Original article

The Significance of Impedance Aggregometry in Cardiac Surgery

DOI:10.5633/amm.2024.0101

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 University of Niš, Faculty of Medicine, Niš, Serbia

2 University Clinical Center Niš, Clinic for Cardiac Surgery, Niš, Serbia

Contact: Dragan Milić

48 dr Zoran Đinđić Bulevard, Niš, Serbia

e-mail: drdraganmilic@gmail.com

tel:+38166333105

Originalni rad

Značaj impedantne agregometrije u kardiohirurgiji

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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, Niš, Srbija

e-mail: drdraganmilic@gmail.com

tel:+38166333105

Abstrakt

Funkcija normalne hemostaze je da spreči gubitak krvi iz nepovređenog krvnog suda i da zustavi prekomerno krvarenje iz oštećenog krvnog suda. Gubitak krvi iz nepovređenog krvnog suda sprečen je normalnom građom krvnog suda i normalnom funkcijom trombocita. Agregacija trombocita posredovana je von Willebrandt-ovim faktorom, polimernim glikoproteinom plazme. Ovaj protein vezuje se za specifične receptore membrane trombocita i kolagen . Primarna agregacija pridošlih trombocita olakšana je dejstvom trombina. Agregirani trombociti zatim oslobađaju serotonin, tromboksan A2 i adenozindifosfat (ADP) koji stimulišu vazokonstrikciju što je dodatni stimulus za agregaciju trombocita i predstavlja sekundarnu agregaciju. Krvarenje u toku i posle kardiopulmonalnog baj-pasa je multifaktorijalno. Impedantna agregometrija je test agregacije trombocita u celoj krvi, što omogućava da se posmatra funkcija trombocita u prisustvu eritrocita i leukocita i prevenira arteficijalna aktivacija trombocita koja nastaje zbog procesa separacije. Agregometrija se primenjuje za dijagnozu poremećaja funkcije trombocita, koja su retko urođena, najčešće stečenog karaktera.

U našem istraživanju smo dokazali da je 31% pacijenata imalo postoperativno pormećenu funkciju trombocita, s tim što je postoperativno krvarenje posle 24h statistički značajno veće kod pacijenata sa vrednostima ADP <300 AU/min 24h od operacije, kao i TRAP<500 AU/min 24h posle operacije (p=0,002). Transfuziju trombocita posle 3h od operacije primilo je 22 pacijenta(22,0%)-ADP test≤300 AU/min, ASPI≤400 AU/min , TRAP≤500 AU/min. Prosečno je davano 11,14±4,45 doza. Posle 24h od intervencije nije bilo pacijenata koji su imali potrebu za transfuzijom koncentrata trombocita.

Savremene metode u kombinaciji sa dokazanim kliničkim protokolima, velikim kliničkim iskustvom osoblja , poštujući princip ,,vreme je život", omogućavaju najbolje moguće zbrinjavanje pacijenata sa detektovanim poremećajem hemostaze u kardiohirurgiji.

KLJUČNE REČI: trombociti, agregometrija, kardiohirurgija, krvarenje

The Significance of Impedance Aggregometry in Cardiac Surgery

Abstract

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 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 which is an additional stimulus for platelet aggregation and represents secondary aggregation. Bleeding during and after cardiopulmonary bypass is multifactorial. Impedance aggregometry is a test of aggregation of platelets in whole blood, which allows 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, 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). 22 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. After 24 hours of the intervention, there were no patients who needed platelet concentrate transfusion.

Modern methods in combination with proven clinical protocols, great clinical experience of the staff, respecting the principle "time is life", enable the best possible care of patients with a detected hemostasis disorder in cardiac surgery.

KEY WORDS: platelets, aggregometry, cardiac surgery, bleeding

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 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 which is 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

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
- 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.

Bleeding during and after cardiopulmonary bypass is multifactorial. It is usually related to the length of the extracorporeal circulation procedure (over 90 minutes), which involves several mechanisms that lead to bleeding.

Prolonged contact of platelets 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]. Platelets of patients who undergo cardiac surgery are very sensitive, because patients are usually preoperatively on mono or dual antiplatelet therapy, which inhibits their function and additionally disrupts postoperative hemostasis. A number of patients preoperatively use oral or parenteral anticoagulation therapy, which inhibits the activity of factors II, VII, IX, X, preventing successful hemostasis.

Also, the contact activation of the coagulation cascade occurs 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 fulfill 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 caused by acute traumatic bleeding, solution infusion and dilutional coagulopathy, use of heparin, antithrombotics, oral anticoagulant therapy... Bleeding usually occurs during and after cardiac surgery. During such an emergency, routine laboratory testing of coagulation using PT, INR, APTT, platelet count is usually slow and insufficient. Point of care (POC) devices for hemostasis monitoring play a real role in the aforementioned acute conditions[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 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, 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, 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, and he was 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 i
- 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

This prospective study included one hundred patients who underwent single, double and triple surgical revascularization of the myocardium, in the Cardiac Surgery Clinic of the University Hospital of Niš, in the period from June 15, 2018. until December 15, 2018. 100 respondents were included in the research (22 female respondents - 22.0% and 78 male respondents - 78.0%). All patients included in the study were preoperatively on mono or dual antiplatelet therapy (acetylsalicylic acid+-clopidogrel/ticagrelor), which was discontinued 5 days before the surgical intervention. After standard cardiac surgical preoperative preparation of patients, patients were operated according to standard

cardiac surgical protocols. Preoperatively, as well as 3 hours and 24 hours postoperatively, parameters of impedance aggregometry were determined:

- parameters of platelet function (platelet activation by adenosine di-phosphate (ADP test) - registers the residual effect of clopidogrel/ticagrelor on platelet function,

- activation of platelets by arachidonic acid (ASPI test) - registers the residual effect of acetylsalicylic acid,

- thrombin-activated platelet function (TRAP test) - represents the natural potential of platelets independent of therapy, and is performed on the impedance aggregometer MULTIPLATE Roch Germany. Blood was sampled in 4 ml test tubes with the anticoagulant Lithium-heparin, and within 30 minutes of sampling, the analyzes were performed.

The values of parameters of the Multiplate test that indicate an increased risk of increased perioperative and postoperative bleeding, which may occur as a result of impaired platelet function, are based on recommendations and guidelines as follows: ADP test ≤310 (reference value 570-1130) aggregation units per minute (AU/ min), ASPI test ≤400 AU/min (ref. values 710-1490AU/min) and TRAP test ≤500AU/min. (ref. values 923-1509 AU/min).

Statistical data processing

Data are presented in the form of arithmetic mean and standard deviation, minimum and maximum values, as well as in the form of absolute and relative numbers.

The normality of continuous variables was tested with the Kolomogor-Smirnov test. If the distribution of the data was normal, the comparison of values preoperatively and postoperatively in two moments (3h and 24h after the operation) was performed with the ANOVA test for repeated measurements. If the data distribution is not normal, the Friedman test was used for this comparison. If the data distribution is normal, the comparison between the two groups was performed using the t test, if the data distribution is not normal, this comparison was performed using the Mann-Whitney test.

The hypothesis was tested with a significance threshold of $p<0.05$. Data analysis was performed in the SPSS 16.0 software package

Results

ADP values decrease in the period up to 3h compared to the period before surgery, and then the values jump significantly between the last two measurements ($p<0.001$). ASPI values preoperatively and 3 hours after surgery are close, then in the period up to 24 hours they increase sharply. It was found that there is a statistically significant difference in ASPI values between the three measurements ($p<0.001$). TRAP values were uniform comparing preoperative and postoperative measurements ($p=0.783$) (Table 1).

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

Parameter[1]	Preoperatively	3h postoperatively	24h 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

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

Preoperatively, 13 people had ADP<300 AU/min (13.0%), after 3 hours after surgery 31 people had ADP<300 AU/min (31.0%), and after 24 hours after surgery 5 people 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 the operation in five patients.

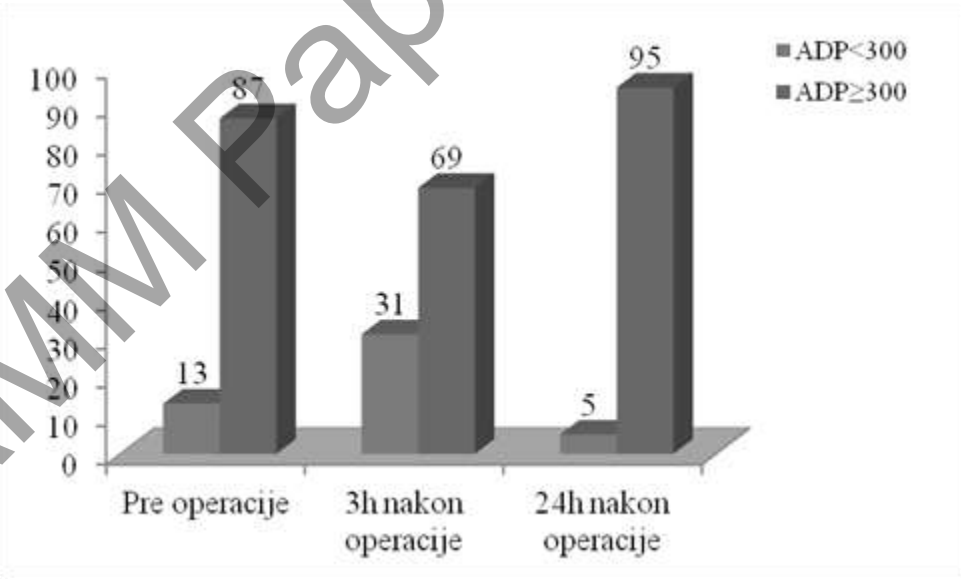


Figure 1. Distribution of patients with low ADP before surgery and 3h and 24h after surgery

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

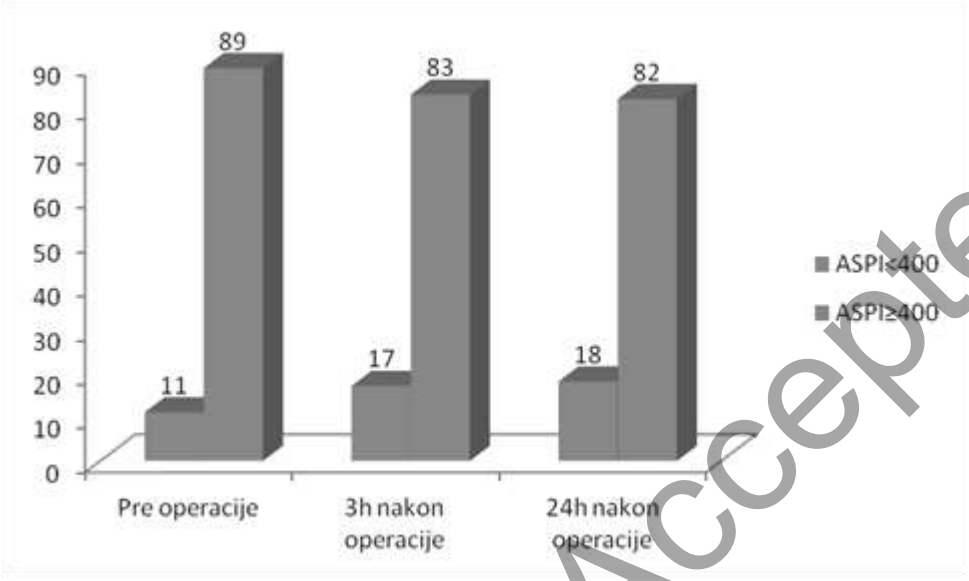
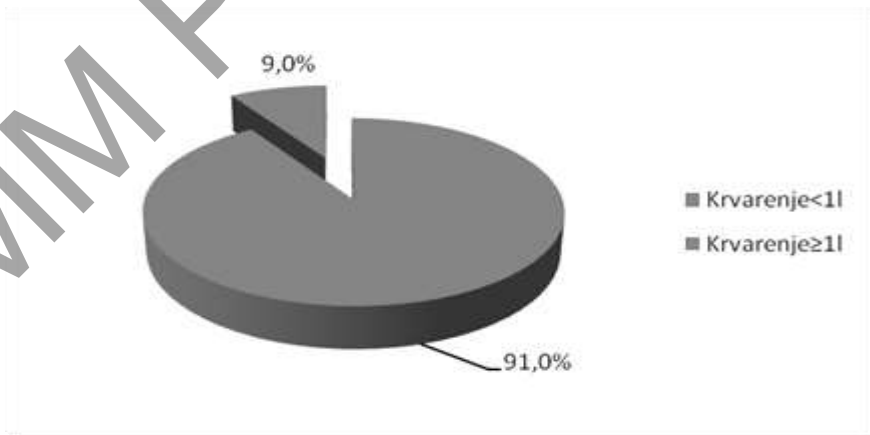


Figure 2. Distribution of patients with low ASPI before surgery and 3h and 24h after surgery

In the studied population, 9 patients (9.0%) had bleeding more than 1 per drain (Figure 3).



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

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

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

Measurement time[1]	ADP	Postoperative bleeding	
		AS±SD	p-value[1]
24h after surgery	<300	3550,00±1286,47	0,002
	≥300	1347,89±319,73	

[1] Arithmetic mean±standard deviation, 1Man-Whitey test

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

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

Measurement time [1]	ASPI	Postoperative bleeding	
		AS±SD	p-value[1]
24h after surgery	<400	1816,67±1282,58	0,725
	≥400	1379,27±323,46	

[1] Arithmetic mean±standard deviation, [1]Man-Whitey test

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

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

Measurement time [1]	TRAP	Postoperative bleeding	
		AS±SD	p-value[1]
24h after surgery	<500	3550,00±1286,47	0,002
	≥500	1347,89±319,73	

[1] Arithmetic mean±standard deviation, [1]Man-Whitey test

22 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. After 24 hours of the intervention, there were no patients who needed platelet concentrate transfusion.

Regarding the systemic hemostatic agents desmopressin-acetate (DDAVP) and prothrombin complex concentrate (PCC), 3 hours after surgery 13 patients received one ampoule of DDAVP (20mcg) - ASPI test ≤300 AU/min, while 24 hours after the surgical intervention, 7 more patients received the same medicine.

Discussion

Transfusion is often necessary during cardiac surgical procedures to correct coagulopathy, blood loss, and hemodilution due to priming[12]. Very often, patients who undergo cardiac surgical procedures have numerous comorbidities, such as anemia or previous myocardial infarctions, which increase the risk of complications and therefore the need for blood transfusion is greater[13].

The authors performed a rigorous statistical analysis of their data and were able to show, using multiple logistic regression, that decreased activity due to ADP activation predicted increased bleeding. In platelet mapping, the percentage of platelet inhibition can be examined, which subtracts the contribution of fibrin from the curve, but also the maximum amplitude due to platelet activators (MAADP). The authors showed that both parameters are equally predictive in this data set. In addition to its predictive effect regarding blood loss, platelet activation due to ADP predicts the need for platelet transfusion. It appears that the MAADP value may have the ability to determine which patients on clopidogrel are likely to require a platelet transfusion[14,15,16]. The results in this study also indicate the importance of preoperative and early postoperative ADP testing as an independent predictor of increased bleeding in cardiac surgery.

In our study, 22% of patients received donor platelet concentrate early after surgery, also based on analysis of point of care (POC) hemostasis tests, primarily on the Multiplate analyzer (ADP, ASPI, TRAP test). Application of the synthetic hemostasis agent desmopressin acetate, for the purpose of correction of platelet function, was performed based on the value of the ASPI test - a total of 20 subjects received the drug after surgery.

In order to reduce the amount of blood loss and blood transfusions required during and after heart surgery, it is important that antiplatelet drugs such as acetylsalicylic acid and clopidogrel, prescribed routinely in patients before heart surgery, especially in those undergoing myocardial revascularization surgery, are timely suspensions before surgery[17,18]. There are no precise data on when and on which day the administration of antiplatelet drugs should be stopped in order to obtain the most optimal results in terms of reducing postoperative drainage and the need for replacement of blood and blood products[19]. Nevertheless, data from the literature show that already stopping the administration of antiplatelet drugs 2 days before performing a cardiac surgical procedure leads to a significant reduction in the need for platelet replacement[20].

No association could be demonstrated between discontinuation of antiplatelet drugs, and preoperative Multiplate values and major adverse cardiovascular and cerebral prothrombotic events, which is in agreement with the results obtained in our study.

Despite the improvements achieved with existing new techniques, most surgeons still tend to accept a significant amount of blood loss as a characteristic of cardiac surgery[21]. The research conducted in our institution also indicates that only 9% of patients had an average postoperative drain loss of more than 1000 ml, primarily thanks to the timely application of hemostatic agents, the so-called Targeted hemostasis therapies guided by point of care hemostasis testing devices.

After careful evaluation, it seems that hemodilution is the most pronounced factor associated with the development of coagulopathy (including thrombocytopenia and thrombocytopathy) after cardiac surgery, and probably plays an important role in the occurrence of blood loss after cardiac surgery[22].
In 2011, Gorlinger et al. retrospectively reviewed more than 3000 patients managed before and after implementation of an algorithm-based approach. The authors noted that the application of a coagulation management algorithm using a POC device significantly reduced the requirements for blood products as well as the frequency of thromboembolic complications[23].
In 2012, Weber et al published the results of a prospective randomized trial 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[24]. Patients diagnosed with diffuse bleeding after heparin reversal or increased blood loss during the first 24 hours were included and randomized to the POC group. Algorithms of hemostatic therapy combined with POC testing reduced the number of RBC units transfused compared with conventional laboratory coagulation testing. Furthermore, POC-guided therapy was associated with reduced use of fresh frozen plasma (FFP) and platelet concentrations and costs, as well as improved clinical outcome.
The use of POC evaluation can provide faster and more complete insight into this delicate balance, creating a more individualized treatment oriented towards each patient. The large variation in patient sensitivity to clopidogrel administration often results in very different individual results before surgery, necessitating further use and determination of POC before, during and after cardiac surgery. An individual approach oriented towards each patient can contribute to the reduction of perioperative and postoperative blood loss and reduce the need for transfusion to a minimum[25].

Conclusion

Due to the complexity and duration of cardiac surgery, pronounced hemostatic changes occur in patients undergoing CABG. Moreover, other hemostatic abnormalities may already be detected in patients preoperatively, due to their type of disease and/or their pharmacological treatments (eg antiplatelet drugs).

Because of all of the above, the priority is to diagnose the most common coagulation disorders in patients who have undergone surgical revascularization of the myocardium and to choose an adequate hemostasis therapy for the timely treatment of coagulation disorders in cardiac surgery patients.

In this context, in this research, preoperative and postoperative impaired platelet function was diagnosed as the most common disorder of the hemostasis system (up to 31% of patients). The described disorders result in bleeding, which in the last case can cause a fatal outcome.

Devices for POC testing of the hemostasis system have a special clinical importance, with the use of which the correct and timely diagnosis of the mentioned coagulation disorders, the prediction of possible bleeding that has not yet manifested itself clinically, as well as the choice of targeted hemostasis therapy that will prevent or stop the bleeding is possible.

Thanks to the described protocols of the POC platelet function testing application, the speed of performing the tests themselves and the quick clinical decision regarding hemostasis therapy, the mortality rate of operated patients included in the research was about 1% (not a consequence of hemostasis disorders), which is in the rank of eminent world institutions that are engaged in cardiac surgery.

Modern methods in combination with proven clinical protocols, great clinical experience of the staff, respecting the principle "time is life", enable the best possible care of patients with a detected hemostasis disorder in cardiac surgery.

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