Original article

UDC: 616.12-089:616-005.1-084
doi: 10.5633/amm.2024.0101

THE SIGNIFICANCE OF IMPEDANCE AGGREGOMETRY IN CARDIAC SURGERY

Dragan Milić[1,2], Milan Lazarević[1,2], Mladjan Golubović[1,2], Velimir Perić[1,2], Aleksandar Kamenov[1,2], Vladimir Stojiljković[1,2], Marija Stošić[1,2], Saša Živić[2], Isidora Milić[1], Dimitrije Spasić[2]

The function of normal hemostasis is to prevent blood loss from an uninjured blood vessel and to stop excessive bleeding from a damaged blood vessel. Blood loss from an uninjured vessel is prevented by normal vessel structure and normal platelet function. Platelet aggregation is mediated by von Willebrand factor, a polymeric plasma glycoprotein. This protein binds to specific platelet membrane receptors and collagen. Primary aggregation of incoming platelets is facilitated by the action of thrombin. Aggregated platelets then release serotonin, thromboxane A2 and adenosine diphosphate (ADP) which stimulate vasoconstriction which is an additional stimulus for platelet aggregation and represents secondary aggregation. Many factors are related to bleeding during cardiac surgical procedures. Impedance aggregometry is a test of aggregation of platelets in whole blood, which allows us to observe the function of platelets in the presence of erythrocytes and leukocytes and prevents the artificial activation of platelets that occurs due to the separation process. Aggregometry is used to diagnose disorders of platelet function, which are rarely congenital, and most often acquired.

In our research, we proved that 31% of patients had post-operatively impaired platelet function, with postoperative bleeding after 24 hours being statistically significantly higher in patients with ADP < 300 AU/min 24 hours after surgery, as well as TRAP < 500 AU/min 24 hours after surgery (p = 0.002). Twenty-two patients (22.0%) received a platelet transfusion 3 hours after surgery - ADP test ≤ 300 AU/min, ASPI ≤ 400 AU/min, TRAP ≤ 500 AU/min. On average, 11.14 ± 4.45 doses were administered. No patient in this study needed a transfusion of platelets 24 h after the procedure. Contemporary principles such as “time is life” together with modern clinical protocols and experienced personnel are essential in the treatment of hemostatic disorders during cardiac interventions.

Acta Medica Medianae 2024;63(1):05-13.

Key words: *platelets, aggregometry, cardiac surgery, bleeding*

[1]University of Niš, Faculty of Medicine Niš, Niš, Serbia
[2]University Clinical Center Niš, Clinic of Cardiac Surgery, Niš, Serbia

Contact: Dragan Milić
48 Dr. Zorana Djindjića Blvd.
E-mail:drdraganmilic@gmail.com
Phone:+38166333105

Introduction

Blood coagulation is a complex process that takes place through a strictly regulated sequence of reactions in order to prevent blood loss from the body. The function of normal hemostasis is to prevent blood loss from an uninjured blood vessel and to stop excessive bleeding from a damaged blood vessel. Blood loss from an uninjured blood vessel is prevented by the normal structure of the blood vessel and the normal function of platelets (1). In the event of a blood vessel injury, the body fights to stop the bleeding using three main mechanisms, through three phases: vascular, platelet and blood coagulation phases. During the vascular phase, vasoconstriction of the blood vessel occurs reflexively and it lasts less than a minute, and is prolonged by serotonin from platelets and fibrinopeptide B, which is produced by the action of thrombin on fibrinogen. During the platelet phase, a platelet plug is formed. During this phase, adhesion of platelets occurs at the site of damaged blood vessels and aggregation of platelets with each other. Platelet aggregation is mediated by von Willebrandt factor, a polymeric plasma glycoprotein. This protein binds to specific platelet membrane receptors and collagen. Primary aggregation of incoming platelets is facilitated by the action of thrombin. Aggregated platelets then release serotonin, thromboxane A2 and adenosine diphosphate (ADP), which stimulate vasoconstriction, an additional stimulus for platelet aggregation, and represents secondary aggregation (2).

The coagulation phase leads to the formation of a permanent coagulum that will prevent bleeding until the injured tissue is repaired. Blood coagulum is created within the bifurcation cascade of proteolytic reactions that include nearly twenty different substances, most of which are glycoproteins synthesized in the liver (3). The coagulation system consists of proteins, lipoproteins and calcium ions. All coagulation factors (except factor III) are normally present in plasma.

Knowing the properties of coagulation factors is of particular importance. Stability to preservation *in vitro*, survival in the recipient organism and a hemostatic level of coagulation factors sufficient to prevent the patient from bleeding are essential.

Seven coagulation factors are present in the form of precursors that are proteolytically activated with the help of serine proteases in the coagulation process. Factors V and VIII are not enzyme precursors but cofactors that circulate as "precofactors". Activated forms of precursors and cofactors are marked with the lowercase letter "a". Fibrinogen (factor I) is converted to fibrin that lacks enzymatic and cofactor activities and is designated as fibrin (not factor Ia). The active form of prothrombin (factor II) is more commonly referred to as thrombin rather than factor IIa (4). Blood coagulation takes place through 4 stages:

Phase I - activation of tissue factor (thromboplastin),

Phase II - conversion of prothrombin into thrombin,

III phase - conversion of fibrinogen into fibrin, and

IV phase - coagulum retraction.

Knowledge about coagulation has changed with the progress of science, and a significant contribution was made by Rapaport when he pointed out the fact that the complex of tissue factor and factor VIIa activates factor X and IX, thus simultaneously activating the external and internal pathways of coagulation (5). Today there is a cellular model of coagulation based on the role of platelets, monocytes and endothelium in coagulation. According to this model, coagulation takes place in four stages:

- initiation phase,
- amplification phase,
- propagation phase, and
- termination phase.

At the site of blood vessel injury, tissue factor (TF) is expressed, which forms a complex with FVIIa, which under normal circumstances circulates in small amounts, but in a biologically inactive state until it forms a complex with tissue factor that leads to the activation of factors X and IX (6). Activated factor X activates factor V on the surface of cells that carry tissue factor and the created complex converts a small amount of prothrombin into thrombin, which represents the initiation phase. In the second phase, the generated thrombin leads to the activation of platelets, factors V, VIII, XI and XIII.

In the propagation phase, activated factor IXa with factor VIIIa builds a complex on the surface of platelets that strongly activates factor X. Activated factor Xa with factor Va on the surface of platelets creates a prothrombinase complex that converts significant amounts of prothrombin into thrombin (7). The generated thrombin converts fibrinogen into fibrin, which is stabilized by FXIIIa and becomes an insoluble fibrin clot.

Thrombin also activates thrombin-activated fibrinolysis inhibitor (TAFI) and thus protects the clot from lysis. At the same time, thrombin is inhibited by its potent inhibitor, antithrombin, and further binds to thrombomodulin, which activates the protein C system that neutralizes activated factors V and VIII (8). Activation of tissue pathway inhibitors stops further activation of coagulation by the tissue factor/FVIIa complex—the termination phase.

Many factors are related to bleeding during cardiac surgical procedures. It is usually related to the length of the extracorporeal circulation procedure (over 90 minutes), which involves several mechanisms that lead to bleeding.

Extended platelets contact with the plastic hoses of the extracorporeal blood flow system disturbs their function. The plastic hoses of the extracorporeal circulation system lead to the activation of platelets and the coagulase cascade, which finally manifests itself in the form of postoperative thrombocytopenia for more than 30%, and consumptive coagulopathy. Also, the pumps of the ECC system perform mechanical destruction of the same (9).

Patients undergoing cardiac intervention have overly sensitive platelets due to the fact the almost all patients referred to cardiac surgery procedures are already on dual antiplatelet therapy which impedes normal hemostatic process. Some patients are on anticoagulation therapy which leads to inhibition of factors II, VII, IX, X, preventing successful hemostasis.

The coagulation cascade is activated when the artificial surface of the intestine comes into contact with blood, and this is primarily activated by factor XII, which cascade activates factor XI, and then factor X, which ultimately leads to increased generation of thrombin. Thrombin is a very potent activator of platelets, but also of fibrinogen and the clot polymerization process, leading to their consumption. On the other hand, thrombin also activates the fibrinolysis system through plasmin, which not only breaks down fibrin threads but also affects the function of platelets by degrading their receptors on the surface of the cell membrane, without which platelets cannot fulfil their role in primary and secondary hemostasis. Increased perioperative blood loss leads to a drop in the concentration of coagulation factors and the number of platelets, but also to anemia, which in combination with the

previously mentioned disorders disrupts normal coagulation.

One of the most difficult tasks in cardiac surgery is the establishment of timely, physiological hemostasis. Hemostasis as an extremely complex process is accompanied by disorders that can be classified as acute and chronic. Chronic hemostasis disorders are most often the result of impaired liver and kidney function, impaired hematopoiesis and hereditary hemostasis disorders.

In surgical practice, acute bleeding is caused by acute traumatic bleeding, solution infusion and dilutional coagulopathy, use of heparin, antithrombotics, oral anticoagulant therapy... Cardiac surgery procedures are often related to extensive bleeding and usual tests such as INR, aPTT and PT or platelet count are insufficient and obtained not in a timely manner. In these critical conditions, point of care (POC) devices play a key role in obtaining fast and reliable hemostasis monitoring (10). A large number of powerful devices for the detection of coagulation disorders have been constructed.

Impedance aggregometry is a test of aggregation of platelets in whole blood, which allows us to observe the function of platelets in the presence of erythrocytes and leukocytes and prevents the artificial activation of platelets that occurs due to the separation process. The method of determination in whole blood detects the electrical impedance between small electrodes immersed in the blood (Multiplate® - Multiplate Platelet Function Analyzer, Roche, Germany), and the kinetics of the impedance change reflects platelet aggregation after the addition of agonists. The kinetics of impedance change reflect platelet aggregation on needles after agonist addition.

Aggregometry is used to diagnose disorders of platelet function, which are rarely congenital, and most often acquired. Acquired damage to platelets is most often caused by drugs or is a consequence of uremia. The widely used acetylsalicylic acid and many other nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit the platelet enzyme cyclooxygenase, which converts arachidonic acid to thromboxane A2 (TXA2). TXA2 is a platelet agonist with a short half-life. NSAIDs can reversibly damage cyclooxygenase or behave in other damage models. There are also platelet ADP receptor blockers such as clopidogrel, ticlopidine, etc. It is also important to monitor IIb IIIa receptor blockers such as abciximab or tirofiban.

Although the monitoring of antithrombotics is certainly one of the most important roles of this device, we must not leave out the role of the MULTIPLATE analyzer in the preparation of patients for surgical intervention, and monitoring after platelet transfusion (11). As already stated, by adding different powerful platelet agonists, the response of platelets to them is monitored and their function, i.e. inhibition of function, is determined.

Regarding the role of impedance aggregometry in the preparation of patients for surgical intervention, whether they are on mono or dual antiplatelet therapy, testing is important. Based on the residual effect of drugs on platelet function, clinicians declare the possible presence of low, moderate or high risk for increased perioperative microcirculatory bleeding depending on platelet function. Not all patients respond equally to antiplatelet therapy. Several mechanisms have been identified that explain the emergence of resistance to aspirin and clopidrogel:

- Inadequate tolerability of the drug or early cessation of its introduction into the body,
- Possible drug interactions,
- Inadequate dose,
- Increased fluctuation of platelets,
- Genetic polymorphism, and
- Potential bypass mechanisms.

The curves that are detected during the analysis show the speed of aggregation of platelets and the total activity of platelets, so based on their appearance and following the reference values prescribed for each test, platelet function is separately assessed. In combination with elastometry, aggregometry can be a postoperative test and play a role in the detection of bleeding that may be a consequence of impaired platelet function.

Materials and Methods

The study included 100 patients who underwent coronary artery bypass grafting (CABG) at the Clinic of Cardiac Surgery, University Clinical Centre of Niš, during the period from June to December 2018. Twenty-two patients were females and 78 were males. All patients included in the study were preoperatively on mono or dual antiplatelet therapy (acetylsalicylic acid+-clopidogrel/ticagrelor). Antiplatelet therapy was stopped 5−7 days before surgery. CABG was performed in a standard manner. Blood samples were taken for impedance aggregometry 24 hours before operation and 3 hours and 24 hours postoperatively.

To monitor the necessary parameters, the following test were used:

- ASPI test (activation of platelets by arachidonic acid) for monitoring residual effect of acetylsalicylic acid,
- ADP test (activation of platelets by adenosine diphosphate) for measuring residual effects of clopidogrel/ticagrelor on platelet function,
- TRAP test (thrombin-activated platelet function) – for measuring the natural potential of platelets regardless of the antiplatelet therapy.

All these tests were performed on an impedance aggregometer (MULTIPLATE Roch Germany).

Blood sampling was performed in 4 ml test tubes with the anticoagulant Lithium-heparin, and

all analyses were performed within 30 minutes of sampling.

Values of monitored parameters indicating increased risk of bleeding were as follows: ADP test ≤ 310 (reference value range 570−1130) aggregation units per minute (AU/min), ASPI test ≤ 400 AU/min (reference values range 710−1490AU/min) and TRAP test ≤ 500AU/min (reference values range 923−1509 AU/min).

Statistical analysis

Arithmetic mean and standard deviation were used to present data.

The Kolomogor-Smirnov test was used to test the normality of continuous variables. In the case of normal distribution of preoperative and postoperative data, the comparison of values at 3h and 24 h was performed with the ANOVA test for repeated measurements. In the case where distribution of data was not normal, the Friedman test was used for this comparison. If distribution of data was normal, the t test was used for comparison and if data distribution was not normal, Mann-Whitney test was used for comparison.

A significance threshold of $p < 0.05$ was used to test the hypothesis. Data analysis was performed using SPSS 16.0 software.

Results

ADP values decreased in the period up to 3 h compared with preoperative values, and then the values jumped significantly between the last two measurements ($p < 0.001$). ASPI values preoperatively and 3 hours after surgery were close, then in the period up to 24 hours they increased sharply. A statistically significant difference in ASPI values between the three measurements was registered ($p < 0.001$). TRAP values were uniform comparing preoperative and postoperative measurements ($p = 0.783$) (Table 1).

Preoperatively, 13 patients had ADP < 300 AU/min (13.0%), 3 hours after surgery 31 patients had ADP < 300 AU/min (31.0%), and 24 hours after surgery, 5 patients had ADP < 300 AU/min (5.0%) (Figure 1.). TRAP < 500 AU/min was not measured preoperatively. Postoperatively, these values of the TRAP test after 3 hours were measured in 4 patients, and within 24 hours of surgery in five patients.

Preoperatively, 11 people had an ASPI < 400 AU/min (11.0%), 3 hours after surgery, 17 people had an ASPI < 400 AU/min (17.0%), and after 24 hours after surgery, 18 patients had an ASPI < 400 AU/min (18.0%) (Figure 2).

Nine patients (9.0%) had bleeding for more than one day per drain (Figure 3).

Postoperative bleeding after 24 h was statistically significantly higher in patients with ADP values < 300 AU/min 24 h after surgery ($p = 0.002$) (Table 2).

Postoperative bleeding did not differ statistically significantly in relation to ASPI values 24 hours after surgery ($p = 725$) (Table 3).

Postoperative bleeding was statistically significantly higher in patients who had TRAP < 500 AU/min 24 hours after surgery ($p = 0.002$) (Table 4).

Twenty-two patients (22.0%) received a platelet transfusion 3 hours after the operation - ADP test ≤ 300 AU/min, ASPI ≤ 400 AU/min, TRAP ≤ 500 AU/min. On average, 11.14 ± 4.45 doses were administered. No patients needed platelet transfusion 24 h after surgery.

Systemic hemostatic agents desmopressin-acetate (DDAVP) and prothrombin complex concentrate (PCC) were administered in 13 patients three hours following the surgical procedure (one ampoule of DDAVP (20 mcg)) while 7 more patients received the same agent 24 h after CABG.

Table 1. ADP, ASPI and TRAP test values before surgery and 3 h and 24 h after surgery

Parameter☐	Preoperatively	3 h postoperatively	24 h postoperatively	p-value[1]
ADP AU/min	450.19 ± 121.56	358.95 ± 145.91	519.56 ± 179.08	< 0.001
ASPI AU/min	634.81 ± 207.81	669.79 ± 326.50	794.44 ± 323.59	< 0.001
TRAP AU/min	1017.83 ± 193.12	1002.91 ± 261.34	1019.30 ± 234.50	0.783

☐ Arithmetic mean ± standard deviation, [1]Friedman's test

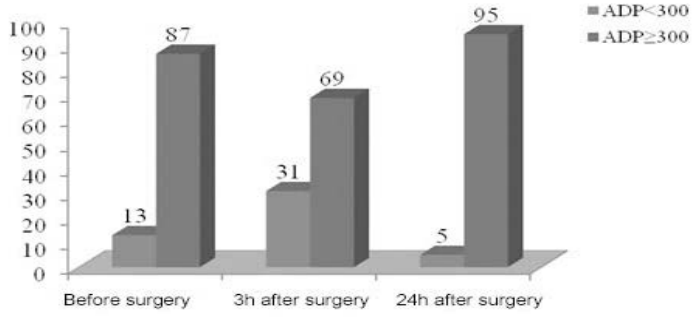

Figure 1. Distribution of patients with low ADP before surgery and 3 h and 24 h after surgery

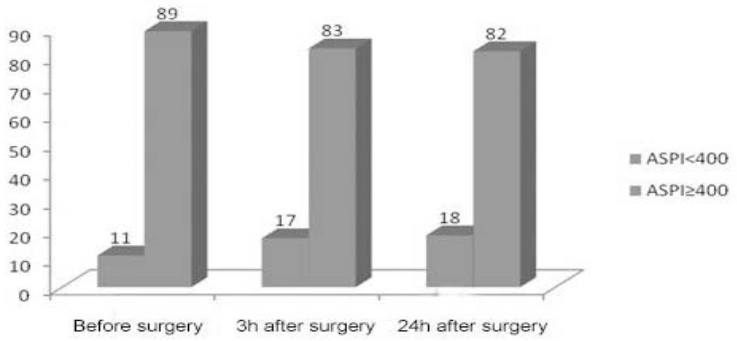

Figure 2. Distribution of patients with low ASPI before surgery and 3 h and 24 h after surgery

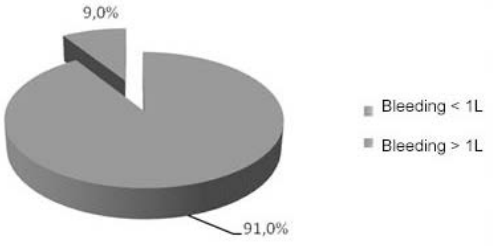

Figure 3. Frequency of drain bleeding ≥ 1 L 24 hours after surgery in the studied patients

Table 2. Postoperative bleeding in relation to low values of ADP parameters

Measurement time ☐	ADP	Postoperative bleeding	
		AS ± SD	p - value[1]
24 h after surgery	< 300	3550.00 ± 1286.47	0.002
	≥ 300	1347.89 ± 319.73	

☐ Arithmetic mean ± standard deviation, [1]Mann–Whitney test

Table 3. Postoperative bleeding in relation to low values of ASPI parameters

Measurement time ☐	ASPI	Postoperative bleeding	
		AS ± SD	p - value[1]
24 h after surgery	< 400	1816.67 ± 1282.58	0.725
	≥ 400	1379.27 ± 323.46	

☐ Arithmetic mean ± standard deviation, [1]Mann–Whitney test

Table 4. Postoperative bleeding in relation to low values of TRAP parameters

Measurement time □	TRAP	Postoperative bleeding	
		AS ± SD	p - value[1]
24 h after surgery	< 500	3550.00 ± 1286.47	0.002
	≥ 500	1347.89 ± 319.73	

☐ Arithmetic mean ± standard deviation, [1]Mann–Whitney test

Discussion

Due to hemodilution as a result of priming, patients undergoing cardiac surgery procedures frequently need a transfusion in order to correct blood loss and coagulopathy after cardiac surgery procedures (12). These patients usually have different comorbidities which may increase the risk of bleeding (13).

Our study demonstrated that decreased activity due to ADP activation was a strong predictor of increased bleeding. It was possible to determine the percentage of platelet inhibition by platelet mapping, subtracting fibrin contribution from the curve and maximizing amplitude due to platelet activators (MAADP). The study proved that either parameter was equally predictive in this dataset. ADP can predict blood loss during the cardiac surgery procedure and the need for blood transfusion. Similarly, MAADP values do have the ability to predict which patients on clopidogrel will need a platelet concentrate transfusion (14, 15, 16). It is clearly demonstrated in this study that ADP testing of patients before and early after performing cardiac surgery interventions is an independent predictor of excessive bleeding.

Using a Multiplate analyzer (ADP, ASPI, TRAP tests) 22% of monitored patients in this study received platelet concentrate. Based on the values of the ASPI test, 20 patients received hemostasis agent desmopressin acetate in order to correct platelet function.

It is very important to emphasize that acetylsalicylic acid and clopidogrel should be discontinued before the planned surgical procedure to reduce the risk of excessive bleeding and the need for blood transfusion (3, 17). No exact data are present in the medical literature describing how many days before surgical procedure antiplatelet drugs should be discontinued (18). However, published data on this issue demonstrates that stopping antiplatelet administration even only 2 days before cardiac surgery procedure significantly reduces the risk of bleeding and the need for platelet concentrate transfusion (19).

The results of our study could not demonstrate any relationship between the discontinuation of antiplatelet drugs and major prothrombotic events (cardiovascular or cerebral).

Old-fashioned surgeons still accept massive blood loss during cardiac surgery procedures as an unchangeable characteristic despite the

improvements in lowering the risk and amount of bleeding using these new techniques (20). Our study also demonstrated that only 9% of patients had an average blood loss of more than 1000 ml probably because of the timely application of hemostatic agents known in the medical literature as targeted hemostasis therapy guided by POC hemostasis testing devices.

Hemodilution is probably the most pronounced factor related to coagulopathy (thrombocytopenia or thrombocytopathy alike) emerging after cardiac surgery procedures playing a significant role in the occurrence of bleeding and excessive blood loss after cardiac surgery operations (21).

In 2011, Gorlinger et al. reviewed retrospectively more than 3000 patients after which they have concluded that implementation of POC devices significantly reduces the need for blood transfusion and thromboembolic complications (6).

In 2012, Weber et al. published the results of a prospective randomized study in which the aim was to study the effects of hemostatic therapy guided by either conventional coagulation assays or POC testing in cardiac surgical patients (22). Patients diagnosed with excessive bleeding after heparin reversal or increased blood loss during the first 24 hours after surgery were randomized into the POC group. POC testing reduced the amount of blood transfusion in comparison to standard laboratory coagulation testing. Even more, POC-guided therapy was associated with reduced use of fresh frozen plasma (FFP) and platelet transfusion leading to lower cost of treatment and better clinical outcome.

POC devices may provide fast and more reliable insight into the hemostasis disbalance creating the treatment tailored for each patient separately. Intensive variations in patient's sensitivity to clopidogrel quiet often results in grossly different tally, necessitating mandatory use of POC before, during and after performing cardiac surgery procedures. This individual approach for each patient could significantly reduce blood loss and need for blood transfusion (23).

Conclusion

Cardiac surgical procedures are complex interventions provoking dramatic hemostatic disorders in many cases. Some patients undergoing cardiac surgery procedures have preoperative hemostatic disorders due to acquired diseases or because they were treated with antiplatelet drugs.

Considering all of these features, the primary goal must be to timely detect possible hemostatic abnormalities in patients undergoing cardiac surgery procedures and to react accordingly.

Our study demonstrated that up to 31% of patients had preoperative and postoperative platelet dysfunction. As a result of these abnormalities bleeding may occur leading even to the death of the patient.

POC devices have an extremely important clinical significance in detecting coagulation disorders in a timely manner predicting excessive bleeding. In this way, the implementation of targeted hemostasis therapy can prevent or even stop the bleeding after a surgical procedure.

Using these protocols in testing platelet function with POC devices, the ease of use and the very short time needed for gaining results were key contributors to the low mortality rate of only 1% in the observed group of patients (not a consequence of hemostasis disorders).

The contemporary approach combining well-established clinical protocols, and the experience of the personnel, respecting the principle "time is life", provides excellent results in the treatment of hemostasis disorders in cardiac surgery patients.

References

1. Rolović Z, Marisavljević D. Fiziologija hemostaze i tromboze. Sprint, Beograd, 2002; 3-13.
2. Biljana Vujičić, Lana Mačukanović-Golubović, Branko Mihailović, Milan Miladinović. Krvarenje i hemostaza u oralnohirurškoj praksi. IP Obeležje Beograd, 2009;39-57.
3. Baklaja R. Hemostaza. Koagulacija krvi i fibrinoliza. U: Baklaja R, Elezović I, Miljić P, Miković D, Lučić AM. Laboratorijska dijagnostika poremećaja hemostaze. Beograd: Interlab; 2008; 7-20
4. Mac Farlan RG. An enzyme cascade in the blood clotting mechanism and its function as a biological amplifier. Nature 1964; 202: 498-9. [CrossRef] [PubMed]
5. Hoffman M, Monroe DM. A cell-based Model of Hemostasis. Tromb Haemost 2001; 85; 958-65. [CrossRef] [PubMed]
6. Roberts HR. Oscar Ranthoff: his contributions to the golden era of coagulation research. Br J Haematol 2003; 122: 180-98. [CrossRef] [PubMed]
7. Monković D, Tracy PB. Activation of human factor V by factor Xa and thrombin. Biochemistry 1990; 29: 1118-28. [CrossRef] [PubMed]
8. Lijenen RH, Kolen D. Molecular and cellular basis of fibrinolysis. In: Hofman et al. Hematology, Basic Principles and Practice, Churchill Livingstone, 4 th ed. 2005; 195-59.
9. Hasan-Ali H, Mosad E.Changes in platelet, coagulation, and fibrinolytic activities in mitral stenosis after percutaneous mitral valvotomy: role of hemodynamic changes and systemic inflammation. Clin Appl Thromb Hemost 2015; 21(4): 339-47. [CrossRef] [PubMed]
10. Mannacio V, Mannacio L, Antignano A, Pinna BG. Antiplatelet therapy suspension in patients undergoing coronary surgery for acute coronary syndrome: Is point-of-care guided strategy the best choice? Journal of Cardiol 2017; 70(4): 402-3. [CrossRef] [PubMed]
11. Ellis J, Valencia O, Crerar-Gilbert A, Phillips S, Meeran H, Sharma V. Point-of-care platelet function testing to predict blood loss after coronary artery bypass grafting surgery: a prospective observational pilot study. Perfusion 2016; 31(8): 676-82. [CrossRef] [PubMed]
12. Koch CG. Tolerating anemia: taking aim at the right target before pulling the transfusion trigger. Transfusion 2014; 54(10 Pt 2): 2595–7. [CrossRef] [PubMed]
13. Ad N, Massimiano PS, Burton NA, Halpin L, Pritchard G, Shuman JD, et al. Effect of patient age on blood product transfusion after cardiac surgery. J Thorac Cardiovasc Surg 2015; 150(1): 209–14. [CrossRef] [PubMed]
14. Mahdi N, Faraoni D. Updates on Coagulation Management in Cardiac Surgery. J Tehran Heart Cent 2014; 9(3): 99-103. [PubMed]
15. Enriquez LJ, Shore-Lesserson L. Point-of-care coagulation testing and transfusion algorithms. Br J Anaesth 2009; 103: 114–22. [CrossRef] [PubMed]
16. Nathaen W. Point of Care Testing and Cardiac Surgery 2014. J Cardiothorac Vasc Anesth 2014; 28(2): 207–9. [CrossRef] [PubMed]
17. Christa B, Meesters MI, Milojević M, Benedetto U, Bollinger D, von Heymann C, et al. 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery.The Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anaesthesiology (EACTA). J Cardiothorac Vasc Anesth 2018; 32(1): 88-120 [CrossRef] [PubMed]
18. Kind SL, Spahn-Nett GH, Emmert MY, Eismon J, Seifert B, Spahn DR, et al. Is dilutional coagulopathy induced by different colloids reversible by replacement of fibrinogen and factor XIII concentrates? Anesth Analg 2013; 117(5): 1063-71. [CrossRef] [PubMed]
19. Gundling F, Seidl H, Gansera L, Schuster T, Hoffmann E, Kemkes BM, et al. Early and late outcomes of cardiac operations in patients with cirrhosis: a retrospective survival-rate analysis of 47 patients over 8 years. Eur J Gastroenterol Hepatol 2010; 22(12): 1466–73. [CrossRef] [PubMed]
20. Jubelirer SJ, Mousa L, Reddy U, Mir M, Welch CA. Coronary artery bypass grafting (CABG) in patients with immune thrombocytopenia (ITP): a community hospital experience and review of the literature. W V Med J 2011; 107(6): 10–4. [PubMed]
21. Vamvakas EC, Carven JH. RBC transfusion and postoperative length of stay in the hospital or the intensive care unit among patients undergoing coronary artery bypass graft surgery: the effects of confounding factors. Transfusion 2000; 40(7): 832–9. [CrossRef] [PubMed]
22. Hoffman M, Monroe DM. A cell-based Model of Hemostasis. Tromb Haemost 2001; 85; 958-65. [CrossRef] [PubMed]
23. Haanschoten MC, van Straten AH, Verstappen F, van de Kerkhof D, van Zundert AAJ, Soliman Hamad MA. Reducing the immediate availability of red blood cells in cardiac surgery, a single-centre experience. Neth Heart J 2015; 23(1): 28-32. [CrossRef] [PubMed]

Originalni rad **UDC: 616.12-089:616-005.1-084**
doi: 10.5633/amm.2024.0101

ZNAČAJ IMPEDANTNE AGREGOMETRIJE U KARDIOHIRURGIJI

Dragan Milić[1,2], Milan Lazarević[1,2], Mlađan Golubović[1,2], Velimir Perić[1,2], Aleksandar Kamenov[1,2], Vladimir Stojiljković[1,2], Marija Stošić[1,2], Saša Živić[2], Isidora Milić[1], Dimitrije Spasić[2]

[1]Univerzitet u Nišu, Medicinski fakultet, Niš, Srbija
[2]Univerzitetski klinički centar Niš, Klinika za kardiohirurgiju, Niš, Srbija

Kontakt: Dragan Milić
Bulevar dr Zorana Đinđića 48, 18000 Niš, Srbija
E-mail: drdraganmilic@gmail.com
Telefon: +38166333105

Hemostaza je složen biološki proces kojim se sprečava gubitak krvi iz neoštećenog krvnog suda, kao i prekomerni gubitak cirkulišuće krvi kod povređenog krvnog suda. Za normalno funkcionisanje hemostaze neophodno je da krvni sud ima histološki normalnu građu zida, kao da je i funkcija trombocita očuvana. Von Willebrandov faktor predstavlja ključni činilac agregacije trombocita. Ovaj glikoprotein plazme vezuje se za receptore trombocita i kolagen. Trombin olakšava primarnu agregaciju prisutnih trombocita, koji nakon toga oslobađaju adenozin-difosfat (ADP), tromboksan A2 i serotonin; svi oni zajedno izazivaju posledičnu vazokonstrikciju, koja dovodi do sekundarne agregacije trombocita. Krvarenje nakon aortokoronarnog bajpasa posledica je delovanja brojnih faktora. Test agregacije trombocita u celoj krvi (impedantna agregometrija) omogućava analizu funkcije trombocita u prisustvu leukocita i eritrocita. Ova metoda se koristi za dijagnostikovanje oštećene funkcije trombocita, koja je uglavnom stečenog, a izuzetno retko urođenog karaktera.

Naše istraživanje pokazalo je da je 31% bolesnika imao postoperativno poremećenu funkciju trombocita, s tim što je postoperativno krvarenje posle 24 sata bilo statistički značajno veće kod bolesnika sa vrednostima ADP < 300 AU/min 24 sata nakon operacije, kao i TRAP < 500 AU/min 24 sata posle operacije (p = 0,002). Tri sata nakon operacije, transfuziju trombocita primila su 22 bolesnika (22,0%): ADP test ≤ 300 AU/min, ASPI ≤ 400 AU/min, TRAP ≤ 500 AU/min. Prosečno je davano 11,14 ± 4,45 doza. Dvadeset četiri časa nakon intervencije nije bilo bolesnika kojima je bila potrebna transfuzija koncentrata trombocita.

Upotreba savremenih metoda, u kombinaciji sa dokazanim kliničkim protokolima i velikim kliničkim iskustvom osoblja i uz poštovanje principa „vreme je život", omogućava najbolje moguće zbrinjavanje bolesnika sa detektovanim poremećajem hemostaze u kardiohirurgiji.

Acta Medica Medianae 2024; 63(1): 05-13.

***Ključne reči**: trombociti, agregometrija, kardiohirurgija, krvarenje*