Point-of-care testing – Thrombelastography and platelet transfusion

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Trauma-induced coagulopathy (TIC)

- Tissue trauma + Consumption
- Tissue trauma + Hyperfibrinolysis
- Thrombomodulin / Protein C
- Blood loss
- Fluid resuscitation + Dilution
- Triad of Malfunction (hypothermia, acidosis, hypocalcaemia)

Pre-existing disorders
- Anticoagulation
- Antiplatelet drugs

Cut vesicles
Limitations of “routine coagulation tests”
aPTT, PT, fibrinogen, platelet count

- no informative test results: aPTT ↑
  factor deficit, hyperfibrinolysis, hypothermia, heparin
- delayed availability of test results > 30 min
- no assessment of fibrinolysis, hypercoagulability
- reflect only plasmatic components (pre-analytical error)
- no validation for monitoring perioperative bleeding
- no prediction of bleeding
- methodological limitations
Goal-directed algorithm management

Algorithm for treating bleeding in patients with trauma-induced coagulopathy

Temperature > 34°C, pH > 7.2, Calcium > 1.0 mmol/L, Haematocrit > 28%

Severe trauma (ISS>15) and/or severe shock

Run ROTEM (TECM, INTEM, FIBTEM, APTEM)

1. Focus on: hyperfibrinolysis
   - EXTEM CT > APTM CT
   - Treat fibrinolysis
   - TXA 15–20 mg/kg BW

2. Focus on: fibrin deficit
   - FIBTEM CAL < 7 mm
   - Increase FIBTEM CAL to 10–12 mm
   - Fibrinogen concentrate 2–6 g (Cryoprecipitate, FFP)

3. Focus on: thrombin generation deficit
   - EXTEM CT > 40 sec
   - EXTEM CAL > 10 mm
   - Treat coagulation factor deficiency
   - FFP 20–30 ml/kg BW

4. Focus on: platelet deficit
   - EXTEM CAL < 40 mm
   - Increase platelet count to >50,000/μl
   - Platelet concentrate
   - TXA 15–20 mg/kg BW

Severe clot deficiency

- EXTEM CAL < 50 mm
- Treat immediately
- Fibrinogen concentrate 6–8 g and FFP 20–30 ml/kg BW
- Platelet concentrate

ROTEM may also identify:

Potential heparin exposure (e.g. cell-saver blood)
- HEPTEM CT < INTEM CT
- Treat heparin effect
- Protamine 1000–2000 U

Clot instability not related to hyperfibrinolysis
- EXTEM ML > 15% and APTEM ML > 15%
- Consider Factor XIII 1.250 U
Intraoperative diagnostic tools

ROTEM® TEM Innovations, Munich

TEG® Analyzer
Haemoscope, USA
Thrombelastometry: Therapeutic approach

- Fibrinogen platelet concentrate
- Maximum clot firmness (MCF in mm)
- Maximum lysis (% ML)
- Clotting time (CT in sec)
- PCC, fresh frozen plasma
- Antifibrinolytics
Normal haemostasis
Management of bleeding and coagulopathy following major trauma: an updated European guideline

**Platelets**

**Recommendation 28** We recommend that platelets be administered to maintain a platelet count above $50 \times 10^9/\text{l}$. (Grade 1C)

We suggest maintenance of a platelet count above $100 \times 10^9/\text{l}$ in patients with ongoing bleeding and/or TBI. (Grade 2C)

We suggest an initial dose of four to eight single platelet units or one aphaeresis pack. (Grade 2C)
Side effects of platelet transfusion

- Incidence 1.5 - 7%, Sepsis 1 : 25.000
- Viral infektion (HBV 1 : 320.000 - 500.000)
- bakterielle Kontamination
- TRALI, incidence 1 : 2000-5000
- Refractory transfusions
Bleeding and \( A_{10_{\text{EX}}} < 45 \text{ mm} \) and \( A_{10_{\text{FIB}}} \geq 10 \text{ mm} \)

Thrombocytopenia (22 G/l) with bleeding but high fibrinogen → transfusion of one platelet concentrate
No bleeding, $A_{10}^{\text{EX}} \approx 45\, \text{mm}$ and $A_{10}^{\text{FIB}} >> 10\, \text{mm}$

Thrombocytopenia (48 G/l) compensated by high fibrinogen → no more platelet transfusion required
The Effects of Fibrinogen Levels on Thromboelastometric Variables in the Presence of Thrombocytopenia

Thomas Lang, MD*†
Kai Johanning, MD*
Helfried Metzler, MD‡
Siegfried Plepenbrock, MD*
Cristina Solomon, MD*
Niels Rahe-Meyer, MD, PhD*
Kenichi A. Tanaka, MD, MSc§

CONCLUSIONS: These in vitro and clinical data indicate that the clot strength increases in a fibrinogen concentration-dependent manner independent of platelet count, when analyzed by ROTEM. The maintenance of fibrinogen concentration is critical in the presence of thrombocytopenia. EXTEM® (extrinsic activation) and FIBTEM may be useful in guiding fibrinogen repletion therapy.

The Effects of Platelet Transfusions Evaluated Using Rotational Thromboelastometry

(Anesth Analg 2009;108:1430–2)

Per Flisberg, MD, PhD*
Malin Rundgren, MD*
Martin Engström, MD, PhD†

BACKGROUND: In this study, we assessed the immediate effects of platelet transfusion on whole blood coagulation.
METHODS: Ten thrombocytopenic patients given a single unit platelet transfusion of 200–300 × 10⁹ platelets had their coagulation status assessed before and immediately after transfusion using rotational thromboelastometry.

Table 1. Results of the Analyses Performed Before and After Platelet Transfusions

<table>
<thead>
<tr>
<th></th>
<th>Before Transfusion</th>
<th>After Transfusion</th>
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</thead>
<tbody>
<tr>
<td>Hb (g/L)</td>
<td>91 (88–101)</td>
<td>88.5 (83–94)</td>
</tr>
<tr>
<td>PT (INR)</td>
<td>1.2 (0.9–1.4)</td>
<td>1.2 (0.9–1.3)</td>
</tr>
<tr>
<td>aPTT (s)</td>
<td>35.5 (27–54)</td>
<td>37 (27–61)</td>
</tr>
<tr>
<td>Platelet count (×10⁹/L)</td>
<td>31.5 (20–44)</td>
<td>43.5 (38–71)*</td>
</tr>
<tr>
<td>Clotting time (s)</td>
<td>103.5 (81–215)</td>
<td>108.5 (51–158)</td>
</tr>
<tr>
<td>Clot formation time (s)</td>
<td>181.5 (108–347)</td>
<td>123 (89–233)*</td>
</tr>
<tr>
<td>Maximum clot firmness (mm)</td>
<td>42 (38–50)</td>
<td>51.5 (45–56)*</td>
</tr>
<tr>
<td>G (dynes/cm²)</td>
<td>3623 (2353–6111)</td>
<td>5319 (3333–7500)*</td>
</tr>
</tbody>
</table>

PT = prothrombin time; aPTT = activated partial thromboplastin time; Hb = hemoglobin.
* P = 0.005, when compared with before transfusion.
Beyond the platelet count: immature platelet fraction and thromboelastometry correlate with bleeding in patients with immune thrombocytopenia

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Division of Hematology/Oncology, Department of Paediatrics, Weill Cornell Medical College, New York, NY, USA

with ABS in any subgroup. Thromboelastometry measures of clot firmness, but not PC, significantly correlated with ABS in all subjects with PC \(<60 \times 10^9/\text{l}\), and children with PC \(<60 \times 10^9/\text{l}\) and \(<30 \times 10^9/\text{l}\). A-IPF demonstrated stronger correlation with ABS than did PC among all subjects, those with PC \(<60 \times 10^9/\text{l}\), all children and children with PC \(<30 \times 10^9/\text{l}\) \((r = -0.37; r = -0.34; r = -0.44; r = -0.60)\) versus ABS with PC \((r = -0.36; \text{ns}; r = -0.32; \text{ns})\). Stronger correlations of both thromboelastometry measures of clot firmness and A-IPF than PC with ABS suggest factors beyond PC, i.e. related to platelet function, contribute to ITP bleeding pathophysiology. Thromboelastometry, A-IPF and ABS can be incorporated into routine or acute visits.

*ABS = acute bleeding score
Platelet transfusion: effect on increment in platelet count and increase in EXTEM (INTEM) MCF (A5, A10)

One therapeutic unit of platelets (either whole blood pooled buffy coat platelets from 4 donors or apheresis platelet from 1 donor) contain about 200-300 $\times 10^9$ platelets

Increment in platelet count in hematology patients with severe thrombocytopenia ($< 50 \times 10^9$/L): $12-18 \times 10^9$/L ($13 \times 10^9$/L in cirrhosis)

Increase in EXTEM (INTEM) MCF (A5, A10): 8-10 mm (only 5 mm in cirrhosis)

No change in EXTEM (INTEM) CT but decreased CFT (x 0.7-0.8); no change in FIBTEM MCF

Increase in impedance aggregometry ADP and TRAP AUC from 3 to 7 U and from 5 to 17 U, respectively

Conclusions – In this prognostic study, we identified clinically significant platelet dysfunction after trauma in the presence of an otherwise reassuring platelet count and standard clotting studies, with profound implications for mortality. Multiple electrode impedance aggregometry reliably identifies this dysfunction in injured patients, and admission arachidonic acid and collagen responsiveness are sensitive and specific independent predictors of both early and late mortality.
Management of bleeding and coagulopathy following major trauma: an updated European guideline

Donat R Spahn¹, Bertil Bouillon², Vladimir Cerny³,⁴, Timothy J Coats⁵, Jacques Duranteau⁶, Enrique Fernández-Mondéjar⁷, Daniela Filipescu⁸, Beverley J Hunt⁹, Radko Komadina¹⁰, Giuseppe Nardi¹¹, Edmund Neugebauer¹², Yves Ozier¹³, Louis Riddez¹⁴, Arthur Schultz¹⁵, Jean-Louis Vincent¹⁶ and Rolf Rossaint¹⁷

Recently, it was shown that identification of impaired platelet function with a platelet function analyzer PFA-100 [454] or whole blood multiple electrode aggregometer [455] might be helpful in the identification of patients who may benefit from desmopressin therapy.
Management of bleeding and coagulopathy following major trauma: an updated European guideline


In addition, TXA was shown to partially improve platelet function in patients treated with dual antiplatelet therapy as measured by multiple electrode aggregometry [459].
Conclusions

- PLTEM A10 (= EXTEM A10 – FIBTEM A10) ($r = 0.85$) shows a better correlation to platelet count than EXTEM A10 ($r = 0.74$). However, PLTEM A10 does not reflect the compensatory effect of high plasma fibrinogen concentration.

- Therefore, the combination **EXTEM A10 < 45 mm and FIBTEM A10 ≥ 10 mm** (which includes the information provided by PLTEM A10) seem to be superior in providing an adequate cut-off value for platelet transfusion in bleeding trauma patients compared to PLTEM (A10 < 25-35 mm) alone.

- **One therapeutic unit of platelets** (either whole blood pooled buffy coat platelets from 4 donors or apheresis platelet from 1 donor) contain about **200-300 x 10^9 platelets**

- The **increment in platelet count** per transfused platelet concentrate in patients with severe thrombocytopenia is **12-18 x 10^9/L**.
Conclusions

- The increase in EXTEM A10 per transfused platelet concentrate in patients with severe thrombocytopenia is 8-10 mm.

- Therefore, one platelet concentrate has to be administered for each targeted increase in EXTEM A10 by 10 mm.

- In the absence of clinical relevant bleeding an EXTEM A10 ≥ 45 mm should not be used as a platelet transfusion trigger.

- Sensitivity of thromboelastometry to the effects of antiplatelet drugs?

- Platelet function tests (e.g. aggregometry, PFA 100) should be used if platelet dysfunction is suspected due to antiplatelet drugs or trauma itself.
Potential conflicts of interest

Travel reimbursement, honoraria for lectures and consulting:

CSL Behring
Fresenius Kabi
Verum Diagnostica
Thank you for your attention!

www.perioperativebleeding.org

gisela.scharbert@meduniwien.ac.at
EXTEM

Aktivierung der Gerinnung im TEM durch Gewebsthromboplastin

Erfassung der Faktoren: VII,X,V,II,I + Thrombozyten

INTEM

Aktivierung der Gerinnung im TEM durch Thromboplastin

Erfassung der Faktoren: XII,XI,IXVIII,X,V,II,I + Thrombozyten
FIBTEM
Aktivierung wie EXTEM unter Zusatz von Cytochalasin D. Dieser Test hilft den Anteil des Fibrinogens an der im TEM gemessenen Gerinnung festzustellen.

APTEM
Aktivierung wie EXTEM unter Zusatz von Aprotinin (Antifibrinolytikum). Im Vergleich zum EXTEM kann nach ca. 5 Minuten eine Aussage zur Hyperfibrinolyse gemacht werden.
HEPTEM

Aktivierung wie INTEM unter Zusatz von Heparinase. Im Vergleich zum INTEM kann eine heparinbedingte Gerinnungsstörung erfasst werden.

NATEM

Bestimmung eines nicht aktivierten TEM aus nativem Vollblut oder rekalzifiziertem Zitratblut
TEG® Analyzer Haemoscope, USA

- Torsion wire
- Pin
- Cup
- Heating element, sensor & controller
- .36 ml whole blood (Clotted)

4°45
"Platelet-Mapping" Haemoscope, USA

1. Citrated kaolin

% MA-Reduzierung durch Thrombozytenmedikamentation 100

Probe: 2/16/2006 09:43:28 - 10:58:08

Kaolin-aktivierte MA\textsuperscript{STANDARD}

P1-aktivierte MA\textsuperscript{THROMBIN}

P3-aktivierte MA\textsuperscript{ADP oder AA}

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<th>R</th>
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<th>Angle</th>
<th>MA</th>
<th>G</th>
<th>EPL</th>
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Citrated kaolin

% MA-Reduzierung durch Thrombozytenmedikament 67.9

Probe: 2/16/2006 09:43:28 - 10:58:08

Kaolin-aktivierte MA\textsuperscript{STANDARD}

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<td>0 – 15</td>
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