Strategies for transfusion therapy and monitoring

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Pathophysiology

**Coagulopathy** related to Trauma/Shock - Acute Traumatic Coagulopathy

**Coagulopathy** secondary to dilution with crystalloids and colloids

**Coagulopathy** secondary to haemotherapy

**Coagulopathy** secondary to consumption (injury, DIC etc.)

**Coagulopathy** due to hypothermia and metabolic acidosis

**Coagulopathy** due to ischemia-reperfusion injury

**Coagulopathy** due to antithrombotics

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**Micro Vascular Bleeding (MVB)**


Brohi K et al. Curr Opinion of Crit Care. 2007
Fluid resuscitation
Bleeding...

- None
- Moderate controllable
- Massive uncontrollable
Massive uncontrollable

1:1:1

4:4:2
Transfusion packages

- Thawed FFP (AB RhD negative) immediately available for transfusion.
- Transfusion Package $4 \text{ RBC} : 4 \text{ FFP} : 2 \text{ Platelet Concentrates}$ (ratio ~ $1 : 1 : 1$)
- Results in
  - Haematocrit ~ 30%
  - Coagulation factor concentration >30%
  - Platelet count of $80 \times 10^9/L$
  - Normal TEG®
- The packages are to be used until surgical control

For patients with uncontrollable haemorrhage

Johansson, Stensballe et al. Transfusion 2007

The Copenhagen Concept
Transfusion of Plasma, Platelets, and Red Blood Cells in a 1:1:1 vs a 1:1:2 Ratio and Mortality in Patients With Severe Trauma
The PROPPR Randomized Clinical Trial

Figure 2. Kaplan-Meier Failure Curves for Mortality at 24 Hours and 30 Days

<table>
<thead>
<tr>
<th>24-h Mortality</th>
<th>30-d Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. at risk</td>
<td>Time to Death From Randomization, h</td>
</tr>
<tr>
<td>1:1:2</td>
<td>342 332 304 296 291 286 284</td>
</tr>
<tr>
<td>1:1:1</td>
<td>338 327 318 305 300 297 295</td>
</tr>
</tbody>
</table>
Before and after study

MT patients (including obstetric calamities)


Intervention group transfused packages and TEG

Control group transfused based on ASA 1996 guidelines

Johansson et Stensballe. Vox Sang 2009

<table>
<thead>
<tr>
<th>Number at risk</th>
<th>2005-2006</th>
<th>2002-2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>442</td>
<td>390</td>
</tr>
<tr>
<td>20</td>
<td>385</td>
<td>308</td>
</tr>
<tr>
<td>40</td>
<td>362</td>
<td>281</td>
</tr>
<tr>
<td>60</td>
<td>352</td>
<td>267</td>
</tr>
<tr>
<td>80</td>
<td>347</td>
<td>257</td>
</tr>
<tr>
<td>100</td>
<td>345</td>
<td>255</td>
</tr>
</tbody>
</table>

Log-rank, $P<0.0001$
Fewer advanced interventional procedures
OR 1.25 [1.07–1.47]; P = 0.008 - the whole cohort
OR 1.58 [1.19–2.10]; P = 0.003 - patients > 1 FFP
Transfusion in Coronary Artery Bypass Grafting is Associated with Reduced Long-Term Survival

Colleen Gorman Koch, MD, MS, Liang Li, PhD, Andra I. Duncan, MD,

"BLOOD"
Cells from human-to-human

Transplantation
Alive cells & DNA
1 Blood = 1 New Donor

Side-effects
Immune system
Physiology
Transfusion reactions
Transfusion-translated infections

Lower versus Higher Hemoglobin Threshold for Transfusion in Septic Shock

Lars B. Holst, M.D., Nicolai Haase, M.D., Ph.D., Jørn Wetterslev, M.D., Ph.D., Jan Werner, M.D., Ph.D., Anne B. Guttormsen, M.D., Ph.D., Sari Karlsson, M.D., Ph.D., Pär I. Johansson, M.D., Ph.D., Anders Åneman, M.D., Ph.D., Marianne L. Vang, M.D., Robert Winding, M.D., Lars Nebrich, M.D., Helle L. Nibro, M.D., Ph.D., Bodil S. Rasmussen, M.D., Ph.D., Johnny R. M. Lauridsen, M.D., Jane S. Nielsen, M.D., Anders Grønne, M.D., Ph.D., Ville Pettinä, M.D., Ph.D., Maria B. Cronhjort, M.D., Lasse H. Andersen, M.D., Ulf G. Petersen, M.D., Nanna Reiter, M.D., Jørgen Wiis, M.D., Jonathan O. White, M.D., Lene Russell, M.D., Klaus J. Thornberg, M.D., Peter B. Hjortrup, M.D., Rasmus G. Müller, M.D., Morten H. Møller, M.D., Ph.D., Morten Carlsen, M.D., Inge Madsen, M.D., Johanna Blom, M.D., Finnja Hjaltadóttir, M.D., Ulrica Odeberg-Werner, M.D., Ph.D., Brit Sjøbø, R.N., Helle Bundgaard, M.D., Ph.D., Maria A. Thyø, M.D., David Lodahl, M.D., Rikke Mærkedahl, M.D., Carsten Albeck, M.D., Dorte Illum, M.D., Mary Kruse, M.D., Per Winkel, M.D., D.M.Sci., and Anders Herner, M.D., Ph.D., on behalf of the RISS-PPD Group* and the Scandinavian Critical Care Trials Group

Age 67 year
Septic shock (Need for NA)
90-d mortality: 45 %

7 versus 9 g/dL
Restrictive or Liberal Red-Cell Transfusion for Cardiac Surgery

C.D. Mazer, R.P. Whitlock, D.A. Fergusson, J. Hall, E. Belley-Cote, K. Connolly,

- 5243 adults
- EuroSCORE I > 6
- Trigger < 7.5 (4.65 mmol/L) vs < 9.5 g/dL
Restrictive or Liberal Red-Cell Transfusion for Cardiac Surgery

C.D. Mazer, R.P. Whitlock, D.A. Fergusson, J. Hall, E. Belley-Cote, K. Connolly,

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Restrictive Threshold (N=2430)</th>
<th>Liberal Threshold (N=2430)</th>
<th>Odds Ratio or Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Composite-outcome event — no./total no. (%)</td>
<td>276/2428 (11.4)</td>
<td>303/2429 (12.5)</td>
<td>0.90 (0.76–1.07)</td>
</tr>
<tr>
<td>Death — no./total no. (%)</td>
<td>74/2427 (3.0)</td>
<td>87/2429 (3.6)</td>
<td>0.85 (0.62–1.16)</td>
</tr>
<tr>
<td>Stroke — no./total no. (%)</td>
<td>45/2428 (1.9)</td>
<td>49/2429 (2.0)</td>
<td>0.92 (0.61–1.38)</td>
</tr>
<tr>
<td>Myocardial infarction — no./total no. (%)</td>
<td>144/2428 (5.9)</td>
<td>144/2429 (5.9)</td>
<td>1.00 (0.79–1.27)</td>
</tr>
<tr>
<td>New-onset renal failure with dialysis — no./total no. (%)</td>
<td>61/2428 (2.5)</td>
<td>72/2429 (3.0)</td>
<td>0.84 (0.60–1.19)</td>
</tr>
</tbody>
</table>
4.3 mmol/L

70 g/dL
Haemostasis!
Plasma-based tests?

INR/PT

EXTRINSIC PATHWAY

INTRINSIC PATHWAY

APTT

...developed to monitor heparin and vitamin K antagonists...
Platelet count?

......nothing but a number.......😊
Viscoelastic Haemostatic Assays (VHA)

* TEG®/ROTEM®

- Whole blood analysis
- Measures the viscoelsational properties of the clot
- Multiple endpoints reflecting clot formation, strength & degradation
- Real-time (15 min.)
NEW Fully Automated VHA’s
(TEG 6s/ROTEM Sigma)
TEG® Tracing and Coagulopathy

![Graph showing TEG tracing and coagulopathy parameters](image)
<table>
<thead>
<tr>
<th><strong>TEG®</strong></th>
<th><strong>Activator</strong></th>
<th><strong>ROTEM®</strong></th>
<th><strong>Activator</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>CK (Standard)</td>
<td>Kaolin</td>
<td>EXTEM</td>
<td>TF</td>
</tr>
<tr>
<td>CK-H</td>
<td>Kaolin Heparinase</td>
<td>HEPTEM</td>
<td>CA Heparinase</td>
</tr>
<tr>
<td>FF</td>
<td>TF</td>
<td>FIBTEM</td>
<td>TF</td>
</tr>
<tr>
<td>Functional Fibrinogen</td>
<td>PLT-Antag.</td>
<td></td>
<td>PLT. Antag.</td>
</tr>
<tr>
<td>Functional Fibrinogen-H</td>
<td>TF</td>
<td>APTEM</td>
<td>TF Aprotinin</td>
</tr>
<tr>
<td>Rapid TEG</td>
<td>TF-Kaolin</td>
<td>INTEM</td>
<td>Contact Activator</td>
</tr>
<tr>
<td>Rapid TEG-H</td>
<td>TF-Kaolin Heparinase</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Functional Fibrinogen TEG® / FIBTEM ROTEM®

MA_{FF} 6.3 mm (normal values 14-24)
# Treatment algorithm

**Table 1.** TEG and ROTEM treatment algorithm for bleeding patients as used in Copenhagen, and adopted across Denmark according to the Danish Society of Blood Banking/Clinical Immunology

<table>
<thead>
<tr>
<th>TEG</th>
<th>ROTEM</th>
<th>Coagulopathy</th>
<th>Treatment option</th>
</tr>
</thead>
<tbody>
<tr>
<td>R 10–14 min</td>
<td>ExTEM CT 80–100 s</td>
<td>Coagulation factors ↓</td>
<td>FFP 20 ml/kg</td>
</tr>
<tr>
<td></td>
<td>InTEM CT 200–240 s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R &gt;14 min</td>
<td>ExTEM CT &gt;100 s</td>
<td>Coagulation factors ↓↓</td>
<td>FFP 30 ml/kg</td>
</tr>
<tr>
<td></td>
<td>InTEM CT &gt;240 s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FF&lt;sub&gt;MA&lt;/sub&gt; 7–14 mm</td>
<td>FibTEM MCF 6–9 mm</td>
<td>Fibrinogen ↓</td>
<td>FFP 20 ml/kg or cryoprecipitate 5 ml/kg or fibrinogen concentrate 20 mg/kg</td>
</tr>
<tr>
<td>FF&lt;sub&gt;MA&lt;/sub&gt; 0–7 mm</td>
<td>FibTEM MCF 0–6 mm</td>
<td>Fibrinogen ↓↓</td>
<td>FFP 30 ml/kg or cryoprecipitate 5 ml/kg or fibrinogen concentrate 30 mg/kg</td>
</tr>
<tr>
<td>MA 45–99 mm and FF&lt;sub&gt;MA&lt;/sub&gt; 14 mm</td>
<td>ExTEM A&lt;sub&gt;10&lt;/sub&gt; 35–42 mm and FibTEM ≥10 mm</td>
<td>Platelets ↓</td>
<td>Platelets 5 ml/kg</td>
</tr>
<tr>
<td></td>
<td>ExTEM MCF &lt;50 mm and FibTEM ≥10 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MA &lt;45 mm or FF&lt;sub&gt;MA&lt;/sub&gt; &gt;14 mm</td>
<td>ExTEM A&lt;sub&gt;10&lt;/sub&gt; &lt;35 mm and FibTEM ≥10 mm</td>
<td>Platelets ↓↓</td>
<td>Platelets 10 ml/kg</td>
</tr>
<tr>
<td></td>
<td>ExTEM Li30 &lt;94%</td>
<td>Hyperfibrinolysis</td>
<td>TXA 1–2 g IV or 10–20 mg/kg</td>
</tr>
<tr>
<td>Ly30 &gt;8%</td>
<td>InTEM CT/HepTEM CT &gt;1.25</td>
<td>Heparinazation</td>
<td>Protamine 50–100 mg or FFP 10–20 ml/kg</td>
</tr>
<tr>
<td>Difference in R Hep TEG vs. standard TEG R &gt;2 min</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If treatment failure – call Bloodbank

Stensballe et al. Curr Opin Anesthesiol 2014
Analysis 1.1. Comparison 1 TEG or ROTEM versus any comparison, Outcome 1 Mortality; grouped by TEG or ROTEM.

Review: Thromboelastography (TEG) or thromboelastometry (ROTEM) to monitor haemostatic treatment versus usual care in adults or children with bleeding

Comparison: 1 TEG or ROTEM versus any comparison

Outcome: 1 Mortality; grouped by TEG or ROTEM

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>TEG or ROTEM</th>
<th>Control</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (95% CI)</td>
<td>364</td>
<td>353</td>
<td></td>
<td>100.0%</td>
<td>0.52 [0.28, 0.95]</td>
</tr>
</tbody>
</table>

Total events: 14 (TEG or ROTEM), 26 (Control)
Heterogeneity: Chi² = 4.08, df = 5 (P = 0.54); I² = 0.0%
Test for overall effect: Z = 2.13 (P = 0.033)
Test for subgroup differences: Chi² = 0.56, df = 1 (P = 0.46), I² = 0.0%
Start of bleeding

- TXA 1 g IV bolus & 1 g IV in 8 hours

Trauma-Induced Coagulopathy
- VHA monitoring → Goal-directed therapy with Plasma, PLT, change of ratio, Cryo, fibrinogen & TXA
- Ratio 1:1:1 (RBC, plasma, PLT)

Risk of coagulopathy
- Arrival → during resuscitation & surgery

Control of bleeding

VTE prophylaxis

The Copenhagen Concept
The Copenhagen Concept

Blood bank specialist on call 24/7
My practical points

- Go for a little crystalloids (1:1)
- Be restrictive with bloods in most patients
- Monitor
  - Hb. (trigger < 70 g/dL ~ < 4.3 mmol/L)
  - Goal-direct therapy with TEG/ROTEM (normal clot)
- Massive bleeding is treated with 1:1:1 (4:4:2) and further goal-direct