What I need to treat our bleeding patients properly

M. Ranucci
Director of Clinical Research
Dept of Cardiothoracic and Vascular Anesthesia and Intensive Care
IRCCS Policlinico S.Donato
Disclosures

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Haemonetics
Werfen-IL
Haemosonics
Roche Diagnostics
CSL Behring
Livanova
Medtronic
THE PRE-REQUISITE: A BLEEDING PATIENT

- The PPV of point-of-care or standard coagulation tests is very poor (< 10%) for prediction of bleeding.
- Therefore, routine application of these tests and the consequent algorithms should be avoided.
- Tests and algorithms should be applied only in:
  a) Patients at very high risk of bleeding due to their characteristics (drugs on board; low platelet count; known coagulopathy) or to the procedure (aortic dissection, very complex surgery)
  b) Evidence of microvascular bleeding in the OR
  c) Evidence of excessive chest drain blood loss in the ICU
THE CORRECT WAY: A STEP-BY STEP RULE OUT

- The NPV of point-of-care tests is very high: > 95%
- Therefore, instead of ruling in the different bleeding causes, a ruling-out approach should be followed
- Vertical algorithms run better than horizontal ones
- The order of approach to the different bleeding causes is important, and depends on (a) the easiness of the therapeutic approach and (b) the probability of the different causes (i.e. platelet dysfunction more likely than low coagulation factors)
BLEEDING PATIENT

Viscoelastic and standard coagulation tests

- Check residual heparin (difference in reaction times)
  - Additional protamine
- Check platelet count and function
  - Platelet transfusion Desmopressin
- Check fibrinogen level (FF or FIBTEM or Clauss)
  - Fibrinogen concentrate or cryoprecipitate or FFP
- Check thrombin generation (reaction times)
  - PCCs or FFP or rFVIIa in extreme cases
- Exclude hyperfibrinolysis (clot lysis index)
  - Tranexamic acid E-aminocaproic acid
BLEEDING PATIENT → Viscoelastic and standard coagulation tests

STEP 1: Check residual heparin (difference in reaction times) → Additional protamine

STEP 2: Check platelet count and function → Platelet transfusion - Desmopressin

STEP 3: Check fibrinogen level (FF or FIBTEM or Clauss) → Fibrinogen concentrate or cryoprecipitate or FFP

STEP 4: Check thrombin generation (reaction times) → PCCs or FFP

STEP 5: Exclude hyperfibrinolysis (clot lysis index) → Tranexamic acid / ε-aminocaproic acid

STEP 6: No signs of coagulopathy → Consider surgical re-exploration

STEP 7: Life-threatening bleeding → Consider rFVIIa
A VISCOELASTIC TESTS-BASED ALGORITHM (TEG-ROTEM)

Rule-out residual heparin

Yes

Protamine supplementation

No

 Proceed to step 2
FORGET THE ACT
A VISCOELASTIC TESTS-BASED ALGORITHM (TEG-ROTEM)

Rule-out low platelet count/function

Yes

Platelet concentrate transfusion and/or DDAVP

No

Proceed to step 3
Cardiac Surgery Intraoperative Targeted Transfusion Algorithm
Non-TEG/ROTEM directed

Consider: Anti-fibrinolytics, ANH, mini-circuits, retrograde autologous priming, or ultrafiltration and the use of red cell salvage using centrifugation
Before coming Off CPB: measure Hb, platelet count, fibrinogen level and heparin-corrected INR

JUST COUNT!

Excessive microvascular bleeding in the field

- Hb < 7.5 g/dL
  - Transfuse RBC to Hb 7.5 g/dL
- PLT < 50,000 μ/L
  - Transfuse PLT to PLT > 50,000 μ/L or hemostasis
- INR > 1.5
  - Transfuse FFP 10-15 ml/Kg or “low dose” PCC*
- Fibrinogen < 200 mg/dl
  - Transfuse cryoprecipitate to fibrinogen > 200 mg/dl or fibrinogen concentrate**
- ACT > baseline
  - Check heparin level to guide additional protamine

If excessive bleeding persists

Re-send labs:
ACT, Hb, PLT, INR, Fibrinogen

DYSFUNCTION?

- Abnormal Labs
  - Transfuse to hemostasis goal: Hb > 7.5 g/dL PLT >100,000 μ/L Fibrinogen > 200 mg/dl INR < 1.5
  - Consider DDAVP 0.3 mcg/kg, if poor kidney function or PLT dysfunction
- If INR > 2 and/or RV failure, consider PCC**

Check and optimize:
T > 36°C pH > 7.2 iCa > 1.0 mmol/L Hb > 7.5 g/dl

Normal Labs
- Surgical re-exploration or rFVIIa (20-40mcg/kg)

Check and optimize:
T > 36°C pH > 7.2 iCa > 1.0 mmol/L Hb > 7.5 g/dl

Exact dosage has not been defined
** Where available and approved for use

Blood Conservation CPI Committee
2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery

The Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anaesthesiology (EACTA)

Authors/Task Force Members: Domenico Pagano* (EACTS Chairperson) (UK), Milan Milojevic (Netherlands), Michael I. Meestersa (Netherlands), Umberto Benedetto (UK), Daniel Bolliger (Switzerland), Christian von Heymanna (Germany), Anders Jeppsson (Sweden), Andreas Koster (Germany), Ruben L. Osnabruggena (Netherlands), Marco Ranuca (Italy), Hanne Berg Ravna (Denmark), Alexander B.A. Vonka (Netherlands), Alexander Wahba (Norway), Christa Boer (EACTA Chairperson) (Netherlands)

Document Reviewers: Moritz W.V. Wyler von Ballmoos (USA), Mate Petricevic (Croatia), Arie Pieter Kappetein (Netherlands), Miguel Sousa-Uva (Portugal), Georg Trummer (Germany), Peter M. Rosseela (Netherlands), Michael Sander (Germany), Pascal Colson (France), Adrian Bauer (Germany)
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<td>B</td>
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<td>Levelb</td>
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<td>Implementation of a PBM protocol for the bleeding patient is recommended.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>The use of PRBCs of all ages is recommended, because the storage time of the PRBCs does not affect the outcomes.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>The use of leucocyte-depleted PRBCs is recommended to reduce infectious complications.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Pooled solvent detergent FFP may be preferred to standard FFP to reduce the risk of TRALI.</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Perioperative treatment algorithms for the bleeding patient based on viscoelastic POC tests should be considered to reduce the number of transfusions.</td>
<td>IIa</td>
<td>B</td>
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<tr>
<td>It is recommended that one transfuse PRBCs on the basis of the clinical condition of the patient rather than on a fixed haemoglobin threshold.</td>
<td>I</td>
<td>B</td>
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<tr>
<td>A haematocrit of 21–24% may be considered during CPB when an adequate DO₂ (&gt;273 ml O₂/min/m²) level is maintained.</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Platelet concentrate should be transfused in bleeding patients with a platelet count below 50 (10⁹/l) or patients on antiplatelet therapy with bleeding complications.</td>
<td>IIa</td>
<td>C</td>
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GUIDELINES

Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology

First update 2016

7.5. Plasma and platelet transfusion
Recommendations

We recommend against the use of plasma transfusion for pre-procedural correction of mild-to-moderately elevated INR. 1C

We recommend early and targeted treatment of coagulation factor deficiencies in the plasma. Sources of coagulation factors are coagulation factor concentrates, cryoprecipitate or high volumes of plasma, depending on the clinical situation, type of bleeding, type of deficiency and resources provided. 1B

In the treatment of acquired coagulation factor deficiency, we suggest the consideration of a ratio-driven protocol (RBC:plasma:platelet concentrates) early in uncontrolled massive bleeding outside the trauma setting followed by a goal-directed approach as soon as possible. 2C

We suggest coagulation factor concentrates for the primary treatment of acquired coagulation factor deficiency due to their high efficacy and their minimal infectiousness. 2C

We recommend against indiscriminate use of plasma transfusion in perioperative bleeding management. 1C

We suggest platelet concentrate transfusion in bleeding situations clearly related to antiplatelet drugs or thrombocytopenia less than 50 x 10^9 l^-1. 2C
Normal reference for TEG

Functional fibrinogen

Standard TEG

<table>
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<tr>
<th>R (min)</th>
<th>K (min)</th>
<th>Angle (deg)</th>
<th>MA (mm)</th>
<th>PMA</th>
<th>G (mmol/L)</th>
<th>EPL</th>
<th>A (mm)</th>
<th>CT</th>
<th>LY30</th>
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<tr>
<td>20.4</td>
<td>3.6</td>
<td>46.9</td>
<td>58.6+</td>
<td>0.0</td>
<td>0.74+</td>
<td>6.0K-13.2K</td>
<td>50.6</td>
<td><em>-11.7</em></td>
<td>-3-3</td>
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</table>
FALSE: roughly indicative of count, not of function because thrombin (kaolin-dependent) always activates platelets
MCF 49
Range (50-72)

MCF 6
Range (9-25)

EXTEM

FIBTEM
<table>
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<th></th>
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<td>67s</td>
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<td></td>
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<tr>
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<td>73°</td>
</tr>
<tr>
<td>ML:</td>
<td></td>
<td></td>
<td></td>
<td>-%</td>
</tr>
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</table>
A normal Rotem-FibTEM
Figure 1
Figure 2: Scatter plot showing the relationship between platelet count (x1,000 cells/μL) and platelet contribution to clot strength, with separate lines for PCS_{el} (pink squares) and PCS_{amp} (blue circles).
MULTIVARIABLE ANALYSIS

Platelet count and ADP-dependent platelet function are independently associated with PCSel.

Platelet count explains 36% of the PCSel variance, Platelet function explains 14%.

Overall, the model explains 50% of the PCSel variance.
DISCRIMINATION (AUC) FOR LOW PLATELET COUNT (< 100,000) OR FUNCTION (ADPtest<12 U) IS VERY GOOD (0.837)
QUANTRA Hemostasis Analyzer

Point-of-Care Coagulation Monitoring

Dr. Ekaterina Baryshnikova, Biol.PhD
San Donato Milanese, Italy
Results display: the dial view
Our study

30 patients undergoing cardiac surgery (any kind)
QUANTRA compared with ROTEM, Multiplate and standard lab
2 time points:
   PRE (after induction, before incision)
   POST (after heparin reversal)

→ NO/weak correlation of Qplus CT and INTEM CT/aPTT
A  Quantra clot stiffness vs. EXTEM Maximum Clot Firmness – All samples

\[ y = -5.339 + 0.0290 \times \]

\( n = 00 \)

\( r = 0.98, P < 0.001 \)
A. Quantra fibrinogen contribution vs. FIBTEM Maximum Clot Firmness – All samples

\[ y = 0.277 + 0.0233 \times x \]
\[ n = 60 \]
\[ r = 0.87, P < 0.001 \]
Quantra fibrinogen contribution vs. Clauss Fibrinogen Concentration – All samples

\[ y = -1.296 + 0.0124 \times x \]
\[ n = 59 \]
\[ r = 0.82, P < 0.001 \]
Quantra platelet contribution vs. Platelet count – All samples

\[ y = 0.544 + 0.112 \times x \]

\( n = 60 \)

\( r = 0.71, P < 0.001 \)
Platelet Contribution related to ADP platelet function?

independently associated at multivariable analysis
PLATFORM

- Prospective cohort study
- Registered at Clinicaltrials.gov
- Adult patients
- 1-year data collection
- Exclusion: emergency surgery; unwillingness to participate; unavailability of reagents; unavailability of study staff
- Externally funded by Roche Diagnostics
PATIENT POPULATION:
494 subjects

DEFINITIONS:
Bleeding: chest drain blood loss 12-hours
Excessive Bleeding: according to the UDPB, > 1,000 mL/12 h and/or surgical revision
Measurements

- aPTT, INR, Platelet count the day before surgery
- aPTT, INR, fibrinogen (Clauss), Platelet count at the arrival in the ICU
- ADPtest and TRAPtest MEA (Multiplate) preoperatively, in the OR
- ADPtest and TRAPtest MEA (Multiplate) post-protamine, in the OR
EXCESSIVE BLEEDING

Chest drain blood loss (mL/kg/12h)

TRAPtest post
EXCESSIVE BLEEDING

Chest drain blood loss (mL/kg/12h)

ADPtest post

0 10 20 30 40 50 60 70 80 90 100 110 120

0 100 200 300 400 500 600 700 800 900 1000 1100 1200 1300 1400 1500 1600 1700 1800 1900 2000
AUC ADP: 0.716
AUC TRAP: 0.630
**POST-PROTAMINE ADPtest**
Rate of events: 8.3%

<table>
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<tr>
<th>CUT-OFF VALUE (U)</th>
<th>PPV</th>
<th>NPV</th>
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<td>4</td>
<td>27.7</td>
<td>88.2</td>
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<tr>
<td>6</td>
<td>33.8</td>
<td>89.4</td>
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<tr>
<td><strong>8</strong></td>
<td><strong>41.7</strong></td>
<td><strong>89.6</strong></td>
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<td>10</td>
<td>36.0</td>
<td>90.4</td>
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<td>12</td>
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<td>16</td>
<td>27.9</td>
<td>93.8</td>
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<td><strong>18</strong></td>
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<td><strong>94.0</strong></td>
</tr>
<tr>
<td>20</td>
<td>20.7</td>
<td>93.9</td>
</tr>
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</table>
A VISCOELASTIC TESTS-BASED ALGORITHM (TEG-ROTEM)

Rule-out low fibrinogen levels

Yes

FIBRINOGEN CONCENTRATE SUPPLEMENTATION

No

Proceed to step 4
POSTOPERATIVE

• Should we supplement with fibrinogen the patient after CPB?
• If yes, when (trigger value?)
• If yes, to reach what level (target value?)
• If yes, how much?
Fibrinogen deficiency

- Due to dilution and consumption
- Rare in routine cardiac surgery
- Factor activity becomes critical below 30%
- More common in long (> 2 hours) pump run
- Associated to extensive use of cell-saver
- Common in aortic surgery
- Common in aortic dissection
Randomized, Double-Blinded, Placebo-Controlled Trial of Fibrinogen Concentrate Supplementation After Complex Cardiac Surgery

Marco Ranucci, MD; Ekaterina Baryshnikova, PhD (Biol.); Giulia Beatrice Crapelli, MD; Niels Rahe-Meyer, MD; Lorenzo Menicanti, MD; Alessandro Frigiola, MD; for the Surgical Clinical Outcome REsearch (SCORE) Group*

Background—Postoperative bleeding after heart operations is still a common finding, leading to allogeneic blood products transfusion. Fibrinogen and coagulation factors deficiency are possible determinants of bleeding. The experimental hypothesis of this study is that a first-line fibrinogen supplementation avoids the need for fresh frozen plasma (FFP) and reduces the need for any kind of transfusions.

Methods and Results—This was a single-center, prospective, randomized, placebo-controlled, double-blinded study. One-hundred sixteen patients undergoing heart surgery with an expected cardiopulmonary bypass duration >90 minutes were admitted to the study. Patients in the treatment arm received fibrinogen concentrate after protamine administration; patients in the control arm received saline solution. In case of ongoing bleeding, patients in the treatment arm could receive prothrombin complex concentrates (PCCs) and those in the control arm saline solution. The primary endpoint was avoidance of any allogeneic blood product. Patients in the treatment arm had a significantly lower rate of any allogeneic blood products transfusion (odds ratio, 0.40; 95% confidence interval, 0.19 to 0.84, *P*=0.015). The total amount of packed red cells and FFP units transfused was significantly lower in the treatment arm. Postoperative bleeding was significantly (*P*=0.042) less in the treatment arm (median, 300 mL; interquartile range, 200 to 400 mL) than in the control arm (median, 355 mL; interquartile range, 250 to 600 mL).

Conclusions—Fibrinogen concentrate limits postoperative bleeding after complex heart surgery, leading to a significant reduction in allogeneic blood products transfusions. No safety issues were raised.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01471730. (J Am Heart Assoc. 2015;4: e002066 doi: 10.1161/JAHA.115.002066)

Key Words: cardiopulmonary bypass • fibrinogen • hemorrhage • surgery
mg/100mL or cells/microL-mean and SEM

Fibrinogen ICU (mg/100mL)
Control
Treatment

P=0.001

Platelet count ICU
PRIMARY ENDPOINT

- Any product: Control 55.2%, Treatment 32.8% (P=0.015)
- PRCs: Control 55.2%, Treatment 32.8% (P=0.015)
- FFP: Control 13.8% (P=0.006)
- PLTs: Control 6.9% (P=0.042)
FIBRINOGEN SUPPLEMENTATION AFTER CARDIAC SURGERY: INSIGHTS FROM THE ZERO-PLASMA TRIAL (ZEPLAST)

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<th>British Journal of Anaesthesia</th>
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<td>Ranucci, Marco; IRCCS Policlinico San Donato, Cardiothoracic Anesthesia and ICU Baryshnikova, Ekaterina; IRCCS Policlinico San Donato, Cardiothoracic Anesthesia</td>
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<td>Key Words:</td>
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Fibrinogen ICU (mg/100 mL)

Postoperative bleeding (mL/12h)

- Control
- Treatment

280 mg/dL NPV: 100%
FIBTEM post-dosing (mm)

Postoperative bleeding (mL/12h)

0 5 10 15 20 25 30

0 500 1000 1500 2000 2500

17 mm (not 22 mm!!!) NPV: 100%
PREDICTION FOR SEVERE BLEEDING (> 1,000 mL)

CUT-OFF VALUES:

- Fibrinogen 285 mg/100 mL  
  Sensitivity 80%, Specificity 65%
- FibTEM 13.5 mm  
  Sensitivity 80%, Specificity 72%
FIBRINOGEN LEVELS AFTER CARDIAC SURGERY: ASSOCIATION WITH POSTOPERATIVE BLEEDING, TRIGGER VALUES, AND TARGET VALUES

Marco Ranucci, MD, FESC, Valeria Pistuddi, Ekaterina Baryshnikova, PhD (Biol), Paolo Bianchi (MD)
Department of Cardiothoracic and Vascular Anesthesia and ICU
IRCCS Policlinico San Donato, San Donato Milanese (Milan) ITALY

Text word count: 4,724
Abstract word count: 242
Figure 1

Graph showing the relationship between postoperative bleeding (mL/12h) and fibrinogen level (mg/dL) at the ICU admission.
<table>
<thead>
<tr>
<th>Fibrinogen level</th>
<th>All cases (N=2,800)</th>
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<th>Excluding patients with other isolated factors (N=2,051)</th>
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<tr>
<td></td>
<td>PPV</td>
<td>NPV</td>
<td>P</td>
<td>PPV</td>
</tr>
<tr>
<td>75 mg/dL</td>
<td>100%</td>
<td>95.4%</td>
<td>0.002</td>
<td>100%</td>
</tr>
<tr>
<td>100 mg/dL</td>
<td>67%</td>
<td>95.4%</td>
<td>0.006</td>
<td>67%</td>
</tr>
<tr>
<td>115 mg/dL</td>
<td>50%</td>
<td>95.4%</td>
<td>0.012</td>
<td>50%</td>
</tr>
<tr>
<td>125 mg/dL</td>
<td>20%</td>
<td>95.4%</td>
<td>0.076</td>
<td>20%</td>
</tr>
<tr>
<td>150 mg/dL</td>
<td>15%</td>
<td>95.6%</td>
<td>0.002</td>
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</tr>
<tr>
<td>175 mg/dL</td>
<td>10%</td>
<td>95.9%</td>
<td>0.001</td>
<td>10%</td>
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<td>200 mg/dL</td>
<td>9.1%</td>
<td>96.4%</td>
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<td>225 mg/dL</td>
<td>7.7%</td>
<td>96.9%</td>
<td>0.001</td>
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<td>275 mg/dL</td>
<td>5.8%</td>
<td>97.2%</td>
<td>0.001</td>
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<tr>
<td>300 mg/dL</td>
<td>5.6%</td>
<td>98.0%</td>
<td>0.001</td>
<td>6.2%</td>
</tr>
</tbody>
</table>

NPV: negative predictive value; PPV: positive predictive value.
Table 4. Levels of negative and positive predictive values at different cut-off values of postoperative fibrinogen

<table>
<thead>
<tr>
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NPV: negative predictive value; PPV: positive predictive value.
### IN THE BLEEDING PATIENT

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<tr>
<td>115 mg/dL</td>
<td>50%</td>
<td>95.4%</td>
</tr>
<tr>
<td>125 mg/dL</td>
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<td>95.4%</td>
</tr>
<tr>
<td>150 mg/dL</td>
<td>15%</td>
<td>95.6%</td>
</tr>
<tr>
<td>175 mg/dL</td>
<td>10%</td>
<td>95.9%</td>
</tr>
<tr>
<td>200 mg/dL</td>
<td>9.1%</td>
<td>96.4%</td>
</tr>
<tr>
<td>225 mg/dL</td>
<td>7.7%</td>
<td>96.9%</td>
</tr>
<tr>
<td>250 mg/dL</td>
<td>6.4%</td>
<td>97.0%</td>
</tr>
<tr>
<td>275 mg/dL</td>
<td>5.8%</td>
<td>97.2%</td>
</tr>
<tr>
<td>300 mg/dL</td>
<td>5.6%</td>
<td>98.0%</td>
</tr>
</tbody>
</table>

NPV: negative predictive value; PPV: positive predictive value.
In the bleeding patient with a low-fibrinogen level (<1.5 g/l), fibrinogen substitution may be considered to reduce postoperative bleeding and transfusions.
A VISCOELASTIC TESTS-BASED ALGORITHM (TEG-ROTEM)

- Rule-out low soluble coagulation factors levels
  - Yes
    - PCC supplementation (better 4-factors)
    - rFVIIa (life-threatening bleeding)
  - No
    - Proceed to step 5
Factors deficiency

- Due to dilution and consumption
- Rare in routine cardiac surgery
- Factor activity becomes critical below 30%
- More common in long (> 2 hours) pump run
- Associated to extensive use of cell-saver
- Common in aortic surgery
- Common in aortic dissection
Regular Article

Plasma activity of individual coagulation factors, hemodilution and blood loss after cardiac surgery: A prospective observational study

Lisa Ternström a,d, Vladimir Radulovic b, Martin Karlsson a,d, Fariba Baghaei b, Monica Hyllner a, Anders Bylock c, Kenny M. Hansson c, Anders Jeppsson a,d,*

a Department of Cardiovascular Surgery and Anesthesia, Sahlgrenska University Hospital, Gothenburg, Sweden
b Department of Medicine/Hematology and Coagulation Disorders, Sahlgrenska University Hospital, Gothenburg, Sweden
c AstraZeneca AB, Mölndal, Sweden
d Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
<table>
<thead>
<tr>
<th>Protein</th>
<th>Time</th>
<th>r</th>
<th>p</th>
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<tbody>
<tr>
<td>Fibrinogen</td>
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<td>0.19</td>
<td>0.15</td>
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<tr>
<td></td>
<td>2 h Postop</td>
<td>0.33</td>
<td>0.019</td>
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<tr>
<td>FII</td>
<td>Preop</td>
<td>0.11</td>
<td>0.42</td>
</tr>
<tr>
<td></td>
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<td>0.22</td>
<td>0.12</td>
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<tr>
<td>FV</td>
<td>Preop</td>
<td>0.04</td>
<td>0.79</td>
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<tr>
<td>FVII</td>
<td>Preop</td>
<td>0.04</td>
<td>0.76</td>
</tr>
<tr>
<td></td>
<td>2 h Postop</td>
<td>0.06</td>
<td>0.66</td>
</tr>
<tr>
<td>FVIII</td>
<td>Preop</td>
<td>0.06</td>
<td>0.65</td>
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<tr>
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<td>2 h Postop</td>
<td>0.07</td>
<td>0.61</td>
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<td>Preop</td>
<td>0.09</td>
<td>0.52</td>
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<tr>
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<td>0.29</td>
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<td>Preop</td>
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<td>0.78</td>
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<tr>
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<td>Preop</td>
<td>0.12</td>
<td>0.39</td>
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<tr>
<td></td>
<td>2 h Postop</td>
<td>0.22</td>
<td>0.12</td>
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<tr>
<td>FXIII</td>
<td>Preop</td>
<td>0.34</td>
<td>0.009</td>
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<tr>
<td></td>
<td>2 h Postop</td>
<td>0.41</td>
<td>0.003</td>
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</table>
Factors deficiency

- LEADS TO DECREASED THROMBIN GENERATION
FACTORS ACTING BEFORE THE GEL POINT

Everything acting before the GEL POINT is directly or indirectly related to a poor thrombin generation or direct thrombin inhibition

- Congenital coagulation disorders
- Poor liver synthesis/consumption
- Heparin
- Warfarin
- Direct thrombin inhibitors
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### WARFARIN

<table>
<thead>
<tr>
<th>R min</th>
<th>K min</th>
<th>Angle deg</th>
<th>MA mm</th>
<th>PMA</th>
<th>G d/sc</th>
<th>EPL %</th>
<th>A mm</th>
<th>CI</th>
<th>LY30 %</th>
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<tbody>
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<td>12.2</td>
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<td>57.4</td>
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<tr>
<td>4-8</td>
<td>0-4</td>
<td>47-74</td>
<td>54-72</td>
<td></td>
<td>6.0K</td>
<td>-13.2K</td>
<td></td>
<td>-3</td>
<td>0-8</td>
</tr>
</tbody>
</table>
Warfarin 36 hours
PCCs 25IU/Kg
FACTORS ACTING BEFORE THE GEL POINT

Everything acting before the GEL POINT is directly or indirectly related to a poor thrombin generation or direct thrombin inhibition

• Congenital coagulation disorders
• Poor liver synthesis/consumption
• Heparin
• Warfarin
• Direct thrombin inhibitors
A VISCOELASTIC TESTS-BASED ALGORITHM (TEG-ROTEM)

Rule-out hyperfibrinolysis

Yes

TRANEXAMIC ACID FIBRINOGEN CONCENTRATE

No

Proceed to step 6
UKIF-TEG

our experience

UKIF-TEG MA not comparable to C - MA

low susceptibility

Application to clinical setting is to be determined
A VISCOELASTIC TESTS-BASED ALGORITHM (TEG-ROTEM)

Rule-out surgical sources

Yes

GO-ON WITH HEMOSTASIS RE-EXPLORATION

No

Other causes