Patient Blood Management In Cardiac Surgery: Principles & Role of TEG - ROTEM

Philippe Van der Linden MD, PhD
Patient Blood Management

- Defined as “the appropriate use of blood and blood components with a goal of minimizing their use”.

- Encompasses an evidence-based medical and surgical approach that is multidisciplinary (transfusion medicine specialists, surgeons, anesthesiologists, and critical care specialists) and multiprofessional (physicians, nurses pump technologists and pharmacists)

Patient Blood Management: Motivation

- Known (and unknown) risk associated with blood products
- Constraints from escalating costs
- Preservation of the national blood inventory
  - Decreased donors' population
  - Increased demand of products
  - Mismatch between recipients and donors regarding ABO blood groups (i.e. sickle cell disease)

- Aging of the population
- Changes in travel pattern
Perioperative Blood Conservation Strategy

- Preop RBC mass
- Periop blood loss
- Reduce the Transfusion Trigger

depending on:
- Surgical procedure and technique
- Patients limitations
- Health Care environment
- Immediate and long term costs
Major Bleeding, Transfusions, and Anemia: The Deadly Triad of Cardiac Surgery

- Retrospective study of the institutional database 2000-2012 (N=16,174)

Massive Hemorrhage

✓ Replacement of one blood mass in less than 24 hours

✓ Dynamic definition more relevant in the acute clinical setting:
  
  • Transfusion of four or more red cell concentrates within one hour when ongoing need is foreseeable
  
  • Replacement of 50% of the total blood volume within 3 hours
Massive Transfusion During Elective Surgery or Major Trauma

<table>
<thead>
<tr>
<th></th>
<th>Elective Surgery</th>
<th>Major Trauma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue trauma</td>
<td>Controlled</td>
<td>Uncontrolled</td>
</tr>
<tr>
<td>Initiation of MT</td>
<td>No delay</td>
<td>Variable</td>
</tr>
<tr>
<td>Volume status</td>
<td>Normovolemia</td>
<td>Hypovolemia</td>
</tr>
<tr>
<td>Temperature</td>
<td>Normothermia</td>
<td>Hypothermia</td>
</tr>
<tr>
<td>Hemostasis monitoring</td>
<td>Ongoing</td>
<td>Late</td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>↓ factors</td>
<td>Complex</td>
</tr>
</tbody>
</table>

Monitoring of Hemostasis During Massive Transfusion

- Preoperative evaluation and preparation

- Clinical evaluation: visual assessment of the surgical field, blood loss measurements, communication with the surgeons...
  - Caution with epistaxis, blood issued from tracheal or gastric tubes, hematomas after venous puncture, hematuria?

Clinical judgment alone is insufficient as an indication for transfusion
Monitoring of Hemostasis During Massive Transfusion: PT (INR) & aPTT

✓ Developed to monitor hemophilia & anticoagulation therapy (50 years ago)

✓ Predictors of mortality in trauma

✓ Not validated to predict hemorrhage in a clinical setting: plasma-based assays reflect only the small amount of thrombin formed during initiation of coagulation
Monitoring of Hemostasis During Massive Transfusion: PT (INR) & aPTT

- High sensitivity, low specificity
- Marked prolongations (1.5 to 1.8 x control)
  - Predict factor V and VIII < 30%
  - Correlates with microvascular bleeding

From blood sampling to results: 30 min to...?
Monitoring of Hemostasis During Massive Transfusion

✓ Platelet count
  • Readily available via automated counters
  • Must be interpreted in the clinical situation:
    ➢ Hypothermia?
    ➢ Expected platelet function?
    ➢ Hemoglobin concentration?
    ➢ Fibrinogen concentration?
    ➢ DIC?

Low platelet count ≠ platelet transfusion
Monitoring of Hemostasis During Massive Transfusion

✓ TEG (thromboelastography) & ROTEM (rotational thromboelastometry)
  • First described in 1948 by H. Hartert as a method to assess the viscoelastic properties of coagulation in whole blood under low shear stress conditions
  • It gives a graphic presentation of clot formation and subsequent lysis
  • Blood is incubated at 37°C in a heated cup
Monitoring of Hemostasis During Massive Transfusion

✓ TEG (thromboelastography)
Monitoring of Hemostasis During Massive Transfusion

✓ ROTEM (rotational thromboelastometry)

1. Oscillating axis
2. Counterforce spring
3. Light beam from LED
4. Mirror
5. Detector (electr camera)
6. Sensor pin
7. Cuvette with blood sample
8. Fibrin strands and platelet aggregates
9. Heated cuvette holder
10. Ball bearing
11. Data processing unit
Monitoring of Hemostasis During Massive Transfusion

✔ TEG (thromboelastography) & ROTEM (rotational thromboelastometry)

- As fibrin forms between the cup and the pin, the transmitted rotation from cup to pin (TEG) or the impedance of the rotation of the pin (ROTEM) are detected at the pin and a trace is generated.
Monitoring of Hemostasis During Massive Transfusion: TEG & ROTEM
## Monitoring of Hemostasis During Massive Transfusion: TEG & ROTEM

<table>
<thead>
<tr>
<th>TEG</th>
<th>ROTEM</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>R: reaction time</td>
<td>CT: clotting time</td>
<td>time of latency from the time that the blood was placed in the analyzer until the initial fibrin formation</td>
</tr>
<tr>
<td>K: clot formation time</td>
<td>CFT: clot formation time</td>
<td>measures the rapidity (kinetics) of fibrin build-up and cross-linking, that is, the speed of clot strengthening</td>
</tr>
<tr>
<td>α: alpha angle</td>
<td>α: alpha angle</td>
<td>a measure of the rapidity to reach a certain level of clot strength</td>
</tr>
<tr>
<td>MA: maximal amplitude</td>
<td>MCF: maximal clot firmness</td>
<td>a direct function of the maximum dynamic properties of fibrin and platelet bonding. It represents the ultimate strength of the fibrin clot</td>
</tr>
<tr>
<td>Ly: clot lysis</td>
<td>CL: clot lysis</td>
<td>measures the rate of amplitude reduction “X” minutes after MA. It gives an indication of the stability of the clot</td>
</tr>
</tbody>
</table>
## Monitoring of Hemostasis During Massive Transfusion: TEG & ROTEM

<table>
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<th>TEG</th>
<th>ROTEM</th>
<th>Cell-based model of coagulation</th>
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<tr>
<td>R: reaction time</td>
<td>CT: clotting time</td>
<td>Initiation phase</td>
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<td>Amplification phase</td>
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<tr>
<td>α: alpha angle</td>
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<td>Thrombin burst</td>
</tr>
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<td>MA: maximal amplitude</td>
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<td>Thrombin generation</td>
</tr>
<tr>
<td>Ly: clot lysis</td>
<td>CL: clot lysis</td>
<td>Fibrinolysis</td>
</tr>
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</table>
TEG & ROTEM: Activators

**TEG**
- Native
- Kaolin
- Tissue factor
- Tissue factor / Kaolin
- Heparinase
- Functional fibrinogen

**ROTEM**
- INTEM
- EXTEM
- HepTEM
- APTEM
- FIBTEM
- ECATEM
## TEG New Development: Platelet Mapping™

<table>
<thead>
<tr>
<th>Channel 1</th>
<th>Channel 2</th>
<th>Channel 3</th>
<th>Channel 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole blood</td>
<td>Whole blood</td>
<td>Whole blood</td>
<td>Whole blood</td>
</tr>
<tr>
<td>Kaolin</td>
<td>Heparin</td>
<td>Novel activator</td>
<td>Novel activator</td>
</tr>
<tr>
<td>Max MA using commonly protocol with Kaoline</td>
<td>Unique contribution of fibrin to MA</td>
<td>Contribution to MA of fibrin and uninhibited platelets by ADP or IIbIIIa inhibitors</td>
<td>Contribution to MA of fibrin and uninhibited platelets by NSAID</td>
</tr>
</tbody>
</table>
TEG & ROTEM: Clinical Interchangeability?

- Prospective observational study: 46 cardiac surgery patients
- Kaolin TEG, Native TEG, InTEM and ExTEM (N=166)
- R time and K time not interchangeable
- Repeatability of the R & K times was poor with both devices
- Repeatability of the MA & α sufficient for clinical purposes
- Kaolin TEG had the best agreement with the ExTEM measurements

Clinical interpretation of thromboelastographic data: caution!

Advantages

• Assessment of the combined influence of circulating plasmatic and cellular elements on clot formation (including platelet function)
• Clinical relevant end-point
• Results available within a short time frame
• Reductions in transfusions

Treatment Strategies Based On TEG / ROTEM in Trauma Patients

Classical hemostatic resuscitation strategy: plasma, platelets and antifibrinolytics are administered as guided by TEG / ROTEM

Pharmacological resuscitation strategy: Different coagulation factor concentrates are administered as guided by TEG / ROTEM

## Blood Products vs. Factors Concentrates?

<table>
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<tr>
<th>Blood products</th>
<th>Pharmacological approaches</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pro</strong></td>
<td><strong>Con</strong></td>
</tr>
<tr>
<td>Contain all factors, fibrinogen</td>
<td>Transfusion-related risks</td>
</tr>
<tr>
<td>MTP</td>
<td>Cross-matched</td>
</tr>
<tr>
<td>Fluid strategy</td>
<td>Large amount of fluid</td>
</tr>
<tr>
<td>Cytokines</td>
<td>No cytokines</td>
</tr>
</tbody>
</table>

Coagulation Management in Cardiac Surgery

✓ Retrospective single-center cohort study
✓ Algorithm implementation (2005) using thromboelastometry (ROTEM®) & blood impedance aggregometry (Multiplate®)
  • In patients at high risk for bleeding or in those with “clinically relevant” diffuse bleeding after heparin antagonization with protamine
  • First-line therapy with fibrinogen & prothrombin complex concentrate

✓ Before (2004; N=1718) & after (2009; N=2147) comparison
✓ ROTEM & Multiplate: used in 17.5% & 10.6% of patients respectively

Coagulation Management in Cardiac Surgery

Coagulation Management in Cardiac Surgery

Coagulation Management in Cardiac Surgery

Hemostatic Therapy in Cardiac Surgery Patients Guided by Point of Care Testing

✓ Prospective randomized parallel-group single-center study
✓ Patients undergoing complex cardiac surgery in whom diffuse bleeding was diagnosed after heparin reversal

- Conventional coagulation analyses
- ROTEM® + whole blood impedance aggregometry (Multiplate®)

✓ First objective:
  - PRBCs units transfused during the first 24 hours after inclusion
  - Study terminated after inclusion of 50 patients in each group

Hemostatic Therapy in Cardiac Surgery Patients Guided by Point of Care Testing

POC group patients received less PRBCs, FFP, platelets units and rFVIIa.

POC group patients had lower postoperative mechanical ventilation time, ICU length of stay, and composite adverse events rate.

Monitoring of Hemostasis During Massive Transfusion: TEG & ROTEM

✓ Limitations

• Easy of use ? Costs ?
• Effects of hypothermia ?
• Effects of hematocrit ?
• Platelet disorders (cf. Von Willebrand Σ) ?
• Antiplatelet therapies
• Moderate correlation with routine coagulation tests
  Preanalytic preparations, test medium, validation (CV < 5% MCF, CT)

  Lang et al. Blood Coagul Fibrinolysis 2005
Patients undergoing cardiac surgery with CPB (N=321)

Chest tube output (end CPB through the first 8 postop hours)

ROTEM In Pediatric Cardiac Surgery Patients

- One year-old baby – 5.5 kg – 66 cm
- Elective atrio-ventricular canal defect repair
- Priming
  - RBCs to maintain Hct > 25%
  - 6% HES 130/0.4: 30 ml/kg
- End-of bypass, after heparin antagonization with protamine (1 mg / 200 IU heparin)
- Temperature: 36.5°C
ROTEM In Pediatric Cardiac Surgery Patients
ROTEM In Pediatric Cardiac Surgery Patients

- Treatment: nihil!
- Normal thorax closing time: 60 minutes
- Post-op blood loss: 30 mL
A change in anticoagulation monitoring improves safety, reduces transfusion, and reduces costs in infants on cardiopulmonary bypass

<table>
<thead>
<tr>
<th></th>
<th>ACT (control)</th>
<th>HMS (intervention)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intraoperative blood products</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total intraoperative products, ml·kg⁻¹</td>
<td>193 (138, 315)</td>
<td>147 (111, 229)</td>
<td>0.01</td>
</tr>
<tr>
<td>RBC, ml·kg⁻¹</td>
<td>97 (67, 132)</td>
<td>67 (53, 100)</td>
<td>0.009</td>
</tr>
<tr>
<td>FP, ml·kg⁻¹</td>
<td>76 (46, 120)</td>
<td>65 (49, 94)</td>
<td>0.28</td>
</tr>
<tr>
<td>Platelets, ml·kg⁻¹</td>
<td>11 (5, 17)</td>
<td>5 (0, 11)</td>
<td>0.006</td>
</tr>
<tr>
<td>Cryoprecipitate, ml·kg⁻¹</td>
<td>16 (0, 31)</td>
<td>13 (0, 21)</td>
<td>0.18</td>
</tr>
<tr>
<td><strong>Intraoperative blood product exposures</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total products, number of units</td>
<td>5 (4, 7)</td>
<td>4 (2, 5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RBC, number of units</td>
<td>2 (1, 7)</td>
<td>1 (1, 2)</td>
<td>0.0006</td>
</tr>
<tr>
<td>FFP, number of units</td>
<td>1 (1, 2)</td>
<td>1 (1, 1)</td>
<td>0.01</td>
</tr>
<tr>
<td>Platelets, number of units</td>
<td>1 (1, 1)</td>
<td>1 (0, 1)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Cryoprecipitate, number of units</td>
<td>1 (1, 1)</td>
<td>1 (0, 1)</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postbypass operating room Time ($)*</td>
<td>1680 (1232, 2064)</td>
<td>1240 (1040, 1584)</td>
<td>0.001</td>
</tr>
<tr>
<td>Total blood products ($)</td>
<td>2378 (1975, 2991)</td>
<td>1975 (163, 2378)</td>
<td>0.0003</td>
</tr>
<tr>
<td>RBC ($)</td>
<td>806 (403, 806)</td>
<td>403 (403, 806)</td>
<td>0.0006</td>
</tr>
<tr>
<td>FFP ($)</td>
<td>210 (210, 420)</td>
<td>210 (210, 210)</td>
<td>0.01</td>
</tr>
<tr>
<td>Platelets ($)</td>
<td>802 (802, 802)</td>
<td>802 (0, 802)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Cryoprecipitate ($)</td>
<td>560 (560, 560)</td>
<td>560 (0, 560)</td>
<td>0.06</td>
</tr>
<tr>
<td>Recombinant factor VIIIa received in OR, %</td>
<td>16 (8)</td>
<td>12 (6)</td>
<td>0.56</td>
</tr>
<tr>
<td>Postbypass operating room time (minutes)*</td>
<td>107 (80, 129)</td>
<td>78 (65, 99)</td>
<td>0.0006</td>
</tr>
<tr>
<td>Postoperative chest tube output</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 h (ml·kg⁻¹)</td>
<td>6.6 (4.6, 14)</td>
<td>7.8 (4.9, 12.6)</td>
<td>0.64</td>
</tr>
<tr>
<td>24 h (ml·kg⁻¹)</td>
<td>23.8 (16.9, 34.9)</td>
<td>25.1 (15.5, 37.2)</td>
<td>0.98</td>
</tr>
</tbody>
</table>

Monitoring of Hemostasis During Massive Transfusion TEG – ROTEM: Conclusions

- Interesting tools to assess hemostasis
- Usefulness to be demonstrated in prospective randomized studies
- Technical limitations

- To be located in the blood banks
- To be used in specific algorithms with «transfusion package» policies