

Utility of Platelet Function Testing in Cardiac Surgery in 2021

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In this issue of the *Journal of Cardiac Critical Care*, Sharan et al and Datta et al are reporting on perioperative and peri-interventional platelet function testing in an attempt to implement personalized antiplatelet therapy in India.^{1,2}

Sharan et al demonstrated that algorithm-based point-of-care thromboelastometry (ROTEM *delta*) combined with whole blood aggregometry (ROTEM *platelet*) helped to guide hemostatic interventions in the intra- and postoperative period of cardiac surgery.¹ On the one hand, this can avoid inappropriate blood transfusion, and on the other hand, excessive bleeding during and after cardiac surgery.^{3,4} Both bleeding and transfusion are associated with worse patient outcomes.⁵ Here, whole blood impedance aggregometry (multiplate or ROTEM *platelet*) has been shown to be a valuable tool to assess platelet function before, during, and after cardiovascular surgery as well as during extracorporeal membrane oxygenation (ECMO).^{6–20} This applies for pediatric cardiac surgery and ECMO too (►Fig. 1 and ►Table 1).^{21–23} Furthermore, platelet function testing has been shown to predict patients' outcome in trauma, bacterial sepsis, and COVID-19.^{24–26} In contrast to drug monitoring of aspirin and P2Y₁₂-receptor inhibitors with arachidonic acid (ASPI test or ARATEM) and adenosine diphosphate (ADP; ADP test or ADP test) activated assays, platelet dysfunction due to diseases (e.g., trauma, cirrhosis, and sepsis) and devices (e.g., cardiopulmonary bypass, ECMO and dialysis) seem to affect predominantly the ADP- and thrombin-pathway (TRAP test or TRAPTEM activated by thrombin-receptor activating peptide 6; TRAP6). Here, a drop in platelet function has to be considered as a biomarker for worse outcome and not as trigger for platelet transfusion. Accordingly, Sharan et al demonstrated that a significant drop in platelet function from postprotamine to 48 hours after surgery in the ICU was associated with adverse fatal

outcome, with an area under the aggregation curve (AUC) threshold value for TRAPTEM, ADPTEM and ARATEM of 53, 43 and 49.5 Ω -min, respectively.¹ This is in line with the results reported by Yassen et al, in that a significant decrease in TRAPTEM AUC between postoperative day 14 and 21 after liver transplantation is associated with increased 3-month nonsurvival.²⁷ On the other hand, increased aspirin resistance after cardiac surgery can be associated with ischemic events. This increase aspirin resistance seems to be mediated by an increased turnover of platelets after cardiac surgery rather than due to a pharmacologic aspirin resistance. Therefore, a switch to dual antiplatelet therapy should be considered in patients with postoperative aspirin resistance to avoid ischemic events.^{28,29}

Datta et al reported on the use of thromboelastography platelet mapping for the assessment of individual platelet response secondary to oral antiplatelet therapy after percutaneous coronary interventions as an attempt to implement personalized antiplatelet therapy in India.² Here, the authors demonstrated that aspirin along with ticagrelor was associated with a higher mean percentage of platelet inhibition and lower high on-treatment platelet reactivity (HPR) as compared with the usage of aspirin combined with clopidogrel or prasugrel. They concluded that platelet function testing may be used effectively to measure the individual response to antiplatelet therapy and personalize antiplatelet therapy for cardiac patients. This is in line with other studies dealing with personalized antiplatelet therapy in cardiology patients.^{30–32} In particular, the use of platelet function testing to deescalate antiplatelet therapy and avoid bleeding complications in hyperresponders seems to be a reasonable and promising approach.^{33,34} Furthermore, platelet function test might be helpful to determine the optimum timing of elective and urgent coronary artery bypass graft (CABG) surgery

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Table 1 Fibrinogen dose calculation

Targeted increase in A5 _{FIB} (mm)	Fibrinogen dose (mg/kg body weight)	Fibrinogen concentrate (mL/kg body weight)	Cryoprecipitate (mL/kg body weight)
2 mm	12.5 mg/kg bw	0.6 mL/kg bw	1 mL/kg bw
4 mm	25.0 mg/kg bw	1.2 mL/kg bw	2 mL/kg bw
6 mm	37.5 mg/kg bw	1.9 mL/kg bw	3 mL/kg bw
8 mm	50.0 mg/kg bw	2.5 mL/kg bw	4 mL/kg bw
10 mm	62.5 mg/kg bw	3.1 mL/kg bw	5 mL/kg bw
12 mm	75.0 mg/kg bw	3.8 mL/kg bw	6 mL/kg bw

Fibrinogen dose (g) = targeted increase in A5_{FIB} (mm) × body weight (kg) / 160.
 Correction factor (140–160 mm · kg · g⁻¹) depends on the actual plasma volume.
 A5_{FIB} levels of 12 to 16 mm may compensate for low platelet count or function.

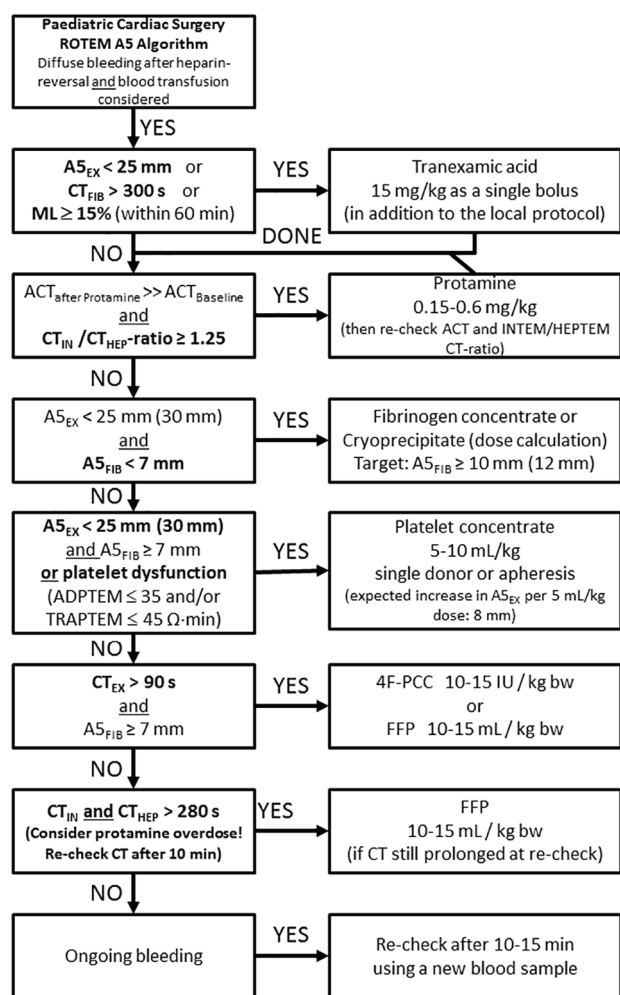


Fig. 1 Evidence-based pediatric cardiac surgery ROTEM A5 algorithm. Abbreviations: 4F-PCC, 4-factor prothrombin complex concentrate; A5_{EX}, EXTEM clot firmness amplitude 5 minutes after CT in mm; A5_{FIB}, FIBTEM clot firmness amplitude 5 minutes after CT in mm; ACT, activated clotting time in seconds; CT_{FIB}, FIBTEM coagulation time in seconds; CT_{HEP}, HEPTM coagulation time in seconds; CT_{IN}, INTEM coagulation time in seconds; EXTEM, extrinsic ROTEM assay activated by tissue factor and heparin neutralization by polybrene; FFP, fresh frozen plasma; FIBTEM, extrinsic ROTEM assay with platelet inhibition by cytochalasin D and heparin neutralization by polybrene; HEPTM, intrinsic ROTEM assay with heparin neutralization by heparinase; INTEM, intrinsic ROTEM assay activated by ellagic acid; MCF, maximum clot firmness in mm; ML, EXTEM or FIBTEM maximum lysis in % of MCF; ROTEM, rotational thromboelastometry (Courtesy of Klaus Görlinger, Essen, Germany).

after P2Y12 inhibitor cessation, in order to minimize bleeding complications.³⁵⁻⁴²

In summary, both platelet function testing studies published in this issue of the *Journal of Cardiac Critical Care* support the use of peri-interventional and perioperative platelet function testing and highlight its potential to personalize and optimize the management of antiplatelet drugs in terms of precision medicine by implementing the therapeutic window concept.⁴³⁻⁴⁷ This approach is also recommended in European and American guidelines, and the time is ripe to implement personalized antiplatelet therapy and bleeding management as an essential part of patient blood management in India.⁴⁸⁻⁵⁰

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Conflict of Interest

KG is the Medical Director of Tem Innovations GmbH, Munich, Germany.

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