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Early Point-of-Care Platelet Function Testing Using Multiple Electrode Aggregometry in Patients Undergoing Cardiac Surgery

To the Editor:

Perioperative coagulopathy in cardiac surgery is common and affects patient outcome due to increased blood loss and transfusion requirements. Platelets are crucial for postoperative hemostasis, and platelet dysfunction is one of the main causes of bleeding in the early period following cardiac surgery.[1] Also, many patients with cardiac disease use antiplatelet therapy, which increasingly is continued throughout surgery. As a result, rapid point-of-care platelet function testing might be of additional value to identify patients at risk for increased postoperative blood loss due to platelet dysfunction.

This study concerns platelet function testing using multiple electrode aggregometry (MEA) in patients undergoing cardiac surgery who were treated with or without antiplatelet therapy prior to surgery. We hypothesized that early platelet function testing, performed 5 minutes after blood sampling, produces reliable results in comparison with testing after a resting time of 30 minutes, as currently recommended by the manufacturer.

Patients eligible for the study were aged >18 years and scheduled for coronary artery bypass grafting (CABG), valve surgery, or both. Exclusion criteria were congenital coagulation disorder, reoperation (within a year), and pregnancy. Handling and analysis of blood samples were standardized locally, and Medical Research Ethics Committees United approval was obtained. After surgical incision, a single blood sample was drawn from an arterial line that was present in all patients and part of routine anesthesia care. For platelet function analysis, 3 mL of blood were added with a syringe to nonvacuumized hirudin-containing blood sampling tubes (25 μg/mL). Hirudin tubes were sealed and kept in an upright position at room temperature. Platelet function was assessed by MEA using the Multiplate analyzer (Roche Diagnostics, Rotkreuz, Switzerland) according to the manufacturer's instructions. In short, after gently pivoting the blood sampling tube, a 300-μL whole-blood sample was aspirated by an electronic pipette and added to the test cuvette. The blood sample then was diluted with preheated (37°C) saline, 0.9% (300 μL), and stirred/incubated for 3 minutes at 37°C before the agonist reagent was added. Reagent delivery was performed using an automatic pipette, and aggregation was recorded for 6 minutes. The recorded aggregation was expressed as arbitrary aggregation units (AU) plotted against time (1U = 10 AU/min).

Platelet aggregation was determined in response to stimulation with 4 specific receptor agonist reagents to test different pathways of aggregation: (1) arachidonic acid (ASPI) with a final concentration of 0.5 mmoL/L (ASPI-test; assay to evaluate the thromboxane pathway), (2) adenosine diphosphate (ADP) with a final concentration of 6.5 μmoL/L (ADP-test; assay to evaluate ADP-receptor function and thienopyridine efficiency), (3) collagen (COL) with a final concentration of 3.2 μg/mL (COL-test; assay for quantitative COL-induced platelet aggregation), and (4) thrombin receptor activating peptide (TRAP)-6 with a final concentration of 32 μmol/L (TRAP-test; assay for quantitative platelet function triggered by TRAP-6 via protease-activated receptor 1 [PAR-1]).

All blood samples were analyzed 5 and 30 minutes after sampling. Platelet aggregation interassay variability was obtained for all 4 reagents at 5 and 30 minutes by concurrently analyzing each sample twice in 2 channels of the 5-channel Multiplate analyzer. Due to the length of time required to perform testing and a maximum of 5 channels in the Multiplate analyzer, only 1 or 2 agonists could be tested for each blood sample. Data regarding routinely measured preoperative platelet count and hemoglobin concentration were collected from electronic patient records.

In total, 50 patients were included in the study for 19 to 21 matched pair tests per agonist. Platelet aggregation measurements were performed in 40 men and 10 women with a median age of 67 years (interquartile range [IQR] 60-74 years). Sixty-six percent (33/50) of patients underwent CABG surgery, and 34% (17/50) had valve surgery or a combination of both CABG and valve surgery. Antiplatelet drugs were continued until the day before surgery in 52% (26/50) of patients. Twenty-six patients used aspirin, and 4 patients were on dual antiplatelet therapy (aspirin combined with a platelet P2Y12 receptor inhibitor). Median preoperative hemoglobin level and platelet count were 9.0 mmoL/L (IQR 8.6-9.4) and 232 × 10^9/L (IQR 201-260), respectively.

Figure 1 displays the correlation between platelet aggregation levels measured at 5 and 30 minutes after blood sampling for all 4 agonists used. Very high correlation was seen for platelet aggregation tests performed with ASPI and COL ($r = 0.95$, $p < 0.01$ and $r = 0.91$, $p < 0.01$, respectively). Five-minute test results for ASPI explained 90% of variability in 30-minute test results, and 5-minute test results for COL explained 81% of variability in 30-minute test results.

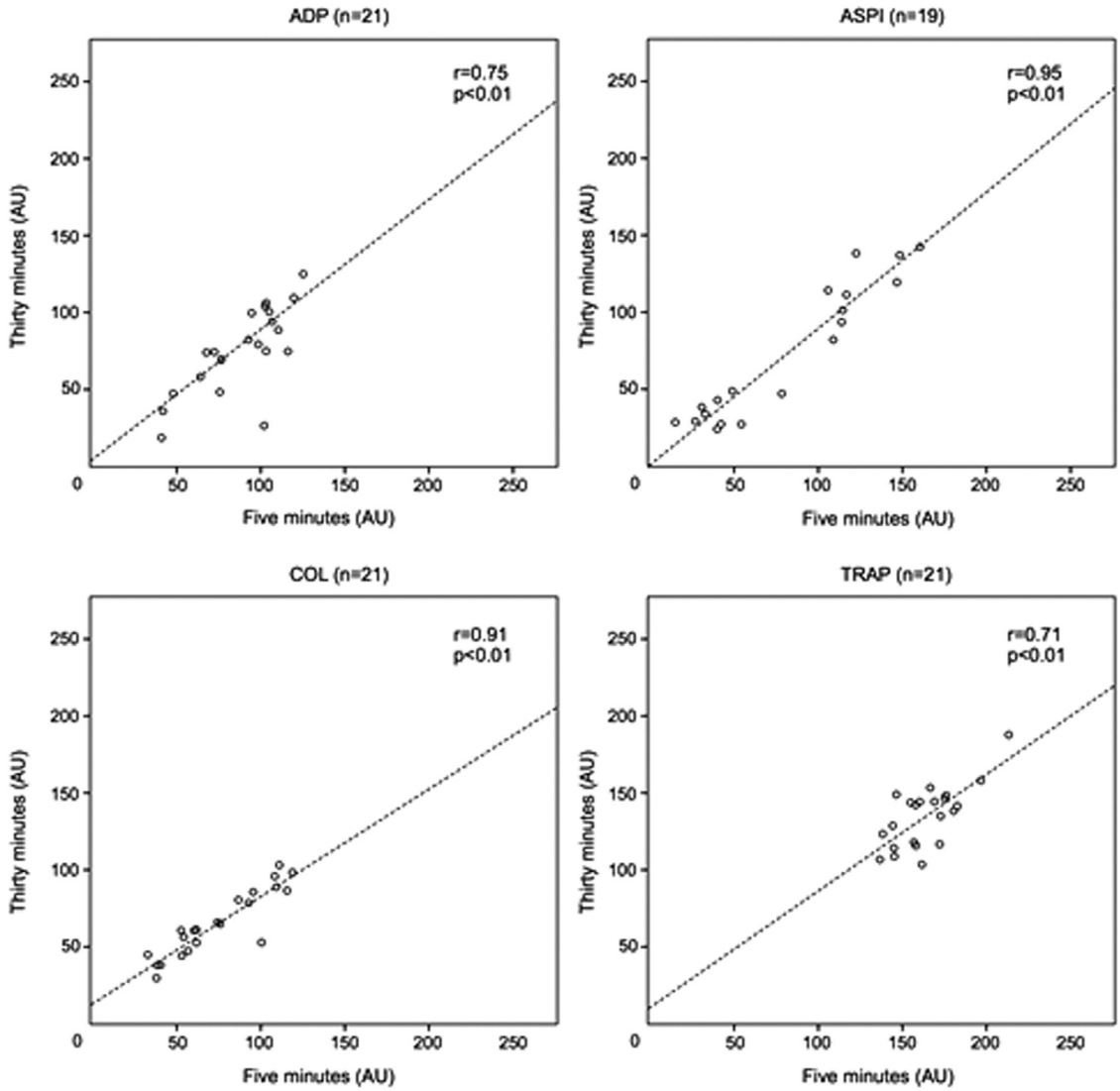

Fig 1. Correlation between platelet aggregation levels measured at 5 and 30 minutes after blood sampling for agonists adenosine diphosphate (ADP), arachidonic acid (ASPI), collagen (COL), and thrombin receptor activating peptide (TRAP)-6.

Interassay variation ranged from 5% (TRAP) to 14% (COL) at 5 minutes and 5% (TRAP) to 9% (ADP) at 30 minutes (Table 1).

The results of this study demonstrated very high correlation between platelet aggregation levels measured at 5 minutes and 30 minutes after blood sampling for ASPI and COL and high correlation for TRAP and ADP in patients undergoing cardiac surgery. For all reagents used, interassay variation of 5-minute test results was below 15%, suggesting good reproducibility.[2]

Table 1. Platelet Aggregation and Interassay Variation at 5 and 30 Minutes

	5 Minutes (AU × min)			30 Minutes (AU × min)			Difference (5-30)	
	Mean (SD)	Range	CV (%)	Mean (SD)	Range	CV (%)	Mean	95% CI
ASPI	69 (48)	2-147	10	61 (44)	12-130	9	8	1-15
ADP	76 (25)	28-113	6	79 (28)	22-128	9	–3	–11 to 5
COL	72 (28)	30-116	14	66 (21)	31-104	6	6	0-12
TRAP	151 (19)	124-201	5	132 (20)	101-185	5	19	13-26

Abbreviations: ADP, adenosine diphosphate; ASPI, arachidonic acid; AU, aggregation units; CI, confidence interval; COL, collagen; TRAP, thrombin receptor activating peptide-6.

Previous reports regarding suitability of MEA for rapid point-of-care platelet function testing have been published.[3–5] Jámbor et al[3] were among the first to question the necessity of a 30-minute resting time in platelet function monitoring using MEA. In 24 healthy adult volunteers, blood samples were drawn at baseline and at multiple time points after intake of an aspirin loading dose. In all blood samples, immediate measurement of platelet aggregation using ASPI and TRAP tests showed similar results compared to measurements after a 30- or 60-minute resting period. Würtz et al[4] studied platelet aggregometry using the Multiplate analyzer at 5 and 30 minutes in patients with stable coronary artery disease using aspirin and healthy patients without medication. A high correlation was present between aggregation levels measured at 5 and 30 minutes, irrespective of the agonist used (ASPI, COL, or ADP). Our study confirmed these results in a cohort of patients undergoing cardiac surgery.

In conclusion, MEA can be used for reliable platelet function testing within 5 minutes after withdrawal in patients undergoing cardiac surgery. This is clinically relevant to further identify patients at increased risk for blood loss and risk of transfusion.

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Cardiac Ultrasound: It's Not Just for Cardiologists!

To the Editor:

Use of bedside ultrasound for assisted physical examination has been well practiced and incorporated into the training curriculum and literature in emergency and critical care medicine for some time. Adoption of bedside ultrasound specifically for physical examination into perioperative practice has been lagging behind in the anesthesia community. While incorporation of ultrasound into the curriculum for anesthesia residents is slated for the near future, at present, the majority of anesthesia training programs are failing to provide adequate basic transthoracic echocardiography training to their trainees.[1]

In recent care of a 5-kg patient requiring surgical placement of a left chest pleural catheter, needle insertion was met with pulsatile bright red blood followed by significant hypotension and tachycardia unresponsive to 50 mL/kg of intravenous fluid. An ultrasound with a transthoracic echocardiography probe was available immediately, allowing the anesthesiologist to scan the chest rapidly and exclude the presence of a pericardial effusion or ventricular function deficit. Use of the bedside ultrasound allowed for rapid determination and management. Identification of a hemodynamically significant pericardial effusion would have necessitated an emergent drainage by the surgeon while absence allowed the team to stabilize the patient with blood transfusion and monitor for hemostasis. Ultimately, it was thought that the intercostal artery was encountered during the procedure.

The future of anesthesia certainly will include the use of bedside ultrasound by the anesthesiologist. Protocols for cardiac evaluation using ultrasound in the perioperative patient exist.[2,3] The time has come for anesthesiologists to incorporate this important skill into our practice. It is, however, critical to properly acquire the skills and knowledge for interpreting ultrasound findings to avoid diagnostic errors. As was demonstrated in this situation, application of cardiac ultrasound allowed for immediate and proper patient management and serves as an example of the utility of bedside ultrasound by the anesthesiologist.

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