Mechanisms of Trauma Coagulopathy

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A continued cause of PREVENTABLE death.

24% of trauma patients are coagulopathic on arrival\(^1\)
- 56% of severe trauma patients have coagulation abnormalities at 25min (samples taken on scene)

Time to Definitive Haemorrhage Control is a key determinant of outcome \(^3\).

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1) Brohi, J Trauma (2003)
2) Floccard et al, Injury (2012)
Coagulopathy is the Harbinger of Mortality

- Pooled data from 5693 patients in 5 countries
- Samples taken on admission

1) Frith et al, J Throm Haemost (2010)
The Triad of Death – The Complete Story?

HYPOTHERMIA

CLOTTING FACTOR LOSS
DILUTION
CONSUMPTION

COAGULOPATHY

ACIDAEMIA

CLOTTING FACTOR DYSFUNCTION
Hypothermia

* BUT…..of 701,491 patients:
  * Only 11,026 (1.57%) had an admission temperature < 35°C

- **CT**: Time to initiation of fibrin formation
- **Alpha Angle**: Rapidity of Fibrin Build up and Cross Linking
- **CFT**: Clot Kinetics (2mm to 20mm)
- **MCF**: Clot strength
Acidosis Impairs the Coagulation: A Thromboelastographic Study

Martin Engström, MD, PhD, Ulf Schött, MD, PhD, Bertil Romner, MD, PhD, and Peter Reinstrup, MD, PhD

$p < 0.00001, r = 0.89$

$p < 0.00001, r = 0.85$
Clot Strength

Maximum Clot Firmness (MCF)

MCF (mm) vs pH
Dilution

Clotting factor DEFICIENCY?

Hypoperfusion in Severely Injured Trauma Patients is Associated With Reduced Coagulation Factor Activity

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* 71 Patients, ISS > 15
* Stratified to degree of hypoperfusion by base deficit
* Similar volume of crystalloid
* Venous sample taken on admission
  • Factor assay

1) Jansen et al, J Trauma (2011)
Base Deficit Vs. Factor Activity

1) Jansen et al, J Trauma (2011)
76% factor activity remained in the normal range
42% of patients had no deficiency
Factor 5 behaves differently
- Significant association between BD and factor activity for 2, 7, 9, 10, & 11
- No association between BD and Factor 5 Activity
- Lowest level of activity of all factors
- 54% had a level below normal range
A significant number of our trauma patients arrive with significant coagulopathy.

Mechanisms traditionally thought to cause coagulopathy appear to only occur in extremes.
Is There Something Else?

**Acute Traumatic Coagulopathy**

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This Next Slide May Contain The Sexiest Graph You Will See Today
1) Frith et al, J Throm Haemost (2010)
Similar Pattern with Mortality

1) Frith et al, J Throm Haemost (2010)
Potential Mechanism?

* **Protein C**
  - Activated by Thrombin-Thrombomodulin Complex
  - Inhibits Factors 5 & 8
  - Promotes Fibrinolysis

* **Cohen et al**
  - 206 patients
  - Serial Blood Samples at 6, 12, and 24 hrs
  - Stratified by Base Deficit and ISS

Increased Activation of Protein C

* Activated Protein C Levels
* Protein C Levels

* $p < 0.05$
Associated with Decreased Factor 5 & 8

Factor Va Level

Factor VIIIa Level

*p < 0.05
Fibrinolysis

- Fibrinogen
- Crosslinked Fibrin
- Thrombin
- Plasminogen
- Plasmin
- Fibrin degradation products
- tPA
APC Associated with De-Repression of Fibrinolysis

*\( p < 0.05 \)
The Thrombin Switch

SHOCK

THROMBOMODULIN

THROMBIN

THROMBIN-THROMBOMODULIN

PROTEIN C

ACTIVATED PROTEIN C

Fibrinolysis
Fibrinogen & Fibrinolysis

- Fibrinogen concentration falls quickly

- Low fibrinogen predictor of mortality at 24hrs and 28 days\(^1\)

- Degree of fibrinolysis related to mortality\(^2\)

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What have we not talked about...

* Platelets
  * Limited knowledge of the role of platelets in Trauma Induced Coagulopathy

* Endothelial Dysfunction
‘Imbalance of the Dynamic Equilibrium Between Procoagulant Factors, Anti-coagulant Factors, Platelets, Endothelium and Fibrinolysis’

Multi-Factorial
- Acute Coagulopathy of Trauma
  - Hyperfibrinolysis
- Factor Deficiency
- (Dilutional)
- (Acidaemia)
- (Hypothermia)

1. Frith and Brohi, Curr Opin Crit Care (2012)
Managing TIC

* Remember
  • Identify the bleeding coagulopathic patient early.
  • Classical tests of coagulation may not detect TIC

* Instigate Damage Control Resuscitation
  • Haemostatic Resuscitation
  • Haemostatic Packaging
  • Minimal, Targeted, Crystalloid Administration
  • Early High Ratio Component Therapy
  • Address Fibrinolysis
  • Point of care coagulation testing
Khan et al 2014
106 patients
  • Median ISS 35 (25-41)
INTERN (International Trauma Research Network)
Lactate and ROTEM analysed at 4, 8 and 12 units PRBC
FFP:PRBC 2:3
Platelets & Cryoprecipitate at 6 PRBC
Hemostatic resuscitation is neither hemostatic nor resuscitative in trauma hemorrhage

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*versus time zero
ROTEM 5min Clot Amplitude (CA5)

ROTEM Mean Clot Firmness (MCF)

ROTEM Clotting Time (CT)
Resuscitation is not an end-point, it is a means to facilitating definitive management.
References (1)

References (2)