The Role of Platelet Function Analyzer Testing in Cardiac Surgery Transfusion Management

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Keywords

PFA-100 · Cardiac surgery · Transfusion management

Summary

Background: Identifying high-risk patients for transfusion after cardiac operations would alter postoperative management. The aim of this study was to investigate closure time (CT) measured by platelet function analyzer (PFA) for prediction of bleeding and transfusions. **Methods:** 66 patients were scheduled for coronary artery bypass graft (CABG) surgery and 30 patients for valve repair and replacement (non-CABG). Measurements of PFA-100[®] CT for collagen and adenosine diphosphate (cADP) and collagen and epinephrine (cEPI) were performed 15 min after protamine administration. Blood loss was measured, and the amount of transfusion products was recorded postoperatively. **Results:** The study demonstrated significant differences between CABG patients with cADP-CT ≥ 118 s and those with cADP-CT < 118 s with regard to blood loss for 24 h ($p = 0.001$) and blood loss for 25–48 h ($p = 0.003$) as well as fresh frozen plasma ($p = 0.015$), platelet ($p > 0.001$) and red blood cell ($p = 0.002$) units given in 48 postoperative h. There were no differences cardiopulmonary bypass when was applied. In non-CABG patients, there were no differences in blood loss and transfusion requirements with respect to cADP-CT and cEPI-CT. **Conclusion:** Postoperative platelet dysfunction measured by a prolonged cADP-CT was significant predictor of blood loss and transfusion in CABG patients.

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Introduction

Patients undergoing cardiac surgery are at risk for excessive bleeding and associated complications [1]. Normal platelet function is essential for proper coagulation and hemostasis [2]. Bleeding often leads to transfusion of allogeneic blood and hemostatic blood components [3]. It is therefore important to assess the real versus the perceived need for transfusion of allogeneic RBCs and other blood products and to establish optimal management of bleeding and transfusion in patients undergoing cardiac surgery [4]. Various tests can be used to monitor the functional abilities of platelets. The PFA-100[®] is simple to use and gives quantitative results based on the principle of high shear stress simulating the environment at the site of vascular tissue injury, possibly making it more relevant than other tests in assessing shear-related platelet dysfunction [5]. Previous studies have shown that the PFA-100 test for assessing the risk of bleeding is subjected to uncertainties, doubts, and controversy. Four studies demonstrated a positive relationship between platelet function tests and postoperative bleeding [6–9]. On the contrary, Forestier et al. [10] and Fattorutto et al. [11] concluded that PFA-100 is not feasible for routine use following cardiac surgery, except for patients with increased risk of post-cardiopulmonary bypass (CPB) bleeding. Only one study has investigated platelet function test for prediction of bleeding and transfusion requirements in non-CPB surgery [12]. Two studies concluded that PFA-100, especially the test sequence with the collagen and adenosine diphosphate (cADP) cartridge, was very useful for platelet function monitoring [13, 14].

The aim of our study was to investigate the association between platelet function as determined by PFA-100 testing and postoperative blood loss and need for transfusion of blood products in i) patients undergoing coronary artery bypass grafting (CABG) and ii) patients with cardiac valve repair and replacement (non-CABG).

Patients and Methods

Study Design

After Medical Ethics Committee of University Hospital Center Split approval (protocol number: 2181-147-01 approved at February 20, 2012) and written consent, 126 patients undergoing cardiac surgery were included between May 2014 and May 2015. After 30 of them were excluded at the different stages of research, 96 patients undergoing cardiac surgery (69 males and 27 females aged between 43 and 84 years) were investigated (fig. 1). According to the prospective study design, the patients were divided into two main groups based on type of surgical intervention. Within each group, patients were divided in two subgroups i) with cADP closure time (CT) ≥ 118 s versus cADP-CT < 118 s or ii) with collagen and epinephrine closure time (cEPI-CT) ≥ 165 s versus cEPI-CT < 165 s. Criteria for non-inclusion in the study: emergency operation, renal insufficiency (creatinine > 120 $\mu\text{mol/l}$, glomerular filtration rate (GRF) < 60 ml/min), hepatic impairment (bilirubin > 50 $\mu\text{mol/l}$), medical history of bleeding tendencies, disorders of coagulation status in standard coagulation tests: platelet (PLT) count $< 100 \times 10^9/\text{l}$, prothrombin time (PT) < 0.70 s, activated partial thromboplastin time (APTT) > 33 s, hemoglobin (Hb) < 10 g/dl, hematocrit (Hct) < 0.28 , fibrinogen < 1.8 g/l, before surgery and usage of anti-PLT agents within 5 days before operation. CTs by PFA-100 longer than the reference ranges may be caused by a Hct less than 28% or PLT count less than $100 \times 10^9/\text{l}$. On the recommendation of Clinical Hematology Laboratory that complies with the manufacturer's recommendations patients with Hct $< 28\%$ or PLT count $< 100 \times 10^9/\text{l}$ measured 15 min following administration of protamine were excluded from the study.

All patients underwent standardized anesthesia and surgical protocol. CPB was performed under moderate hypothermia (34°C) and with usage of heparin-coated circuits. Heparin was administered as a loading dose of 150 IU/kg of body weight and supplemented to maintain an activated clotting time (ACT) of more than 280 s during CPB. After CPB, heparin was neutralized with protamine sulfate (1.5 mg of protamine/100 IU of heparin) to an ACT of less than 130 s. In patients without use of CPB, heparin was administered as a loading dose of 150 IU/kg of body weight to reach ACT ≥ 280 s and was neutralized with protamine sulfate at the same dosage as in patients with CPB. Red blood cells (RBCs), PLTs and fresh frozen plasma (FFP) were administered in accordance with recent recommendations and guidelines according to the decision of the cardiac anesthesiologists in charge [15]. RBCs were transfused to maintain Hb concentrations between 9 and 11 g/dl, considering the dynamics of bleeding [15, 16]. FFP was given to maintain hemostasis when the international normalized ratio exceeded 1.5 [17]. In the postoperative period, PLTs were administered as indicated in patients with microvascular bleeding and in those with PLT counts below $100 \times 10^9/\text{l}$ [17].

Blood samples were collected and analyzed at one time point, 15 min after administration of protamine. Additionally, the following demographic and sur-

gical data were collected: sex, body weight (kg), age (years), chest tube drainage (ml) at 24 and 48 h after admission in the intensive care unit (ICU) – a measure of postoperative blood loss, use of blood products (FFP, PLTs and RBCs) given during the operative or postoperative 48-hour period. Hct, Hb and PLT counts were measured in a hematology analyzer (Advia 120; Bayer, Tarrytown, NY, USA). PT, aPTT, and fibrinogen were analyzed with a coagulation analyzer Behring Coagulation System (Siemens Diagnostic Inc., Marburg, Germany) using manufacturer's kits and recommendations.

Platelet function was tested using the PFA-100 (Siemens AG, Erlangen, Germany); citrated whole blood was aspirated at high shear rates through disposable cartridges containing an aperture within a membrane coated either with cADP or cEPI [18]. These agonists induced platelet adhesion, activation, and aggregation leading to rapid occlusion of the aperture and cessation of blood flow. The time needed for blood flow cessation is termed CT and measured in seconds. An abnormally prolonged CT was considered to be ≥ 165 s for a cEPI cartridge, and ≥ 118 s for a cADP cartridge. As recommended by the manufacturer, blood samples were collected into 3,2% sodium citrate tubes of 4,5 ml (Vacutainer; Becton-Dickinson, Franklin Lakes, NJ, USA).

Statistical Analysis

Data were defined as continuous and categorical variables. Categorical variables are expressed as percentages and continuous variables as mean $\pm$ standard deviation (SD). Patients were divided in two subgroups i) with cADP-CT ≥ 118 s versus cADP-CT < 118 s, or ii) with cEPI-CT ≥ 165 s versus cEPI-CT < 165 s. Comparison between subgroups was made by using the Student's t-test to test the differences between the two arithmetic means in the subgroups. According to power analysis, an estimated number of 33 patients in each subgroup was needed at a statistical power of 90% and significance level of 5% to detect clinically meaningful differences of blood loss and transfusion requirements in the CABG group. For sample size analysis, PASS 11 (NCSS Inc., Kaysville, UT, USA) was used. A p value ≤ 0.05 was considered statistically and clinically significant with respect to the effect size and performed power analysis. All statistical analyses were performed using computer software (SPSS 17.0; SPSS, Inc., Chicago, IL, USA).

Results

Out of 126 patients, 30 patients were excluded because of i) insufficient blood sample for PFA-100 testing (n = 10), iii) Hct < 0.28 (n = 6), iii) PLT count $< 100 \times 10^9/\text{l}$ (n = 4), and iv) revision for postoperative bleeding (n = 10) (fig. 1).

Fig. 1. Flow diagram.

Table 1. Patient-related preoperative, perioperative and postoperative variables

	CABG (n = 66)	non-CABG (n = 30)
Age, years	67 ± 11	69 ± 8
Male sex (%)	55 (83%)	14 (47%)
Body mass index, kg/m ²	29 ± 4	26 ± 4
Hypertension (%)	49 (74%)	12 (40%)
Hyperlipidemia (%)	41 (62%)	10 (33%)
Diabetes mellitus (%)	12 (18%)	6 (20%)
Smokers (%)	25 (38%)	11 (27%)
Creatinine, μmol/l	84 ± 1 8.5	89.6 ± 23.6
GRF, ml/min	82.9 ± 13.2	85.6 ± 14.1
Bilirubin, μmol/l	30.4 ± 22.2	31.5 ± 18.3
Previous myocardial infarction (%)	10 (15%)	0
Withdrawal of clopidogrel at least 5 days before surgery (%)	33 (50%)	5 (17%)
Without of clopidogrel therapy in medical history (%)	33 (50%)	25 (83%)
Withdrawal of ASA at least 5 days before surgery (%)	42 (74%)	20 (67%)
Without of ASA therapy in medical history (%)	24 (26%)	10 (33%)
CPB	22 (33%)	30 (100%)
PLT number × 10 ⁹ /l	197 ± 59	160 ± 43
Hct	0.35 ± 0.04	0.31 ± 0.02
Hb, g/l	120 ± 15	114 ± 13
Fibrinogen, g/l	3.3 ± 0.9	2.7 ± 0.8
cEPI-CT, s	180 ± 77	232 ± 62
cADP-CT, s	141 ± 83	195 ± 77
24-hour drain volume, ml	664 ± 446	282 ± 155
25- to 48-hour drain volume, ml	338 ± 237	229 ± 166
≥2 units of RBCs / 48 h (%)	28 (42%)	9 (30%)
≥1 units of FFP / 48 h (%)	15 (23%)	6 (20%)
≥4 units of PLTs / 48 h (%)	23 (35%)	2 (7%)

Table 2. The difference between groups with cADP-CT ≥ 118 s and cADP-CT < 118 s in CABG patients

	cADP-CT ≥ 118 s (n = 32)	cADP-CT < 118 s (n = 34)	p
Age, years	66 ± 10	67 ± 5	0.063
Body mass index, kg/m ²	27 ± 2	29 ± 3	0.062
Hypertension (%)	29 (90%)	20 (59%)	0.003
Hyperlipidemia (%)	18 (56%)	23 (68%)	0.062
Diabetes mellitus (%)	5 (16%)	7 (20%)	0.065
Smokers (%)	16 (50%)	9 (26%)	0.004
Creatinine, μmol/l	83 ± 16.5	84 ± 10.5	0.623
GRF (ml/min)	80.7 ± 11.2	82.8 ± 10.2	0.675
Bilirubin, μmol/l	30.1 ± 16.2	33.2 ± 15.2	0.545
CPB	12	10	0.064
Time of CPB, min	160 ± 50	154 ± 35	0.567
PLT number × 10 ⁹ /l	190 ± 54	202 ± 62	0.444
Hb, g/l	116 ± 14	124 ± 15	0.535
Hct	0.34 ± 0.04	0.36 ± 0.04	0.020
Fibrinogen, g/l	3.0 ± 0.9	3.5 ± 1.0	0.051
cEPI-CT, s	211 ± 74	152 ± 69	0.001
24-hour drain volume, ml	847 ± 493	486 ± 317	0.001
25- to 48-hour drain volume, ml	423 ± 271	257 ± 163	0.003
Intraoperatively			
RBCs, U	3.2 ± 1.8	1.8 ± 1.7	0.002
FFP, U	3.6 ± 1.2	2.8 ± 0.7	0.003
Postoperatively			
RBCs, U	2.5 ± 2.2	1.0 ± 1.5	0.002
FFP, U	1.5 ± 2.4	0.4 ± 1.3	0.015
PLTs, U	5.1 ± 5.6	0.8 ± 2.6	<0.001

Fig. 2. Correlation between values of cADP-CT and blood loss for 24 h in CABG group.

Fig. 3. Correlation between values of cADP-CT and PLT for 48 h in CABG group.

Preoperative, perioperative and postoperative variables in CABG and non-CABG groups are summarized in table 1. The CABG group included 55 males and 11 females. On-pump surgery was performed in 22 (33%) and off-pump surgery in 44 (67%) of the CABG cases. In the non-CABG group (14 males and 16 females) single-valve surgery (replacement or repair, all on-pump surgery) was performed in 21 (70%) patients and multiple valve procedure in 9 (30%) subjects. The median CPB time in patients on CPB was 150 min (range 140–285 min).

In CABG patients, blood loss postoperatively was 664 ± 446 ml / 24 h and 338 ± 237 ml / 25–48 h. Of the 66 patients in the CABG group, 15 (23%) received FFP, 23 (35%) PLTs, and 28 (42%) two or more RBC units in the first 48 postoperative h.

In non-CABG patients, blood loss was 282 ± 155 ml / 24 h and 229 ± 166 ml / 25–48 h. Of the 30 patients in the non-CABG group, 6 (20%) received FFP, 2 (7%) PLTs, and 9 (30%) two or more RBC units in the first 48 postoperative h.

There were no differences between subgroups regarding age, gender, body mass index, levels of bilirubin, creatinine and Hb, GFR, and PLT count. There were no differences between subgroups of CABG and non-CABG patients with cADP-CT ≥ 118 s and < 118 s with respect to the use of CPB and duration of CPB.

Univariate comparison of the variables between subgroups of CABG patients with cADP-CT ≥ 118 s and < 118 s, demonstrated significant differences of hypertension and smoking habit in medi-

cal history, Hct values, blood loss in 24 h, blood loss in 25–48 h as well as FFP, PLT and RBC units given in the first 48 postoperative h (table 2). 14 (20%) patients had a cADP-CT > 200 s. They consumed 140 (70%) of total of 194 units of PLTs. The scatter diagrams showed strong correlations between cADP-CT and blood loss in 24 h (fig. 2) and between cADP-CT and PLT in 48 h (fig. 3). In the subgroups of CABG patients with cEPI-CT ≥ 165 s and < 165 s, there were significant differences of Hct values, but no differences with regard to blood loss in 24 h and in 25–48 h as well as FFP, PLT and RBC units given in the first 48 postoperative h (table 3). In contrast, in the subgroups of non-CABG patients with cADP-CT ≥ 118 s and < 118 s (table 4) and in those with cEPI-CT ≥ 165 s and < 165 s (table 5), blood loss in 24 h 25–48 h as well as FFP, PLT and RBC units given during 48 h postoperatively did not differ.

Discussion

To our knowledge, this is the first study to investigate postoperative cADP-CT and cEPI-CT in relation with postoperative blood loss and transfusion requirements in two specific groups of patients (CABG and non-CABG). So there is no possibility to compare our study to any other. We took into consideration cADP-CT and cEPI-CT. CADP-CT is prolonged in all cases of impairment of

Table 3. The difference between groups with cEPI-CT ≥ 165 s and cEPI-CT < 165 s in CABG patients

	cEPI-CT ≥ 165 s (n = 31)	cEPI-CT < 165 s (n = 35)	p
Age, years	66 $\pm$ 8	67 $\pm$ 4	0.367
Body mass index, kg/m ²	28 $\pm$ 3	29 $\pm$ 2	0.421
Hypertension (%)	22 (71%)	27 (77%)	0.067
Hyperlipidemia (%)	20 (65%)	21 (60%)	0.420
Diabetes mellitus (%)	7 (23%)	5 (14%)	0.410
Smokers (%)	13 (42%)	12 (34%)	0.375
Creatinine, μ mol/l	82.8 $\pm$ 16.5	83 $\pm$ 12.5	0.645
GRF, ml/min	82.7 $\pm$ 10.2	80.5 $\pm$ 9.2	0.667
Bilirubin, μ mol/l	31.5 $\pm$ 14.2	32.2 $\pm$ 14.5	0.589
CPB	15 (48%)	7 (20%)	0.020
Time of CPB, min	165 $\pm$ 30	140 $\pm$ 15	0.030
PLT number $\times 10^9$ /l	192 $\pm$ 53	201 $\pm$ 64	0.430
Hb, g/l	115 $\pm$ 14	124 $\pm$ 15	0.470
Hct	0.33 $\pm$ 0.04	0.37 $\pm$ 0.04	0.001
Fibrinogen, g/l	2.9 $\pm$ 0.7	3.6 $\pm$ 1.0	0.007
cADP-CT, s	176 $\pm$ 78	122 $\pm$ 47	0.001
24-hour drain volume, ml	693 $\pm$ 462	632 $\pm$ 438	0.582
25- to 48-hour drain volume, ml	347 $\pm$ 244	329 $\pm$ 231	0.766
Intraoperatively			
RBCs, U	3.0 $\pm$ 1.6	1.9 $\pm$ 2.0	0.021
FFP, U	3.4 $\pm$ 1.4	3.0 $\pm$ 0.6	0.183
Postoperatively			
RBCs, U	2.1 $\pm$ 2.3	1.3 $\pm$ 1.6	0.102
FFP, U	1.1 $\pm$ 2.3	0.8 $\pm$ 1.7	0.186
PLTs, U	3.7 $\pm$ 5.7	2.2 $\pm$ 3.7	0.153

Table 4. The difference between groups with cADP-CT ≥ 118 s and cADP-CT < 118 s in non-CABG patients

	cADP-CT ≥ 118 s (n = 23)	cADP-CT < 118 s (n = 7)	p
Age, years	70 $\pm$ 5	69 $\pm$ 2	0.425
Body mass index, kg/m ²	25 $\pm$ 7	26 $\pm$ 3	0.402
Hypertension (%)	9 (40%)	3 (43%)	0.456
Hyperlipidemia (%)	8 (35%)	2 (29%)	0.064
Diabetes mellitus (%)	4 (17%)	2 (29%)	0.058
Smokers (%)	9 (39%)	2 (29%)	0.077
Creatinine, μ mol/l	89.3 $\pm$ 19.6	87.6 $\pm$ 21.6	0.467
GRF, ml/min	82.6 $\pm$ 12.1	84.8 $\pm$ 13.5	0.478
Bilirubin, μ mol/l	30.8 $\pm$ 16.3	31.4 $\pm$ 17.3	0.523
Time of CPB, min	170 $\pm$ 30	160 $\pm$ 40	0.065
PLT number $\times 10^9$ /l	153 $\pm$ 36	182 $\pm$ 59	0.266
Hb, g/l	110 $\pm$ 13	98 $\pm$ 11	0.310
Hct	0.32 $\pm$ 0.04	0.30 $\pm$ 0.03	0.115
Fibrinogen, g/l	2.7 $\pm$ 0.6	2.7 $\pm$ 1.3	0.900
cEPI-CT, s	241 $\pm$ 54	201 $\pm$ 80	0.252
24-hour drain volume, ml	294 $\pm$ 147	238 $\pm$ 185	0.482
25- to 48-hour drain volume, ml	240 $\pm$ 179	190 $\pm$ 114	0.492
Intraoperatively			
RBCs, U	3.7 $\pm$ 1.8	2.9 $\pm$ 2.2	0.250
FFP, U	3.0 $\pm$ 1.1	3.6 $\pm$ 0.8	0.267
Postoperatively			
RBCs, U	0.9 $\pm$ 1.2	1.0 $\pm$ 1.5	0.817
FFP, U	0.4 $\pm$ 1.0	0.7 $\pm$ 1.5	0.508
PLTs, U	0.2 $\pm$ 0.8	0.6 $\pm$ 1.5	0.527

Table 5. The difference between groups with cEPI-CT ≥ 165 s and cEPI-CT < 165 s in non-CABG patients

	cEPI-CT ≥ 165 s (n = 26)	cEPI-CT < 165 s (n = 4)	p
Age, years	68 $\pm$ 8	69 $\pm$ 3	0.587
Body mass index, kg/m ²	25 $\pm$ 6	26 $\pm$ 4	0.562
Hypertension (%)	10 (38%)	2 (50%)	0.056
Hyperlipidemia (%)	9 (35%)	1 (25%)	0.058
Diabetes mellitus (%)	6 (23%)	0 (0%)	0.002
Smokers (%)	9 (35%)	2 (50%)	0.054
Creatinine, μ mol/l	87.3 $\pm$ 17.6	89.1 $\pm$ 16.5	0.592
GRF, ml/min	82.68 $\pm$ 10.5	84.5 $\pm$ 14.3	0.534
Bilirubin, μ mol/l	30.4 $\pm$ 15.1	31.2 $\pm$ 18.3	0.621
Time of CPB, min	180 $\pm$ 30	150 $\pm$ 50	0.003
PLT number $\times 10^9$ /l	154 $\pm$ 36	202 $\pm$ 67	0.249
Hb, g/l	107 $\pm$ 14	105 $\pm$ 7.0	0.599
Hct	0.32 $\pm$ 0.04	0.30 $\pm$ 0.02	0.304
Fibrinogen, g/l	2.8 $\pm$ 0.8	2.4 $\pm$ 0.4	0.930
cADP-CT, s	201 $\pm$ 72	146 $\pm$ 77	0.252
24-hour drain volume, ml	296 $\pm$ 160	180 $\pm$ 43	0.166
25- to 48-hour drain volume, ml	223 $\pm$ 169	199 $\pm$ 159	0.707
Intraoperatively			
RBCs, U	3.9 $\pm$ 1.6	0.8 $\pm$ 0.5	0.001
FFP, U	2.9 $\pm$ 0.9	4.8 $\pm$ 1.0	0.001
Postoperatively			
RBCs, U	1.0 $\pm$ 1.3	0.5 $\pm$ 1.0	0.508
FFP, U	0.5 $\pm$ 1.2	0.0 $\pm$ 0.0	0.374
PLTs, U	0.3 $\pm$ 1.0	0.0 $\pm$ 0.0	0.581

PLT activity associated with cardiac surgery, including the residual effect of clopidogrel [19] and external effects on PLTs by heparin as well as usage of CPB and colloid and crystalloid solutions [20, 21]. The reason for the use of CT The time point for blood sample withdrawal 15 min after administration of protamine was the result of previous investigations showing that the CT after cardiac surgery was the best predictor of blood loss [6, 7]. This measurement will give information regarding differences in baseline hemostatic capacity of the blood among the patients and information about the influence of all hemostatic disturbances related to cardiac surgery.

In our study group of CABG patients, significant differences were found with regard to blood loss/24 h and blood loss/25–48 h between patients with cADP-CT ≥ 118 s and those with cADP-CT < 118 s, confirming similar finding by Poston and colleagues [12]. We showed that the higher the values of cADP-CT in the CABG group the higher were the intra- and postoperative blood loss and transfusion requirements (fig. 2, 3).

In non-CABG patients we did not find any association either between cADP-CT and blood loss / transfusion requirements postoperatively or between cEPI-CT and blood loss / transfusion requirements. Our observations can be explained by the fact that primary hemostasis disturbance is a reversible process in non-CABG patients, and after elimination of external triggers hemostasis recovers spontaneously. Similarly Pappalardo and colleagues [21] showed that a defective primary hemostasis in these patients is not associated with an increased risk of bleeding. In our study, volume of bleeding and consumption of blood products were higher in the

CABG group than in the non-CABG group. In CABG patients, recovery of primary hemostasis, if there is a disturbance, cannot be achieved without blood product transfusions [16, 17].

We therefore conclude that cADP-CT testing following administration of protamine in the CABG group may identify patients in need for higher amounts of blood products. These patients would be the ones who could receive early initiation of cADP-CT testing and therefore derive the most benefit. In contrast, cEPI-CT was not predictive of bleeding and transfusion requirements either in the CABG and or in the non-CABG group. Cardiosurgery-related bleeding and transfusions requirements are strongly influenced by antiplatelet therapy before surgery [22]. The antiplatelet therapy before surgery was different in CABG and non-CABG patients. Clopidogrel therapy in CABG group is characterized by a large interindividual variability in pharmacodynamic response and in time to recover normal platelet reactivity following cessation of clopidogrel [23]. Theoretically, the PFA-100 cADP cartridge may be more suitable for monitoring clopidogrel therapy than the cEPI cartridge, but both collagen activation and ADP acting through the P2Y1 receptor, along with the high shear conditions, may be normally sufficient to largely overcome P2Y12 blockade. Some studies have shown that cADP is not suitable for assessing the efficacy of clopidogrel therapy [24–26]. The Innovance PFA P2Y was found to have a high sensitivity for the detection of platelet P2Y12-receptor blockade in patients undergoing therapy with a P2Y12 receptor antagonist [26], but clopidogrel therapy is not the only reason for the impairment of platelet function in CABG patients. Effects of heparin, hypothermia and fibrinolytic activity may also contribute

to the platelet function defect, as well as commonly used medications such as nonsteroidal anti-inflammatory drugs, some antibiotics, diuretics, and antihypertensives. Platelet plug formation in the PFA system is affected by a reduced level or function of von Willebrand factor (vWF). The severity of the cardiovascular disease indicated by higher vascular wall shear stress may produce changes of vWF structure. This was supported by the fact that approximately 90% patients with hypertension had prolonged PFA time (subgroup of cADP-CT value ≥ 118 s). A normal concentration of vWF, therefore, is not sufficient to support platelet adhesion and aggregation if the molecular structure of vWF is not preserved. During aging, the arterial system narrows thus increasing shear stress; this may result in activation of platelets and also in adsorption and prolonged loss of large multimers of vWF unlike transitory and reversible loss and dysfunction of vWF caused by CPB [27]. We showed significant differences of cEPI-CT values depending on the use of CPB, but cEPI-CT was not predictive of bleeding and transfusions requirements.

On the other hand, patients with impairment of platelet function and with subsequently increased consumption of blood products can be identified by cADP-CT testing.

In our study, there were significant differences of Hct values in cADP-CT and cEPI-CT subgroups of the CABG group. These differences were only clinically significant for the cADP-CT subgroups as cEPI-CT subgroups did not differ with respect to blood loss and transfusions requirements.

Further, there were no significant differences of plasma fibrinogen levels in subgroups with cADP-CT ≥ 118 s versus cADP-CT < 118 s in CABG and non-CABG group.

This study has some limitations. PFA-100 testing is very sensitive to vWF levels, and vWF measurement was not done. However,

thorough and careful history of bleeding tendencies was performed for all the patients included in the study compensating for the missing vWF determination. The differences in blood loss between subgroups in the non-CABG group did not have any clinical or statistical significance because they did not result in increased consumption of blood products. Therefore, a sample of 30 non-CABG patients is sufficient for statistical analysis. Another possible limitation is that CABG patients were not divided according to the fact whether or not CPB was applied. However, we could demonstrate that there were no significant differences in cADP-CT values between CAPG patients with and without CPB. This is in line with an article by Poston [28] who also did not find any of bleeding rates in patients with or without CPB. Therefore, we abstained from dividing our CABG group into additional subgroups. Thus the main limitation of our study is that in many cases routine administration of transfusion products mainly depended on the discretion of individual anesthesiologist in charge.

In summary, our study demonstrates that cADP-CT at time point of 15 min following administration of protamine may predict blood loss as well as FFP, PLT and RBC transfusion requirements only in CABG patients. Identifying high-risk patients for transfusion would alter postoperative patient management. In our opinion prediction models based on a postoperative PFA-100 test may facilitate blood component management following cardiac surgery and, at the same time, decrease potential negative influence of excessive transfusion of blood products.

Disclosure Statement

The authors declare no conflict of interest.

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