Platelet function in cardiovascular surgery

ROTEM® User Meeting, UZ Leuven, 9 November 2015

Klaus Görlinger, MD
Munich, Germany
Disclosures

• Senior Consultant for Anesthesiology, Emergency and Intensive Care Medicine, Haemostaseology, and Pain Therapy

• Dec 1986 - June 2012: Senior Consultant at the Department of Anesthesiology and Intensive Care Medicine, University Hospital Essen, Germany (Trauma, Liver Transplant and Cardiac Surgery)

• 2010 - 2012: Chair of the Section Clinical Haemotherapy and Haemostasis Management of the German Interdisciplinary Association of Critical Care and Emergency Medicine (DIVI)

• 2010 - 2012: Member of the European Society of Anaesthesiology (ESA) Scientific Subcommittee Transfusion and Hemostasis and the Task Force / co-author of the ESA Guidelines on the Management of Severe Perioperative Bleeding

• Honoraria for Scientific Lectures from CSL Behring GmbH, Marburg, Germany, and Octapharma AG, Lachen, Switzerland
Disclosures

• Since July 2012, KG is the Global Medical Director of Tem International GmbH, Munich, Germany.

• Some statements in this presentation are based on the clinical experience of more than 25 years of KG as an anesthesiologist, intensivist, haemostaseologist, and ROTEM® user in Germany as well as on publications in US and non-US peer-reviewed medical journals. This includes ROTEM® and coagulation factor concentrate use approved in Germany/Europe but not in the US. However, KG does not promote the off-label use of the ROTEM® device in the US.

• Tem International/Tem Systems does not necessarily endorse or approve KG’s statements provided from his physician’s experience.
"The All-rounder"

ROTEM® delta and platelet

"The Specialist"

Multiplate®
Platelet activation

ADPtem

TRAPtem

ARAtem

GPIIbIIIa receptor (fibrinogen receptor) expression and activation
Multiple Electrode Whole-Blood Aggregometry and Bleeding in Cardiac Surgery Patients Receiving Thienopyridines

Marco Ranucci, MD, Ekaterina Baryshnikova, PhD, Giorgio Soro, MD, Andrea Ballotta, MD, FCCP, Donatella De Benedetti, MD, and Daniela Conti, MD; for the Surgical and Clinical Outcome Research (SCORE) Group

Department of Cardiothoracic-Vascular Anesthesia and Intensive Care, Istituto Di Ricovero e Cura a Carattere Scientifico (IRCCS) Policlinico S. Donato, Milan, Italy

Fig 1. Graph analysis (nonlinear regression) for the association of the adenosine diphosphate (ADP) test and postoperative bleeding.

Fig 2. Receiver operating characteristic curve analysis for excessive bleeding prediction by the ADP test. The best predictive value corresponds to an ADP value of 307 (sensitivity 72%, specificity 66%). (ADP = adenosine diphosphate; AUC = area under the curve; c.i. = confidence interval.)
Multiple Electrode Whole-Blood Aggregometry and Bleeding in Cardiac Surgery Patients Receiving Thienopyridines

Marco Ranucci, MD, Ekaterina Baryshnikova, PhD, Giorgio Soro, MD, Andrea Ballotta, MD, FCCP, Donatella De Benedetti, MD, and Daniela Conti, MD; for the Surgical and Clinical Outcome Research (SCORE) Group

Department of Cardiothoracic-Vascular Anesthesia and Intensive Care, Istituto Di Ricovero e Cura a Carattere Scientifico (IRCCS) Policlinico S. Donato, Milan, Italy

Table 4. Postoperative Bleeding and Transfusion Rates According to the ADP Test Cutoff Value

<table>
<thead>
<tr>
<th>Type of Transfusion</th>
<th>ADP Test AUC &lt; 31 U (n = 35)</th>
<th>ADP Test AUC ≥ 31 U (n = 52)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding (mL/12 hours)</td>
<td>666 (367)*</td>
<td>444 (212)*</td>
<td>0.002</td>
</tr>
<tr>
<td>Excessive bleeding</td>
<td>10 (28.6%)</td>
<td>4 (7.7%)</td>
<td>0.009</td>
</tr>
<tr>
<td>Overall</td>
<td>21 (60%)</td>
<td>23 (44.2%)</td>
<td>0.149</td>
</tr>
<tr>
<td>Packed red cells</td>
<td>17 (48.6%)</td>
<td>20 (38.5%)</td>
<td>0.350</td>
</tr>
<tr>
<td>Fresh frozen plasma</td>
<td>9 (25.7%)</td>
<td>6 (11.5%)</td>
<td>0.086</td>
</tr>
<tr>
<td>Platelet concentrates</td>
<td>10 (28.6%)</td>
<td>6 (11.5%)</td>
<td>0.044</td>
</tr>
</tbody>
</table>

* Mean (standard deviation).

ADP = adenosine diphosphate; AUC = area under the curve.
Effect of preoperative P2Y12 and thrombin platelet receptor inhibition on bleeding after cardiac surgery

M. Ranucci1*, D. Colella2, E. Baryshnikova1 and U. Di Dedda1 for the Surgical and Clinical Outcome Research (SCORE) Group

Fig 3 Logarithmic association between preoperative MEA-ADP test and MEA-TRAP test. Dashed lines are 95% confidence interval. Orange diamonds are patients with severe bleeding. ADP, adenosine diphosphate; MEA, multiple electrode aggregometry; TRAP, thrombin receptor-activating peptide.
Effect of preoperative $P_2Y_{12}$ and thrombin platelet receptor inhibition on bleeding after cardiac surgery

M. Ranucci$^{1*}$, D. Colella$^2$, E. Baryshnikova$^1$ and U. Di Dedda$^1$ for the Surgical and Clinical Outcome Research (SCORE) Group

**Results.** Both the ADPtest and the TRAPtest were significantly ($P=0.001$) associated with postoperative bleeding. A threshold of 22 U for the ADPtest yielded a negative predictive value (NPV) of 94% and a positive predictive value (PPV) of 20%, and a threshold of 75 U for the TRAPtest yielded an NPV of 95% and a PPV of 23%. In the subgroup of patients with ADPtest $<22$ U, TRAPtest $>75$ U was not associated with severe bleeding (NPV of 100% and PPV of 37%).

**Conclusions.** In patients taking $P_2Y_{12}$ receptor inhibitors, residual platelet reactivity to thrombin stimulation limits the risk of severe postoperative bleeding.

- Multiplate electrode aggregometry platelet function testing predicted postoperative bleeding with high negative and low positive predictive values.
- $P_2Y_{12}$ receptor inhibition by the ADPtest can be compensated by normal protease-activated receptor (PAR) function by the TRAPtest.
Platelet count and function in paediatric cardiac surgery: a prospective observational study

B. S. Romlin1*, F. Söderlund1, H. Wählander2, B. Nilsson1, F. Baghaei3 and A. Jeppsson4,5

Fig 2  (a) Prevalence of intraoperative transfusions for patients with none, one, two, or three of the ADP-, AA-, and TRAP-induced aggregation measurements ≤30 U. (b–d) Prevalence of intraoperative transfusions in patients with ADP-induced (a), AA-induced (c), or TRAP-induced (d) aggregation ≤ or >30 U. ADP, adenosine diphosphate; AA, arachidonic acid; TRAP, thrombin receptor-activating peptide.
Drugs that Affect Platelet Function*
Rüdiger E. Scharf, MD, PhD, FAHA

- **Drugs** represent the most common cause of platelet dysfunction in our **overmedicated society**.
- There is a large variety of **agents that have not been designed for antiplatelet therapy** but nevertheless interfere with platelet reactivity or induce platelet inhibition.
- This is especially relevant in **patients with preexisting hemostatic defects** of any kind.
- Nonsteroidal anti-inflammatory drugs, antibiotics, cardiovascular and lipid-lowering drugs, selective serotonin reuptake inhibitors, and volume expanders can also impair platelet function.
- **Identification of individual patients with preexisting hemostatic defects remains crucial**
  - to minimize the risk from invasive procedures and
  - to avoid unnecessary patient exposure to blood products
Combination of a selective serotonin reuptake inhibitor and a non-steroidal anti-inflammatory drug.
Point-of-Care Assessment of Hypothermia and Protamine-Induced Platelet Dysfunction with Multiple Electrode Aggregometry (Multiplate®) in Patients Undergoing Cardiopulmonary Bypass

Erik Ortmann, MD,* Andrew A. Klein, MBBS, FRCA,* Linda D. Sharples, PhD,† Racheal Walsh, BSc (hons) BiomedSci, BSc (hons) MedChem,† David P. Jenkins, BSc, MBBS, FRCS(Eng), MS(Lond), FRCS(CTh),§ Roger J. Luddington, MPhil, PhD,† and Martin W. Besser, MRCP, FRCPath†

Figure 3. Marginal mean (95% confidence interval) platelet aggregation measured at body temperature (AUC-CT) and at 37°C (AUC-37) over time. CPB = cardiopulmonary bypass; ICU = intensive care unit.
LB11
Reference values in the ROTEM® platelet device
Lang T.1, Tollnick M.2, Martynenko L.1, Rieke M.1
1Gerinnungsambulanz Südheide, Hohne, Germany, 2MedLab Südheide, Hohne, Germany

Aim: Establishment of reference values in ROTEM® platelet (impedance aggregometry) using different anticoagulants: Citrate, Heparin and Hirudin

Materials and methods: Samples were collected from 48 healthy volunteers. Medication of Aspirin or NSAR were denied at least for one week before sample collection. Measurement was performed using three different activators for platelet aggregation (TRAP, ADP, Arachidonic Acid=AA) for each sample. Results of platelet aggregation are given as area under curve (AUC) in $\Omega^\text{min}$.

Results: Mean age of the volunteers was 46 y (±15; range: 18 - 84 y, m=25, f=23).

Mean AUC for citrated samples: TRAP 108 (±21), ADP 82 (±15), AA 85 (±20); for heparin samples: TRAP 104 (±27), ADP 87 (±24), AA 86 (±23); for hirudin samples TRAP 115 (±23), ADP 91 (±18), AA 107 (±22); The coefficient of variation (CV) ranged between 19% and 27%. Correlation between different anticoagulants was poor (range of r-value: 0.32 - 0.66). There was no correlation between age and platelet aggregation ($r<0.3$). There was no significant difference between male and female in AUC ($p>0.25$).

Discussion: As expected in platelet aggregation the CV was rather high, which may reflect known analytical problems in platelet aggregation and the individual biological variation as well. Since platelet aggregation is usually completely abolished after ingestion of Aspirin and Clopidogrel, ROTEM® platelet will be a useful tool in monitoring of platelet aggregation inhibitors anyway.
Normal platelet function

Aspirin effect

Clopidogrel effect
Severe platelet dysfunction
GPIIbIIIa receptor antagonist
Severe thrombocytopenia
Dual antiplatelet therapy
Vorapaxar effect
Results: Using AUC = 30 as cut-off for Aspirin-effect all Aspirin samples are discriminated in both systems. In both systems 2 Aspirin samples show an AUC > 30 suggesting ASS-non-responder. Two samples with no Aspirin ingestion showed an AUC < 30 in both systems suggesting an Aspirin effect.

Discussion: The discrimination between normal an Aspirin samples was identical between Multiplate® and ROTEM® platelet using AUC = 30 as cut-off and arachidonic acid for stimulation. Also Aspirin resistance is reliably detected by both devices.

Conclusion: There is no difference between ROTEM® platelet and Multiplate® in detection/exclusion of Aspirin effect in citrated whole blood.
ADP - AUC

ROTEM® platelet ADP AUC [Ohm x min]

Multiplate® ADP AUC [AU]
Electric impedance platelet aggregometry in cardiac surgery patients: A comparative study of two technologies

Marco Ranucci, Ekaterina Baryshnikova, Giulia Beatrice Crapelli, Matteo Ranucci, Silvia Meloni, & Valeria Pistuddi; For the Clinical and Surgical Outcome Research (Score) Group

Platelet function tests are suggested to assess platelet reactivity before cardiac and major non-cardiac surgery. Different point-of-care platelet function tests are available. Among these, electric impedance platelet aggregometry (EIPA) (Multiplate®, MP) is one of the most widely used techniques. Recently, a new EIPA system (Rotem Platelet®, RP) was released. This is a comparative study of platelet function measured with MP and RP. Fifty cardiac surgery patients were admitted to this study. All the patients received a preoperative platelet function test with both the MP and the RP; for each technology, two tests were performed: the ADP test (investigating P2Y12 receptor platelet reactivity) and the TRAP test (investigating the thrombin-dependent platelet reactivity). ADP-based platelet reactivity values demonstrated a significant ($p = 0.019$) correlation between the MP and the RP; and a marginally significant ($p = 0.042$) correlation for TRAP-based tests.
Bleeding Risk Assessment in Patients Undergoing Elective Cardiac Surgery Using ROTEM® platelet and Multiplate® Impedance Aggregometry (NCT02277379) Petricevic M, et al. [submitted for publication]

ROC Cut-off at T3: ≤ 26 AU ≤ 33 AU ≤ 78 AU

Multiplate®

a) Area under the Curve

b) Area under the Curve
c) Area under the Curve

ROTEM® platelet

d) Area under the Curve
e) Area under the Curve
f) Area under the Curve

ROC Cut-off at T3: ≤ 15 Ω·min ≤ 36 Ω·min ≤ 78 Ω·min
Bleeding Risk Assessment in Patients Undergoing Elective Cardiac Surgery Using ROTEM® platelet and Multiplate® Impedance Aggregometry (NCT02277379) Petricevic M, et al. [submitted for publication]

1025 mL (262.5 / 1533)

270 mL (0 / 865)
Bleeding Risk Assessment in Patients Undergoing Elective Cardiac Surgery Using ROTEM® platelet and Multiplate® Impedance Aggregometry (NCT02277379) Petricevic M, et al. [submitted for publication]
CONCLUSION: TEG PM is least suited to monitor effects of antiplatelet agents. Multiplate impedance aggregometry was the only method to demonstrate an acceptable reliability coefficient among healthy volunteers and donors on both aspirin and clopidogrel therapy.

© 2014 American Association for Clinical Chemistry
Expert position paper on the role of platelet function testing in patients undergoing percutaneous coronary intervention

Figure 1: Inter-individual variability in platelet reactivity after 600 mg clopidogrel loading dose. Inter-individual variation in platelet reactivity values in consecutive stable angina patients tested 6–24 h after a 600 mg clopidogrel loading dose with four different platelet function assays. Notably, each platelet function plot represents a unique stable angina patient population after a 600 mg clopidogrel loading dose. Patients in (A) were recruited for light transmission aggregometry, vasodilator-stimulated phosphoprotein phosphorylation (VASP-PRI) and Multiplate testing in the Heart Institute, University of Pécs, Hungary, while those in (B) represent a similar patient population enrolled in Institut de Cardiologie, Pitié-Salpêtrière Hospital, Paris, France. LTA, light transmission aggregometry; VASP-PRI, vasodilator-stimulated phosphoprotein phosphorylation index.
Consensus summary

Monitoring platelet reactivity during clopidogrel treatment with ADP-stimulated platelet assays is more specific to the drug action and more predictive for thrombotic events than the assessment of aspirin responsiveness. Based on the currently available evidence, the recommended assays for monitoring platelet inhibition during P2Y₁₂-inhibitors are the VerifyNow P2Y12 assay, the Multiplate device with the ADP kit and the VASP assay. Although the optimal thresholds to define a higher risk for thrombotic events may depend on the clinical situation and are still under investigation, available evidence suggests 208 PRU with the VerifyNow, 46 U with the Multiplate assay and 50% with the VASP assay. (Supplementary material online, Table S2) LTA is only recommended when no standardized assays are available. Measurement of response to aspirin therapy is not recommended.
Platelet Aggregation and Its Association With Stent Thrombosis and Bleeding in Clopidogrel-Treated Patients

Initial Evidence of a Therapeutic Window

30-day incidence of ST and major bleeding

hyper normal low
First-line Therapy with Coagulation Factor Concentrates Combined with Point-of-Care Coagulation Testing Is Associated with Decreased Allogeneic Blood Transfusion in Cardiovascular Surgery

A Retrospective, Single-center Cohort Study

Klaus Görlinger, Dr. med,* Daniel Dirkmann, Dr. med,† Alexander A. Hanke, Dr. med,‡ Markus Kamler, PD Dr. med,‡ Eva Kottenberg, PD Dr. med,* Matthias Thielmann, PD Dr. med,† Heinz Jakob, Prof. Dr. med,§ Jürgen Peters, Prof. Dr. med||

Methods: In a retrospective cohort study including 3,865 patients, we analyzed the incidence of intraoperative allogeneic blood transfusions (primary endpoints) before and after algorithm implementation.
Point-of-Care Testing

A Prospective, Randomized Clinical Trial of Efficacy in Coagulopathic Cardiac Surgery Patients

Christian Friedrich Weber, Dr. med.,* Klaus Görlinger, Dr. med.,† Dirk Meininger, P.D. Dr. med.,‡ Eva Herrmann, Prof. Dr. rer. nat.,§ Tobias Bingold, Dr. med.,‖ Anton Moritz, Prof. Dr. med.,¶ Lawrence H. Cohn, M.D., Ph.D.,# Kai Zacharowski, Prof. Dr. med., Ph.D., F.R.C.A.**

What We Already Know about This Topic

- Cardiac surgical patients experience rapid changes in coagulation status
- Point-of-care coagulation testing may speed up diagnosis of coagulopathies and improve management
Incidence of MT, RT, Re-Exploration and Outcomes
Incidence of adverse events

- ARF: CON = 20, POC = 6; p = 0.071
- Sepsis: CON = 14, POC = 2; p = 0.059
- TAE: CON = 4, POC = 0; p = 0.495
- Allergy: CON = 0, POC = 0
- CAE: CON = 38, POC = 8; p < 0.001
Fig. 4. Kaplan–Meier curve demonstrating survival by type of performed coagulation management during the 6-month follow-up period. POC = point-of-care.
Protocol guided bleeding management improves cardiac surgery patient outcomes

Fig. 4. Total number of blood product units transfused intra-operatively and postoperatively before and after the implementation of bleeding management. PRBCs = packed red blood cells, FFP = fresh frozen plasma and platelets = pooled or apheresis platelets.
Total incidence of large volume transfusion
≥ 5 units of PRBCs: 15.9% vs. 8.5%; P < 0.0001;
RR 0.535 (95 CI, 0.429-0.666)

Total incidence of large volume transfusion
≥ 10 units of PRBCs: 4.6% vs. 2.6%; P < 0.007;
RR 0.565 (95 CI, 0.370-0.863)

Re-exploration for bleeding: 5.6% vs. 3.4%; P = 0.01
Superficial chest wound infection: 3.3% vs. 1.4%; P = 0.002

Leg wound infection: 4.6% vs. 2.0%; P < 0.0001

Reduction in mean length of stay from operation to discharge: 12% (95% CI, 9-16%; P < 0.0001)

Acquisition cost of blood products decreased by AU$ 1,029,118 within 15 months
Conclusion: This tailored bleeding management protocol guided by POCT facilitated early identification of patients at risk of bleeding and rapid identification of the cause of bleeding to support appropriate treatment. The observed improvements in patient outcomes, decreases in blood product use and cost, indicate improved haemostasis management. This initiative has also led to a department wide change from a culture of ‘transfusion practice’ to one of ‘PBM’.
The role of point-of-care platelet function testing in predicting postoperative bleeding following cardiac surgery: a systematic review and meta-analysis

C. Corredor, M. Wasowicz, K. Karkouti and V. Sharma

30 observational studies incorporating 3044 patients were included in the qualitative assessment

9 RCTs including 1057 patients were included in the meta-analysis

Conclusion: Incorporation of point-of-care platelet function testing into transfusion management algorithms is associated with a reduction in blood loss and transfusion requirements in cardiac surgery patients.
Meta-analysis: Effect of POCT on Bleeding

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean Difference</th>
<th>SE</th>
<th>Weight</th>
<th>Mean Difference IV, Random, 95% CI</th>
<th>Mean Difference IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.1.1 TEG/ROTEM only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ak 2009</td>
<td>-110.9</td>
<td>46.144</td>
<td>26.9%</td>
<td>-110.90 [-201.34, -20.46]</td>
<td></td>
</tr>
<tr>
<td>Girdauskas 2010</td>
<td>-60</td>
<td>139.388</td>
<td>2.9%</td>
<td>-60.00 [-333.20, 213.20]</td>
<td></td>
</tr>
<tr>
<td>Nuttall 2001</td>
<td>-260</td>
<td>355.054</td>
<td>0.5%</td>
<td>-260.00 [-957.07, 437.07]</td>
<td></td>
</tr>
<tr>
<td>Royston 2001</td>
<td>80</td>
<td>105.798</td>
<td>5.1%</td>
<td>80.00 [-127.36, 287.36]</td>
<td></td>
</tr>
<tr>
<td>Shore-Leeterson 1999</td>
<td>-199</td>
<td>135.433</td>
<td>3.1%</td>
<td>-199.00 [-464.44, 66.44]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>-90.55</td>
<td></td>
<td>38.5%</td>
<td>-90.55 [-166.11, -14.99]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.00; Chi² = 3.71, df = 4 (P = 0.45); I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 2.35 (P = 0.02)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14.1.2 TEG/ROTEM+PFT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agarwal 2014</td>
<td>-95</td>
<td>56.775</td>
<td>17.8%</td>
<td>-95.00 [-206.28, 16.28]</td>
<td></td>
</tr>
<tr>
<td>Weber 2012</td>
<td>-300</td>
<td>110.358</td>
<td>4.7%</td>
<td>-300.00 [-516.29, -83.71]</td>
<td></td>
</tr>
<tr>
<td>Westbrook 2009</td>
<td>-85</td>
<td>67.52</td>
<td>12.6%</td>
<td>-85.00 [-217.34, 47.34]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>-111.79</td>
<td></td>
<td>61.5%</td>
<td>-111.79 [-174.49, -49.09]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 4.91, Chi² = 3.22, df = 3 (P = 0.36), I² = 7%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 3.49 (P = 0.0005)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 2 Effect of point-of-care platelet function test-guided transfusion algorithm vs control group on bleeding after cardiac surgery at longest follow-up, grouped by studies using TEG/ROTEM alone and TEG/ROTEM plus other point-of-care platelet function test.
Meta-analysis: Effect of POCT on Proportion of Patients receiving Red Cells

**Corredor et al. | Predictive ability of point-of-care platelet function testing**

**Anaesthesia 2015**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Risk Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Risk Ratio IV, Random, 95% CI</th>
<th>Risk Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.1.1 TEG/ROTEM only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ak 2009</td>
<td>-0.1791</td>
<td>0.1339</td>
<td>11.0%</td>
<td>0.84 [0.64, 1.09]</td>
<td></td>
</tr>
<tr>
<td>Girdauskas 2010</td>
<td>-0.046</td>
<td>0.0847</td>
<td>24.5%</td>
<td>0.96 [0.81, 1.13]</td>
<td></td>
</tr>
<tr>
<td>Shore-Lesserson 1999</td>
<td>0.3624</td>
<td>0.1992</td>
<td>5.2%</td>
<td>0.70 [0.47, 1.03]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>40.6%</td>
<td>0.88 [0.75, 1.03]</td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.00; Chi^2 = 2.44, df = 2 (P = 0.30); I^2 = 18%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.64 (P = 0.10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

15.1.2 TEG/ROTEM + PFT

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Risk Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Risk Ratio IV, Random, 95% CI</th>
<th>Risk Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agarwal 2014</td>
<td>-0.3425</td>
<td>0.1303</td>
<td>11.5%</td>
<td>0.71 [0.55, 0.92]</td>
<td></td>
</tr>
<tr>
<td>Avidan 2004</td>
<td>-0.0305</td>
<td>0.136</td>
<td>10.6%</td>
<td>0.97 [0.74, 1.27]</td>
<td></td>
</tr>
<tr>
<td>Weber 2012</td>
<td>-0.1543</td>
<td>0.0647</td>
<td>37.3%</td>
<td>0.86 [0.75, 0.97]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>59.4%</td>
<td>0.84 [0.73, 0.97]</td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.01; Chi^2 = 2.86, df = 2 (P = 0.24); I^2 = 30%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 2.40 (P = 0.02)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th>100.0%</th>
<th>0.86 [0.79, 0.94]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heterogeneity: Tau^2 = 0.00; Chi^2 = 5.65, df = 5 (P = 0.34); I^2 = 11%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 3.24 (P = 0.001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for subgroup differences: Chi^2 = 0.15, df = 1 (P = 0.70); I^2 = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 3** Effect of point-of-care platelet function test-guided transfusion algorithm vs control group on proportion of patients receiving red cells, grouped by studies using TEG/ROTEM alone and TEG/ROTEM plus other point-of-care platelet function test.
The multifactorial nature of postoperative bleeding in cardiac surgery may necessitate a need for the use of combinations of point-of-care tests. The incorporation of point-of-care platelet function tests into blood transfusion management algorithms is associated with a reduction in blood loss and transfusion requirements. The use of a combination of viscoelastic methods and platelet agonist assays achieved the greatest reduction in blood loss and blood transfusion requirements.
Management of severe perioperative bleeding

Guidelines from the European Society of Anaesthesiology

Sibylle A. Konrad-Langebeck, Ariash Afshari, Pierre Albaladejo, Cesar Aldecoa Alvarez Santuliano, Eduardo de Robertis, Daniela C. Filipescu, Dietmar Fries, Klaus Görtlinger, Thorsten Haas, Georgina Imberger, Matthias Jacob, Marcus Lancé, Juan Llau, Sue Mallett, Jens Meier, Niels Rahe-Meyer, Charles Marc Samama, Andrew Smith, Cristina Solomon, Philippe Van der Linden, Anne Juel Wikkelso, Patrick Wouters and Piet Wyffels

We recommend the application of transfusion algorithms incorporating predefined intervention triggers to guide haemostatic intervention during intraoperative bleeding.

1B

We recommend the application of transfusion algorithms incorporating predefined intervention triggers based on point-of-care (POC) coagulation monitoring assays to guide haemostatic intervention during cardiovascular surgery.

1C
Practice Guidelines for Perioperative Blood Management

An Updated Report by the American Society of Anesthesiologists Task Force on Perioperative Blood Management*

* Revised by the American Society of Anesthesiologists Committee on Standards and Practice Parameters: Jeffrey L. Apfelbaum, M.D. (Committee Chair), Chicago, Illinois; Gregory A. Nuttall, M.D. (Task Force Chair), Rochester, Minnesota; Richard T. Connis, Ph.D., Woodinville, Washington; Chantal R. Harrison M.D., San Antonio, Texas; Ronald D. Miller, M.D., San Francisco, California; David G. Nickinovich, Ph.D., Bellevue, Washington; Nancy A. Nussmeier, M.D., Boston, Massachusetts; Andrew D. Rosenberg, M.D., Roslyn Heights, New York; Linda Shore-Lesserson M.D., New Hyde Park, New York; and John T. Sullivan M.D., M.B.A., Chicago, Illinois. These Guidelines have been endorsed by the Society of Cardiovascular Anesthesia, the Society for Obstetric Anesthesia and Perinatology, and the Society of Critical Care Anesthesiologists.

- How does this statement differ from existing guidelines?
  - New evidence presented includes greater emphasis of the preoperative assessment of the patient, assessment of the risk for transfusion, and the use of adjunct medications to prevent and/or treat bleeding.
  - The updated ASA practice guidelines differ from those published by other organizations in that:
    - They include greater use of pharmacologic therapies to minimize blood transfusions, such as erythropoietin for the anemic patient, prothrombin complex concentrates for urgent reversal of warfarin, and intraoperative antifibrinolytic therapy during selected cardiac and noncardiac procedures having a high risk for bleeding.
    - They advocate the use of transfusion algorithms, especially those based on thromboelastographic testing, blood ordering schedules, and restrictive transfusion strategies.
Practice Guidelines for Perioperative Blood Management

An Updated Report by the American Society of Anesthesiologists Task Force on Perioperative Blood Management*

Multimodal Protocols or Algorithms. Multimodal protocols are strategies that typically consist of a predetermined “bundle” of interventions intended to reduce blood loss and transfusion requirements. The bundle components may include consultation with multiple medical specialties, institutional support, using transfusion algorithms, and point-of-care testing in addition to other perioperative blood conservation interventions. Algorithms are intended to identify decision points or “pathways” during a procedure whereby certain interventions should be employed.
Practice Guidelines for Perioperative Blood Management

An Updated Report by the American Society of Anesthesiologists Task Force on Perioperative Blood Management*

Intraoperative and Postoperative Interventions

- Monitoring for non-RBC transfusion—coagulopathy
  - Platelet function monitoring
  - Viscoelastic hemostatic assays
  - TEG
  - ROTEM
Therapeutic Window Concept

ADPTEM 30-45 Ω • min (patients with DES)
KNOWLEDGE IS POWER, BUT ENTHUSIASM_PULLS THE SWITCH

—James Tartt