrate-fibrinogen concentrate group (FC-PCC group) (dark gray) was compared with the fibrinogen concentrate group (FC group) (light gray) and patients receiving no coagulation therapy (NCT group) (white). *$P$ <0.05; **$P$ <0.01; ***$P$ <0.001; ****$P$ <0.0001; no indication = not significant. Data are presented as box and whisker plots (Tukey). Student $t$-test or Mann-Whitney rank sum test was used as appropriate for between-group comparisons.

Schöchl *et al. Critical Care* 2014, **18**:R147
http://ccforum.com/content/18/4/R147

# Bleeding or thrombosis?

**Between Scylla & Charybdis…**

# RDCR Considerations

- “Coagulopathy” can be assumed in badly injured patients.
- The good news: if you don’t know what you’re supposed to be monitoring, don’t bother with the monitors (not available anyway).
- First do no harm: go with Mother Nature (whole blood or at least blood products).
- Pretty good evidence that TXA and “fibrinogen” and/or plasma are **reasonable** adjuncts or bridges to whole blood.
- Respect physiology and do what makes sense.

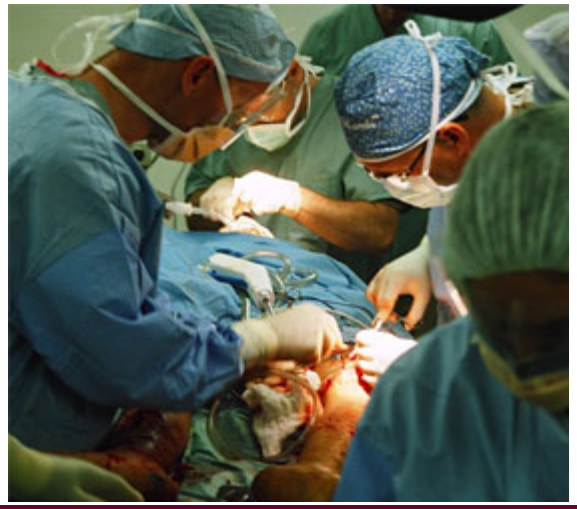
# Destiny of TIC Theories

# Damage Control for Combat Trauma

- Stop the bleeding!
  - Don't try to fix everything at once, just stabilize
- Treat shock!
  - Lack of tissue perfusion = death; need oxygen
- Don't worsen coagulopathy!
  - Blood that doesn't clot will leak out, but don't overdo it…

How do you do this?

***Surgical control of hemorrhage + whole blood!***




# Thank You.