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Use of thrombin generation test for monitoring hemostasis in coronary bypass surgery

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Abstract. To evaluate the parameters of the thrombin generation test (TGT) in coronary artery disease (CAD) patients on prolonged aspirin therapy during on-pump coronary artery bypass grafting (CABG) after donor platelet concentrate transfusion. A total of 148 patients with CAD on prolonged aspirin therapy (75–100 mg/day) who have undergone elective on-pump CABG were consecutively included in the study. Patients were divided randomly into two groups. Group 1 ($n = 76$) received donor platelet transfusions after cardiopulmonary bypass, whereas Group 2 ($n = 72$) did not. TGT parameters were measured using an analyzer at pre-, intra-, and early postoperative periods. Activation of the endogenous thrombin potential was observed in patients on prolonged aspirin therapy in the pre- and intraoperative periods, as confirmed by high peak thrombin and increased velocity index. The activation time of the prothrombinase complex and thrombin generation time were greater than the control group. The blood hemostatic potential in patients who did not receive transfusions in the early postoperative period decreased up to the level of the control group in the extended time parameters. Hemostatic potential in plasma in patients on aspirin was preserved. Given the laboratory test results and clinical data, platelet concentrate transfusion is unnecessary for prevention.

Keywords: Thrombin generation test, coronary artery disease, aspirin therapy, platelet transfusion.

Abbreviations

CABG	Coronary artery bypass grafting
CAD	coronary artery disease
CPB	cardiopulmonary bypass

1. Introduction

On-pump coronary artery bypass grafting (CABG) is the gold standard treatment of coronary artery disease (CAD). This treatment eliminates the symptoms of angina and prolongs the life of patients with severe CAD (severe left main coronary artery stenosis) and three-vessel disease (or two-vessel disease involving stenosis of the proximal left anterior descending artery) with left ventricular dysfunction.

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Bleeding in patients on prolonged aspirin therapy is a major complication during CABG. It may be caused by extensive surgical trauma, prolonged blood contact with the cardiopulmonary bypass (CPB) circuit, high doses of heparin, low levels of clotting factors due to dilution after infusion and transfusion therapy, and hypothermia [16, 25].

Platelet dysfunction and structural platelet disorder [6, 20, 26] play an important role in the development of postoperative bleeding. Therefore, transfusion of platelet concentrate is speculated to be significant in pathogenetic therapy and in hemorrhagic complication prevention. However, no clear criteria for transfusion of platelet concentrate are available. Moreover, platelet transfusions may lead to further aggravation of hemostasis in some cases. Therefore, adequate monitoring of platelet-vascular (primary) and coagulation (secondary) hemostasis in these patients is necessary. The thrombin generation test (TGT) is one of the promising methods for comprehensive assessment of the hemostatic potential; it can capture the end result of the interaction between pro- and anti-coagulant mechanisms of the hemostatic system [2, 13, 19]. In this study, we aim to evaluate the parameters of the TGT in CAD patients on prolonged aspirin therapy during on-pump CABG after donor platelet concentrate transfusion.

2. Methods

The local Ethics Committee of the Federal State Budgetary Institution "Research Institute for Complex Issues of Cardiovascular Diseases" approved the conduct of the study. All patients provided written informed consent.

A total of 148 patients with CAD who have undergone elective on-pump CABG were consecutively selected from the CABG Registry using the case–control method. The diagnosis was confirmed according to clinical assessment and electrocardiographic and echocardiographic findings.

The inclusion criteria were as follows: prolonged aspirin therapy for at least 1 year (75–100 mg daily); age <75 years; capacity to provide written informed consent; and aspirin reaction unit (ARU) values <550, which are consistent with a patient who is receiving the therapeutic benefit of aspirin (VerifyNow Aspirin).

The exclusion criteria were as follows: concurrent bypass surgery; redo procedures and prior surgeries; acute coronary syndrome with the need for the use of dual antiplatelet therapy; intraoperative complications, requiring the re-start of CPB or the application of intra-aortic balloon counterpulsation; resternotomy in the early postoperative period, associated with surgical bleeding; chronic kidney disease stages II–III (S.I. Ryabov's classification); ARU ≥550% (VerifyNow Aspirin Test); a positive history of hemorrhagic disease; hematocrit <30% and hemoglobin <100 g/l; platelet count <100 and >450×109/l; administration of drugs containing plasma coagulation factors; perioperative transfusion of donor red blood cell (RBC) units, fresh frozen plasma; concomitant inflammatory disease and/or cancer; pregnancy; hormone replacement therapy; and patient refusal to participate in the study.

Patients were divided randomly into two groups by the drawing of envelopes. Group 1 ($n = 76$) patients received donor platelet transfusions after CPB, and Group 2 ($n = 72$) patients did not. Transfusion of platelet concentrates was performed after the assessment of platelet function after protamine administration. A main indication for platelet concentrate transfusion is reduced adenosine diphosphate and epinephrine-induced platelet aggregation activity by 20% below the normal range [8].

Table 1 shows clinical and demographic data of the study groups. Male patients prevailed in the study groups ($n = 112$, 75.7%) with a mean age of 57.4 (55.3; 59.47) years. The study groups were matched for age and presence of CAD risk factors, namely, hypertension, smoking, clinical signs and symptoms of angina before the onset of myocardial infarction, congestive heart failure, and dyslipidemia. Patients in both groups had the same incidence rates of type 2 diabetes and postinfarction cardiosclerosis.

Table 1
Baseline clinical characteristics of patients, n (%)

Variable	Patients with platelet transfusions, $n = 76$	Patients without platelet transfusions, $n = 72$	P
Age, years	55.3 (52.3;56.7)3	58.72 (56.2;59.1)	0.25
Men, *n* (%)	56 (73.6)	56 (77.7)	0.45
Arterial hypertension, *n* (%)	36 (42.1)	40 (55.5)	0.59
Current smoking, *n* (%)	56 (73.8)	60 (83.3)	0.12
Chronic heart failure	62 (81.5)	64 (88.8)	0.42
Dyslipidemia	18 (23.6)	24 (33.3)	0.45
Angina pectoris signs prior to MI onset	76 (100)	68 (98)	0.53
Type 2 diabetes in the anamnesis	22 (28.9)	16 (22.2)	0.059
Comorbidities			
Diseases of the digestive tract	16 (21)	20 (27.7)	0.21
Iron-deficiency anemia	6 (7.8)	8 (10)	0.36
In-hospital treatment			
- β-AB	72 (94.7)	68 (94.4)	0.82
- ACEs	60 (78.9)	48 (66.6)	0.68
CCB	52 (68.4)	48 (66.6)	0.98
Diuretics	20 (26.3)	20 (27.7)	0.83
Nitrates	14 (18.4)	12 (16.6)	0.77
Aspirin	76 (100)	72 (100)	0.92
Statin	76 (100)	72 (100)	0.98

The study groups were comparable in preoperative hematocrit levels, number of RBCs and platelets, and coagulation profile. All patients underwent elective, primary CABG without discontinuation of antiplatelet therapy (aspirin 75–100 mg/day). All patients received standard therapy, including beta-blockers, angiotensin-converting enzyme inhibitors, and lipid-lowering drugs (statins).

All surgical procedures were performed by the same surgical team using the standard protocol adopted in the Research Institution. The mean CPB time, mean aortic cross-clamp time, mean temperature during CPB, and average graft number were 86.5 min, 53 min, 35.3°C, and 3, respectively. The harvesting of the internal thoracic artery and vein grafts was performed according to the standard technique. Heparin administration and neutralization by protamine sulfate were performed according to the protocol adopted in the Research Institute. Secondary hemostasis in the perioperative period was assessed by determining the activated clotting time (ACT) in whole blood samples on an ACT Plus Automated Coagulation Timer System (Medtronic, USA) using ACT PLUS disposable test cartridges. The mean ACT before surgery was 122 s; after protamine administration, 139 s; and in the immediate postoperative period, 144 s. All these parameters corresponded to the protocol of on-pump CABG adopted in the Research Institute.

The study groups did not differ in the type of anesthesia and doses used during the surgeries. The perfusion index was 2.5–2.7l/min/m^2. The CPB circuit was primed with 1300 ml of volume expanders: crystalloids and colloids. Cold blood cardioplegia was used to protect the myocardium (4 : 1 ratio of RBCs to crystalloids). The intra- and postoperative blood loss (for 6, 12, and 24 h) did not differ significantly between the study groups (Table 2). The increased chest tube drainage rate in the postoperative period was considered in the following cases: >7 ml/kg body weight in the first hour after surgery, >5 ml/kg body weight per hour in the first 2–3 h, and 2 ml/kg body weight per hour in the first 4 h.

Table 2
Thrombin generation test parameters (platelet poor plasma)

Variable	Control ($n=20$)	Patients without platelet transfusions			Patients with platelet transfusions		
		Before surgery	After protamine	Early postoperative period (median 1 h)	Before surgery	After protamine	Early postoperative period (median 1 h)
	1	2	3	4	5	6	7
Lag time, min	2.8 (3.0;3.4)	5.65 (4.2;9.05) $P_{1,2}=0.011$	6.7 (5.4;8.9) $P_{1,3}=0.002$ $P_{2,3}=0.0196$	7.6 (6.5;10.4) $P_{1,4}=0.0001$ $P_{2,4}=0.001$ $P_{3,4}=0.23$	5.3 (2.5;5.2) $P_{1,5}=0.03$	5.0 (2.6;6.6) $P_{1,6}=0.002$ $P_{5,6}=0.011$ $P_{3,6}=0.028$	4.3 (3.0;6.0) $P_{1,7}=0.001$ $P_{5,7}=0.005$ $P_{6,7}=0.004$ $P_{4,7}=0.007$
Time to peak, min	9.5 (8.9;10.2)	11.6 (9.4;16.1) $P_{1,2}=0.0014$	14.15 (10.2;17.65) $P_{1,3}=0.012$	14.8 (11.7;17.6) $P_{1,4}=0.025$	11.0 (8.9;13.1) $P_{1,5}=0.014$ $P_{2,5}=0.02$	11.0 (7.5;14.2) $P_{1,6}=0.052$ $P_{3,6}=0.002$	10.75 (8.4;14.05) $P_{1,7}=0.024$ $P_{4,7}=0.036$
Peak thrombin, nM/l	122.8 (115;130.1)	168.9 (68.0;277.9) $P_{1,2}=0.03$	149.7 (92.050;235.650) $P_{1,3}=0.025$	105.400 (56.8;144.8) $P_{1,4}=0.049$ $P_{2,4}=0.007$ $P_{3,4}=0.0002$	197 (172.0;276) $P_{1,5}=0.021$	181 (132.5;274) $P_{1,6}=0.0005$ $P_{5,6}=0.081$ $P_{3,6}=0.045$	184 (127,5;253) $P_{1,7}=0.0016$ $P_{5,7}=0.001$ $P_{4,7}=0.034$
V1, nM/min	20.4 (17.2;22.1)	32.300 (7.5;61.800) $P_{1,2}=0.028$	28.150 (12.35;39.5) $P_{1,3}=0.014$	14,85 (6.6;25.35) $P_{1,4}=0.027$ $P_{2,4}=0.006$ $P_{3,4}=0.002$	40,9 (24.7;32.5) $P_{1,5}=0.001$	31,3 (19.9;60.5) $P_{1,6}=0.005$ $P_{5,6}=0.002$	32,5 (16.7;67.5) $P_{1,7}=0.001$ $P_{5,7}=0.001$ $P_{4,7}=0.045$
AUC, nM	1604.2 (1517;1690)	2556.5 (1524.4;2738.8) $P_{1,2}=0.0021$	2062.9 (1381,8;2690.1) $P_{1,3}=0.045$ $P_{2,3}=0.056$	1593.95 (955;1893.9) $P_{2,4}=0.002$ $P_{3,4}=0.0001$	2963 (2850;4111) $P_{1,5}=0.0002$	2562 (1726;2868) $P_{1,6}=0.043$ $P_{5,6}=0.01$ $P_{3,6}=0.032$	2724 (1881;3247) $P_{1,7}=0.002$ $P_{5,7}=0.0001$ $P_{6,7}=0.0001$ $P_{4,7}=0.006$

Platelet concentrate was obtained by automatic apheresis using a Haemonetics MCS + cell separator (Haemonetics, USA) and filtration (Kemerovo Regional Blood Center). Filter-prepared platelet concentrate was stored in a platelet mixer and PRESVAC Platelet incubator (PRESVAC, Argentina) in the transfusion office in the operating room unit. Transfusion was performed based on the AB0 and Rh systems at a dose of $>50–70\times10^9$ platelets per 10 kg body weight after 20 min since protamine sulfate was administered. The mean volume of platelet concentrate transfused to a patient was 312.0 ± 15.9 ml. The control group consisted of 20 healthy subjects aged 40–60 years without clinical signs and symptoms of CAD. The average storage period of the platelet concentrate before transfusion was 42.6 ± 10.1 hours, allowable storage period – 5 days. The number of platelets in a dose of platelet concentrate was on average $4.8 \pm 2.1*10^{11}$, residual leukocytes – $0.23\pm 0.10*10^6$, ph of the medium varied from 6.4 to 7.0.

The preoperative efficiency of antiplatelet therapy with aspirin was evaluated using a VerifyNow® (Accumetrics, USA) based on light transmittance aggregometry. Whole venous blood was collected for the automatic bedside test. ARU values <550 are consistent with a patient who is receiving the therapeutic benefit of aspirin.

The study material contained platelet-rich plasma (PRP) and platelet-poor plasma (PPP). Venous whole blood was collected by gravity using a central venous catheter. PRP was obtained through centrifugation of whole blood at 1500 rpm for 7 min. The upper layer was then centrifuged at 3000 rpm for 15 min (PPP).

Blood samples were collected at preoperative (1 h before the induction of anesthesia), intraoperative (15 min after protamine administration and before platelet concentrate transfusion), and early postoperative periods (approximately 1 h after the patient's transfer from the operating room unit to the intensive care unit). The TGT parameters were measured using a kit (Technothrombin TGA, Technoclone, Vienna, Austria) and a Ceveron Alpha analyzer (Technoclone, Vienna, Austria).

The following parameters were measured to assess quantitative and dynamic characteristics of thrombin generation:

- Lag time (LT, min) – the moment that the signal deviates by >2 standard deviations from the horizontal baseline;
- Peak thrombin (nM/l) – maximum thrombin concentration;
- Time to peak (TTP, min) – the time of maximum thrombin concentration;
- AUC – area under the thrombin generation curve (nM);
- Velocity index (VI) – the effective rate of thrombin generation between lag time and TTP (nm/min).

Mann–Whitney and Wilcoxon tests were performed to statistically analyze independent and paired samples, respectively. The obtained results are presented as median (Me) and 25% and 75% quartiles (Me: Q1; Q3). $P < 0.05$ was considered statistically significant.

3. Results

The clotting time in the PPP of CAD patients in the preoperative period was 1.88-times higher compared with the control group. The TTP and VI were 1.2- and 1.6-times higher than those in the control group. Despite an increase in thrombin generation time, the peak thrombin generation was 1.4-times higher compared with the control group. The AUC exceeded 1.6-times the same parameter in the control group (Table 3). The obtained results showed increased thrombin generation in the PPP of CAD patients in the preoperative period.

After protamine administration, a further increase in the lag time and TTP was observed at the intraoperative period compared with the pre-operative and corresponding values in the control group.

Table 3
Parameters of thrombin generation test (platelet rich plasma)

Variable	Control ($n = 20$)	Patients without platelet transfusions			Patients with platelet transfusions		
		Before surgery	After protamine	Early postoperative period (median 1 h)	Before surgery	After protamine	Early postoperative period (median 1 h)
	1	2	3	4	5	6	7
Lag time, min	3.2 (3.0;4.0)	4.6 (3.9;6.9) $P_{1,2} = 0{,}026$	5.3 (3.9;7.0) $P_{1,3} = 0.032$	6,20 (5.4;10.2) $P_{1,4} = 0.001$ $P_{2,4} = 0.0001$ $P_{3,4} = 0.004$	4.90 (3.42;5.85)	5.0 (2.3;6.6) $P_{1.6} = 0.002$	4.55 (3.1;8.1) P1,7 = 0.032 P4,7 = 0.02
Time to peak, min	9.40 (9.0;10.0)	9.45 (7.9;12.25)	9.7 (9.7;8.29)	11.25 (9.1;16.35) $P_{1,4} = 0.012$ $P_{2,4} = 0.006$ $P_{3,4} = 0.0001$	9.55 (6.35;12.2)	11.10 (5.1;13.7) $P_{1.6} = 0.023$	10,90 (7.8;16.6) $P_{1,7} = 0.02$ $P_{5,7} = 0.0004$
Peak thrombin, nM/l	132.5 (130.1;141.2)	249.9 (136.65;422.35) $P_{1,2} = 0.001$	275.7 (152.1436.4) $P_{1,3} = 0.01$	171.85 (108.8;281.25) $P_{1,4} = 0.02$ $P_{2,4} = 0.001$ $P_{3,4} = 0.0003$	261 (204;421) P1,5 = 0.001	283 (137;315) P1,6 = 0.002 P 5,6 = 0.028	225 (132;292) P1,7 = 0.002 P 5,7 = 0.0001 P4,7 = 0.012
V1, nM/min	21.95 (19.8;23.7)	54.7 (26.15;115.4) $P_{1,2} = 0{,}02$	64.6 (36;119.1) $P_{1,3} = 0.005$	32.4 (26.7;41.2) $P_{1,4} = 0.012$ $P_{2,4} = 0.0001$ $P_{3,4} = 0.0003$	49.3 (27.8;114) $P_{1,5} = 0.0023$	71.2 (17;217) $P_{1,6} = 0.021$	48.3 (17.1;66.5) $P_{1,7} = 0.022$ $P_{4,7} = 0.022$
AUC, nM	1665.2 (1523;1855.1)	3448.2 (1677.4;3958.6) $P_{1,2} = 0.014$	2487.7 (1426.0;2957.8) $P_{1,3} = 0.023$	2075.25 (1285.2;2314.1) $P_{1,4} = 0.042$ $P_{2,4} = 0.00012$ $P_{3,4} = 0.001$	2958 (2036;3175) P1,5 = 0.0002	2650 (2334;3061) $P_{1,6} = 0.001$	3204 (2056;3648) $P_{1,7} = 0.001$ $P_{4,7} = 0.023$

A slight decrease in peak thrombin generation and VI accompanied by 20% reduction in AUC were considered as a decrease in thrombin generation compared with the preoperative values. However, thrombin generation was higher compared with the controls; the AUC increased 1.6 times (Table 3).

Further reduction of thrombin generation was observed at the early postoperative period, i.e., peak thrombin generation decreased with reduced TTP, and the initiation phase. Despite the fact that the AUC reduced up to the levels in the control group, other parameters, such as peak thrombin generation and VI, were significantly altered compared with the controls (Table 3). In general, thrombin is generated faster in the early postoperative period, but its concentration is lower than that in the control group. The results indicated a partial normalization of thrombin generation with the development of the enzyme deficiency in blood plasma.

As expected, platelet transfusions increased thrombin generation; the clotting time and TTP reduced, but the VI and peak thrombin generation increased. However, the latter did not reach the preoperative levels. The initiation time after protamine administration and at the early postoperative period reduced by 40% on average compared with patients without transfusion and by 80% compared with the control group (Table 3). The TTP reduced by 23%, but its concentration increased by 1.8-times compared with the group of patients in the postoperative period who did not receive platelet transfusions (Table 3). Despite the increase in thrombin concentration, the VI slightly decreased in the postoperative period but remained elevated compared with the controls. The AUC was 1.6–1.7-times higher than those of the reference values (Table 3). Platelet transfusion generally stimulated thrombin generation by increasing the VI and thrombin concentration in PPP.

Almost all the TGT values in the PRP of CAD patients were different from those in the PPP particularly the shorter lag phase and thrombin generation. Moreover, the VI increased 2-fold at the intraoperative and early postoperative periods compared with those in the PPP (Table 3).

Platelet transfusion reduced the clotting initiation time in the early postoperative period by 1.4-times and peak thrombin generation increased by 1.3-times. Moreover, the VI and endogenous thrombin capacity increased by 1.5-times on average.

4. Discussion

Prolonged aspirin therapy is significant in the prevention and treatment of CAD [22, 24]. The antithrombotic action of aspirin (acetylsalicylic acid) is due to the inhibition of cyclooxygenase-1 [7]. However, aspirin affects secondary hemostasis and inhibits fibrin formation by preventing thrombin generation and the functional state of fibrinogen; it also affects fibrinolysis activation by releasing plasminogen activators and unravelling fibers [27]. Meanwhile, recent studies have reported new experimental data on the pro-coagulation effect of aspirin, i.e., increased fibrinogen concentration and prothrombin index [25].

The question of whether antiplatelet therapy should be discontinued in the preoperative period in patients undergoing elective CABG remains the subject of debate. On the one hand, antiplatelet therapy can reduce thrombosis and ischemic events, as well as improve graft patency [12] and survival after CABG [8]. However, it is associated with a higher risk of bleeding [3, 15]. Therefore, discontinuation of antiplatelet agents in the preoperative management of patient undergoing elective CABG is quite common [27]. On the other hand, the discontinuation of aspirin (7–30 days) is associated with 3-fold increased risk for cardiovascular events [4]. This finding indicates that preoperative management should be specifically designed to an individual patient. Health care practitioners should focus on the balance between the effectiveness of antiplatelet therapy and its safety to minimize the rate of bleeding. Hemostasis monitoring in cardiac patients at the intraoperative and early postoperative periods remains an important issue of transfusion therapy and anesthesia.

Currently, laboratory methods are commonly used to assess blood hemostatic potential. One of the promising methods is TGT, which can capture the end result of the interaction between pro- and anti-coagulant mechanisms on the formation and inactivation *in vitro* of the key enzyme of hemostasis – thrombin. The estimation of thrombin generation using the TGT allows the assessment of hemostatic profile in general and can be an integral indicator of the balance of pro- and anti-coagulant mechanisms [1].

In this study, we performed serial thrombin generation testing in patients undergoing on-pump CABG without the discontinuation of antiplatelet therapy in the perioperative period. The results obtained in the preoperative period showed an increase in thrombin potential in the plasma of patients in the study groups compared with the control group. Moreover, the values of thrombin generation parameters were higher in PRP compared with PPP. This point emphasizes the contribution of platelets to blood hemostatic potential despite the ongoing antiplatelet therapy. Notably, the time of the test performance in patients on prolonged aspirin therapy was longer and consistent with other studies [1, 23, 25].

In the intraoperative period after protamine administration, thrombin generation decreased compared with the preoperative values. However, the TGT parameters in PRP and PPP were higher than the control group; the AUC increased 1.6-fold. Furthermore, an increase was observed in time parameters compared with the preoperative values and the control group. The findings indicated that platelet dysfunction worsened during CABG because of the following factors:

- Blood contact with the synthetic surfaces of the extracorporeal circuit, resulting in degranulated platelets after CPB [21];
- The use of heparin, which inhibits thrombin activity and binds to antithrombin III, contributing to its inactivation, inhibition of thrombus formation, and development of heparin-induced thrombocytopenia [8, 15];
- The use of protamine to neutralize heparin, which in a dose-dependent manner alters the structure of the fibrin clot, reducing platelet function and increasing the ACT [18];
- Hemodilution coagulopathy [5], both due to mechanical blood dilution and the direct interaction of the molecules of colloid volume expanders with platelet membranes, causing the blockage of platelet fibrinogen receptors – GP IIb/IIIa [10, 11];
- Hypothermia and acidosis, which leads to damages in the initial stages of thrombus formation (initiation phase) and clot formation (proliferation phase) [14].

The thrombin potential continued to reduce in the early postoperative period in patients who did not receive platelet concentrate transfusion. The most pronounced reduction was defined in PRP; the AUC reduced up to the levels in the control group, and other parameters, such as peak thrombin and VI, were significantly lower compared with the control group. The values of the generation test in PPP were also decreased but remained higher than those of the controls, indicating the preserved platelet ability to generate thrombin. The results showed a partial normalization of thrombin generation with the development of enzyme deficiency in blood plasma.

Transfusion of donor platelets increased blood hemostatic potential, as evidenced by higher quantitative parameters with reduced time compared with the group of patients without donor platelet transfusion and the control group. Apparently, donor platelets enhance thrombin generation by releasing platelet alpha granules of the coagulation factors (V, VIII, XIII, tissue factor), which promote activation of the prothrombinase complex [17] and increase thrombin concentrations. Moreover, the phospholipids in the platelet membrane provide the surface for forming coagulation factor complexes from plasma (V, X, VIII, IX, XI, prothrombin, fibrinogen) and protect them from the effects of inhibitors, which also contribute to thrombin generation. However, own platelets can increase thrombin generation despite the antiplatelet therapy. Thrombin binds to PAR-1 and PAR-4 receptors, involving Gi GqG12/13b protein, and leads to the synthesis of thromboxane A2, and the activation of integrins

increases the concentration of intracellular calcium by stimulating platelet aggregation. Low thrombin concentrations (50 pmol/l) may cause a similar effect [9]. Even low thrombin concentration during CABG probably promotes platelet aggregation. Additional transfusion of donor platelets may cause thrombosis and adverse ischemic events due to the mutual activation of platelet and coagulation phases of hemostasis.

5. Conclusion

Hemostatic potential in plasma in patients on aspirin is preserved; thus, own platelets fully contribute to hemostatic potential in blood, increasing thrombin generation. On-pump CABG is associated with a breach in thrombin generation in the perioperative period. The thrombin potential in the intra- and postoperative periods under the influence of the factors that affect hemostasis is reduced without developing hemorrhagic complications. Considering that patient's platelets retain their ability to participate in thrombin generation and donor platelets stimulate endogenous thrombin potential, platelet concentrate transfusion is suggested to increase the risk of thrombosis and ischemic events. Given the results of laboratory test and clinical data, platelet concentrate transfusion is unnecessary for prevention. The rationale for the transfusion of donor platelets should be individual and based on the laboratory parameters of the TGT, which minimize the risk of perioperative ischemic and hemorrhagic complications.

Ethical approval

This case report was approved by the local institutional review board (Federal State Budgetary Scientific Institution Research Institute for Complex Issues of Cardiovascular Diseases) and the patient gave written informed consent to participate for this manuscript.

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