PREDNOSTI *POINT-OF-CARE* METODA U PERIOPERATIVNOJ KONTROLI KRVARENJA

PREGLEDNI RAD

REVIEW ARTICLE

ADVANTAGES OF POINT-OF-CARE METHODS IN PERIOPERATIVE BLEEDING CONTROL

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SAŽETAK

Perioperativna kontrola krvarenja je kompleksan zadatak koji ima značajan uticaj na ishod operativnog zahvata. Većina poremećaja hemostaze nastalih intraoperativno je akutna, uzrokovana masivnim krvarenjem, i može se objasniti principom gubitka, nadoknade i dilucije cirkulišućeg volumena krvi. Poremećaj na nivou hemostaznog sistema može se meriti primenom različitih testova; standardnih laboratorijskih testova (SLT) kao što su: protrombinsko vreme, aktivirano parcijalno tromboplastinsko vreme, broj trombocita, koncentracija faktora koagulacije, koncentracija nivoa antitrombina, koncentracija D-dimera; ili primenom *point-of-care (POC) metoda*.

Standardni laboratorijski testovi imaju svoja ograničenja. Pomoću njih se ne može detektovati povećana tendencija ka intraoperativnom krvarenju, te se preporučuje primena metoda kao što su *POC*, kojima se brzo i precizno procenjuje koagulacioni status pacijenta, kako bi se u što kraćem roku primenila adekvatna terapija. Od *POC* metoda najčešće se primenjuju agregometrijske metode *(Multiplate, PFA-100 i Platelet Mapping Assay)*, koje se koriste u perioperativnoj proceni funkcije trombocita, i viskoelastični testovi (rotaciona tromboelastometrija – *ROTEM*; tromboelastografija – *TEG*), koji daju grafički prikaz celokupne hemostatske aktivnosti mereći vreme do početka formiranja ugruška, dinamiku formiranja kao i čvrstinu i stabilnost ugruška tokom vremena.

Glavne prednosti *POC* metoda jesu: brza dostupnost rezultata (do 15 minuta) i veoma mala količina uzorka krvi (do 5 ml) koja je potrebna za izvođenje testa; dok su glavni nedostaci ovih metoda: njihova cena, koja prevazilazi cenu izvođenja standardnih laboratorijskih testova, i nemogućnost detektovanja koagulopatija, koje nastaju usled poremećaja normalnog fiziološkog stanja pacijenta.

POC metode imaju izuzetno veliki značaj u smanjenju perioperativnog krvarenja, smanjenju transfuzije krvi i krvnih derivata i formiranju adekvatnih terapijskih algoritama.

Ključne reči: tromboelastografija, krvarenje, multiplejt, transfuzija, *point-of-care* metode

ABSTRACT

Perioperative bleeding management is a complex task which has significant impact on surgery outcome. Most hemostasis disorders occurring intraoperatively are acute, caused by massive bleeding, and can be explained by the principle of loss, compensation, and dilution of circulating blood volume. Disorders at the level of the hemostatic system can be assessed both by various standard laboratory tests, such as: prothrombin time, activated partial thromboplastin time, platelet count, coagulation factor concentrates, levels of antithrombin and D-dimer; or by point-of-care (POC) methods.

Standard laboratory tests have their limitations. They do not detect increased intraoperative bleeding tendency, and it is recommended to use methods such as POC, which quickly and accurately assess the patient's coagulation status, thus enabling the administration of the appropriate therapy, as soon as possible. The most commonly used POC methods are the aggregometry methods (Multiplate, PFA-100, and Platelet Mapping Assay), used in perioperative platelet function evaluation, and viscoelastic tests (rotational thromboelastometry – ROTEM; thromboelastography – TEG), which provide a graphic representation of all hemostatic activity by measuring the time elapsed until the onset of clot formation, formation dynamics, as well as clot firmness and stability over time.

The main advantages of the POC method are: the swift availability of results (up to 15 minutes) and the very small blood sample size (up to 5 ml) necessary for performing the test; while the main disadvantages are: their cost, which exceeds the cost of performing standard laboratory tests, and their inability to detect coagulopathies, resulting from the disturbance of the patient's normal physiological state.

POC methods are very important in reducing perioperative bleeding, reducing blood transfusions, and forming adequate therapeutic algorithms.

Keywords: thromboelastography, bleeding, Multiplate, transfusion, point-of-care methods

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UVOD

Perioperativna kontrola krvarenja je kompleksan zadatak koji ima značajan uticaj na ishod operativnog zahvata. Kontrola faktora koagulacije i hemostaze je jedan od najznačajnijih zadataka anesteziologa, hirurga, transfuziologa, hematologa, ali i lekara drugih specijalnosti. Većina poremećaja koagulacije nastalih intraoperativno je akutna, uzrokovana masivnim krvarenjem i može se objasniti principom gubitka, nadoknade i dilucije cirkulišućeg volumena krvi. Tada dolazi do poremećaja vrednosti rezultata testova praćenja koagulacije kao što su: protrombinsko vreme (engl. *prothrombin time – PT*), aktivirano parcijalno tromboplastinsko vreme (engl. *activated partial thromboplastin time – aPTT*), tromboelastografija, broj trombocita, kao i koncentracija antitrombina, fibrinogena, faktora koagulacije, i D-dimera [1,2]. Perioperativno krvarenje zavisi od tipa hirurške intervencije, koagulacionog statusa i komorbiditeta bolesnika. Obilnije perioperativno krvarenje se očekuje u kardiohirurgiji, ortopedskoj, abdominalnoj i vaskularnoj hirurgiji, ali se pojačano krvarenje može javiti i u ostalim granama hirurgije [3]. Takođe, pojačano perioperativno krvarenje može biti posledica određenih bolesti (fon Vilebrandova bolest, hemofilija A i B, trombocitopenijska purpura, itd.) ali i primene antikoagulacionih lekova (aspirin, vitamin K-antagonisti, antagonisti ADP receptora, i drugi) [4,5]. Ozbiljno krvarenje, kao potencijalna komplikacija svih invazivnih procedura, i njegov tretman, u vidu transfuzije krvi i njenih produkata, povezani su sa povećanjem morbiditeta i mortaliteta [6].

U literaturi postoje opisane različite strategije tretmana krvarenja. Jedni autori opisuju dve strategije tretmana krvarenja, koje su zasnovane na transfuziji sveže zamrznute plazme (SZP) i koncentrovanih eritrocita u odnosu 1:2, ili na transfuziji koncentrata fibrinogena i koncentrovanih eritrocita, u zavisnosti od nivoa hemoglobina u krvi. Drugi autori preporučuju tri strategije tretmana krvarenja:

1. Strategija „kontrole štete" (engl. *damage control resuscitation*; *damage control hematology*) predstavlja nadoknadu krvi, SZP i trombocita u odnosu 1:1:1;
2. Individualni terapijski koncept, zasnovan na standardnim laboratorijskim testovima (*PT*, *aPTT* i broj trombocita);
3. Individualni terapijski, tzv. *near-patient* koncept, zasnovan na *POC* testiranju, gde se koagulacioni status i funkcija trombocita ispituju viskoelastističnim i agregometrijskim testovima (tromboelastografija – *TEG*, rotaciona tromboelastometrija – *ROTEM*, multiplejt – *MULTIPLATE*).

Standardni laboratorijski testovi, kao što su *PT* i *aPTT*, su slabi prediktori krvarenja i nisu adekvatni za

INTRODUCTION

Perioperative bleeding management is a complex task which has significant impact on surgery outcome. For anesthesiologists, surgeons, transfusiologists, hematologists, but also for doctors of other specialties, monitoring coagulation factors and hemostasis is one of the most important tasks. Most coagulation disorders occurring intraoperatively are acute, caused by massive bleeding and can be explained by the principle of loss, compensation, and dilution of circulating blood volume. This is when disruption occurs in the values of coagulation monitoring test results, such as: prothrombin time (PT), activated partial thromboplastin time (aPTT), thromboelastography, platelet count, as well as the concentrations of antithrombin, fibrinogen, coagulation factors and D-dimer [1,2]. Perioperative bleeding depends on the type of surgical procedure, the coagulation status, and the comorbidities of the patient. Heavy perioperative bleeding is expected in cardiac, orthopedic, abdominal, and vascular surgery, but more profuse bleeding can also occur in other branches of surgery [3]. Also, profuse perioperative bleeding can be the result of certain illnesses (von Willebrand disease, hemophilia A and B, thrombocytopenic purpura, etc.), but also of anticoagulation drug application (aspirin, vitamin K antagonists, ADP receptor antagonists, and others) [4,5]. Serious bleeding, as a potential complication of all invasive procedures, and its treatment, in the form of transfusion of blood and blood products, are linked to the increase in morbidity and mortality [6].

Different strategies for treating bleeding have been described in literature. Some authors describe two strategies of bleeding treatment based either on the transfusion of fresh-frozen plasma (FFP) and red blood cell concentrates, in the ratio 1:2, or on the transfusion of the fibrinogen concentrate and red blood cell concentrates, adjusted according to the blood hemoglobin level. Other authors recommend three strategies of bleeding treatment:

1. Strategy of damage control (damage control resuscitation; damage control hematology) is the replacement of blood, FFP, and thrombocytes, in the ratio: 1:1:1;
2. Individual therapy concept, based on standard laboratory tests (PT, aPTT and platelet count);
3. Individual therapy near-patient concept, based on POC testing, whereby the coagulation status and the platelet function are tested by means of viscoelastic and aggregometry tests (TEG, ROTEM, MULTIPLATE).

Standard laboratory tests, such as PT and aPTT, are weak predictors of bleeding and are not appropriate

procenu koagulacionog statusa pacijenta. Ukoliko postoji adekvatna oprema, treći koncept može lako da zameni prva dva terapijska koncepta [7,8].

POINT-OF-CARE (*POC*) METODE

POC metode obezbeđuju informacije o početku koagulacije, stabilnosti ugruška i fibrinolizi. Rezultati o prisutnom poremećaju koagulacije, kao i njegovim uzrocima, dobijaju se u kratkom vremenskom periodu i mogu se primenjivati u svim fazama hirurškog lečenja: preoperativno, intraoperativno i postoperativno. Nijedna od trenutno dostupnih *POC* metoda ne može sama pružiti informacije o koagulacionom sistemu u celini. *POC* metode se dele na agregometrijske i viskoelastične testove [9].

Agregometrijski testovi se koriste u perioperativnoj proceni funkcije trombocita. Oni se razlikuju u odnosu na to koji se agonista koristi u aktiviranju trombocita (kolagen, adenozin difosfat, epinefrin, arahidonska kiselina, trombin). Najčešće korišćen agregometrijski test je multiplejt.

Multiplejt (engl. *Multiplate – multiple electrode aggregometry*, *MEA*) jeste test ispitivanja funkcije trombocita. Može se koristiti za otkrivanje poremećaja funkcije trombocita, praćenje antitrombocitne terapije, kao i za procenu rizika od krvarenja. Ovaj test koristi uzorak pune krvi u postupku kvantifikacije agregacijske funkcije trombocita, tako što se trombociti iz uzorka pune krvi zalepe za metalne elektrode, kojih ima po dva para u svakoj kiveti, a između njih se kontinuirano meri električni otpor. Korišćenjem različitih reagenasa (adenozin difosfat, kolagen, arahidonska kiselina, ristocetin, peptid-6 aktivator receptora trombina - *TRAP-6*) dolazi do aktivacije trombocita preko različitih receptora, koji se nalaze na njihovoj površini, i na taj način se, pored funkcije trombocita, može ispitati i efekat antitrombocitne terapije. Rezultati se dobijaju u vidu grafikona, na kojem površina ispod krivulja označava funkciju trombocita i efekat antitrombocitne terapije, pri čemu veća površina predstavlja bolju funkciju trombocita (Slike 1 i 2) [10,11].

Viskoelastični testovi (rotaciona tromboelastometrija - *ROTEM* i tromboelastografija - *TEG*) obezbeđuju podatke o vremenu početka formiranja ugruška, dinamici formiranja kao i čvrstini i stabilnosti ugruška tokom vremena. Oni omogućavaju paralelno praćenje ovih parametara na jednom uzorku krvi, nakon aktiviranja koagulacije različitim agonistima, a posebna prednost je mogućnost detektovanja hiperfibrinolize [12].

TEG test je otkriven 1948. godine. U početku se koristio samo u proceni koagulacionog statusa tokom transplantacije jetre, dok se danas koristi u kardiohirurgiji, ginekologiji, ortopediji i drugim granama

for assessing the patient's coagulation status. If appropriate equipment is available, the third concept can easily replace the first two therapeutic concepts [7,8].

POINT-OF-CARE (POC) METHODS

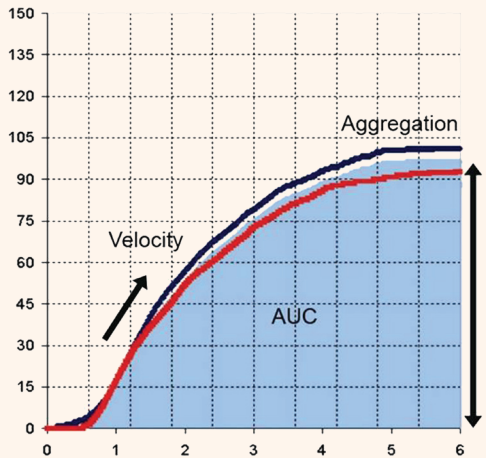
POC methods provide information on coagulation initiation, clot stability and fibrinolysis. Results confirming coagulation disorder and its origin are obtained within a short space of time and can be carried out in any of the phases of surgical treatment: perioperatively, intraoperatively and postoperatively. On its own, none of the currently available POC methods can offer information on the coagulation system, as a whole. There are two types of POC methods: aggregometry tests and viscoelastic tests [9].

Aggregometry tests are used in perioperative platelet function assessment. They differ depending on the agonist applied for platelet activation (collagen, adenosine diphosphate, epinephrine, arachidonic acid, thrombin). The most commonly used aggregometry test is the Multiplate test.

Multiplate (multiple electrode aggregometry – MEA) is a platelet function test. It can be used for discovering platelet function disorder, monitoring antiplatelet therapy, as well as for assessing the risk of bleeding. This test uses a full blood sample in platelet aggregation function quantification, through the process of sticking the platelets from the full blood sample to metal electrodes, with two pairs of electrodes placed in each cuvette, while electrical resistance between them is continuously measured. The use of different reagents (adenosine diphosphate, collagen, arachidonic acid, ristocetin, thrombin receptor activating peptide 6 - TRAP-6) results in platelet activation via different receptors located on their surface, and, in this way, not only platelet function, but also the effect of antiplatelet therapy can be tested. Results are obtained in the form of graphs, where the surface below the curves marks the platelet function and the effect of antiplatelet therapy, with a larger surface representing better platelet function (Figures 1 and 2) [10,11].

Viscoelastic tests (rotational thromboelastometry - ROTEM and thromboelastography – TEG) provide data on clot formation initiation time, clot formation dynamics, clot firmness, and clot stability over time. They enable parallel monitoring of these parameters in a single blood sample, after clot activation with different agonists, while the possibility of also detecting hyperfibrinolysis is a particular advantage [12].

The TEG test was discovered in 1948. In the beginning it was used only for assessing coagulation status during liver transplantation, while today it is used in cardiac surgery, gynecology, orthopedics, and other branches of



Slika 1. Multiplejt kriva

**AUC* – Površina ispod krive

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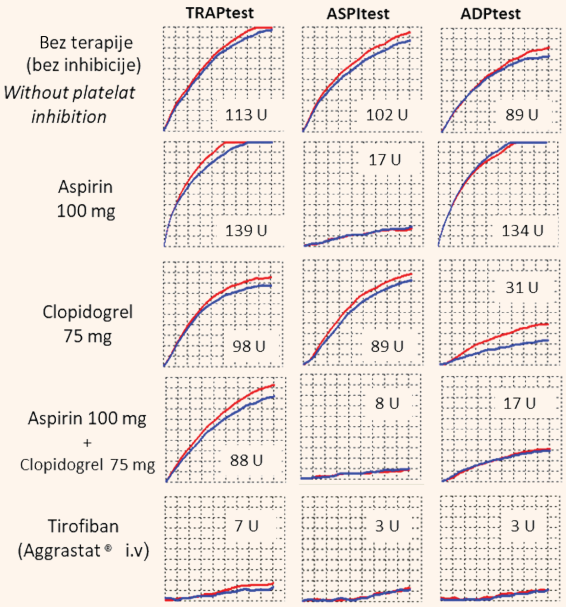
Figure 1. The Multiplate Curve

**AUC* – Area under the Curve

From: Dimić N, et al. Procena obima intraoperativnog krvarenja i strategije za smanjenje rizika i nadoknadu volumena, in: Kalezić N. Perioperativna medicina 1. Medicinski fakultet, Beograd; 2020; 303-324.

hirurgije [13]. Uz pomoć *TEG* metode dobijaju se informacije o formiranju fibrina, interakciji trombocita i fibrina, čvrstini ugruška i fibrinolizi. Kao aktivatori koagulacije koriste se: selit, kaolin ili tkivni faktor. Izvođenjem *TEG* metode prati se pet parametara u različitim stadijumima formiranja ugruška: R-vrednost, K-vrednost, α ugao, maksimalna amplituda (*MA*) i maksimalnu amplituda nakon 60 minuta (*MA60*). Uz to, prate se i indeksi razgradnje ugruška nakon 30 i 60 minuta od postizanja maksimalne amplitude (engl. *LY-lysis index – LY30; LY60*). Referentne vrednosti zavise od aktivatora koji se koristi. R-vrednost predstavlja

surgery [13]. With the aid of the TEG method, information on fibrin formation, interaction between thrombocytes and fibrin, clot firmness, and fibrinolysis, is obtained. The following are used as coagulation activators: celite, kaolin, or the tissue factor. The implementation of the TEG method enables the monitoring of five parameters in different stadiums of clot formation: R value, K value, α angle, maximum amplitude (*MA*), and maximum amplitude after 60 minutes (MA60). Additionally, clot lysis indices are also monitored, 30 and 60 minutes after maximum amplitude (LY30; LY60). Reference values depend on the activator being used. The R value represents clotting time

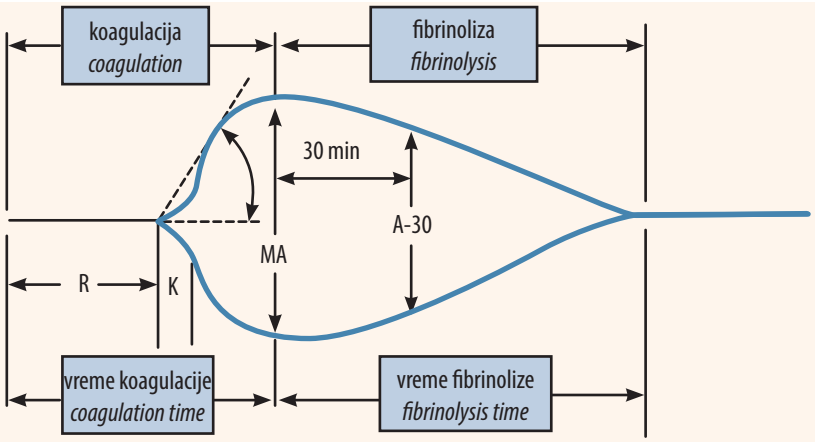


Slika 2. Praćenje efekta antitrombocitne terapije

Preuzeto iz: Dimić N i dr. Procena obima intraoperativnog krvarenja i strategije za smanjenje rizika i nadoknadu volumena, u: Kalezić N. Perioperativna medicina 1. Medicinski fakultet, Beograd; 2020; 303-324.

Figure 2. Monitoring the effects of antiplatelet therapy

From: Dimić N, et al. Procena obima intraoperativnog krvarenja i strategije za smanjenje rizika i nadoknadu volumena, in: Kalezić N. Perioperativna medicina 1. Medicinski fakultet, Beograd; 2020; 303-324.



Slika 3. Tromboelastografija – parametri praćenja

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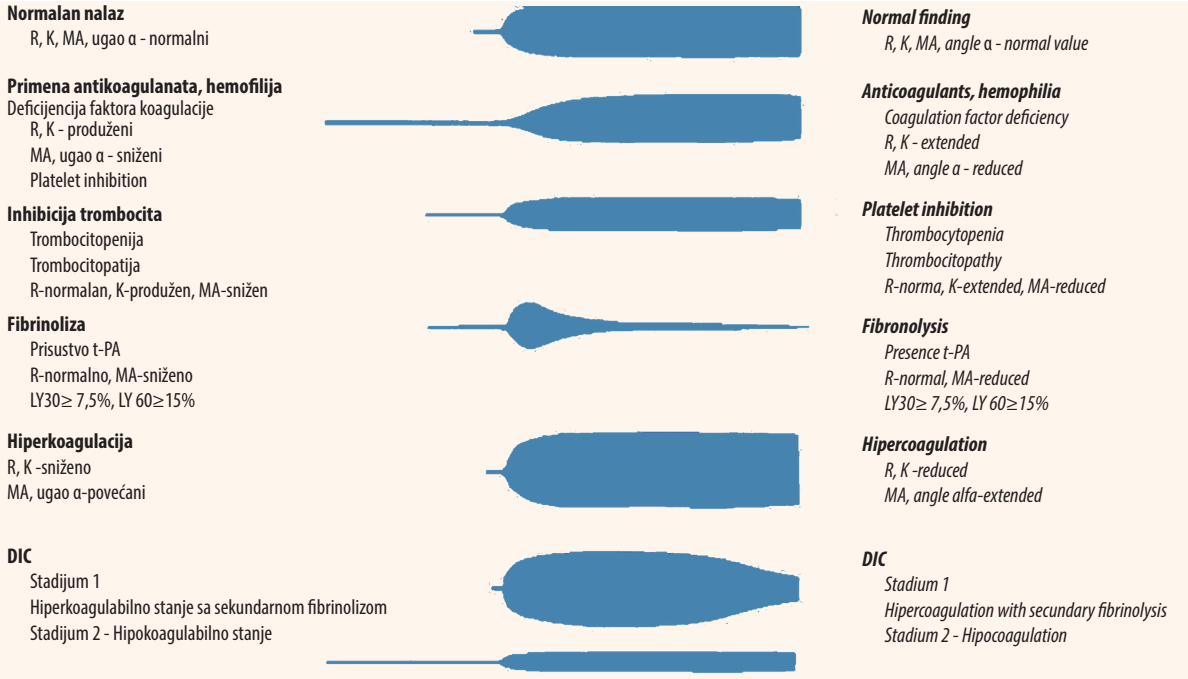
Figure 3. Thromboelastography – monitored parameters

From: Dimić N, et al. Procena obima intraoperativnog krvarenja i strategije za smanjenje rizika i nadoknadu volumena, in: Kalezić N. Perioperativna medicina 1. Medicinski fakultet, Beograd; 2020; 303-324.

vreme zgrušavanja (engl. *clotting time – CT*) odnosno period od trenutka početka testa do trenutka početka formiranja fibrina. K-vrednost predstavlja kinetiku formiranja ugruška, odnosno brzinu zgrušavanja kojom se dostiže određeni nivo čvrstine ugruška (vreme od početka formiranja ugruška do trenutka kada amplituda dostigne 20 mm). Ugao α je ugao koji formira tangenta kada je amplituda 2 mm. On predstavlja brzinu formiranja fibrina (jačanja ugruška). Maksimalna amplituda (*MA*) predstavlja čvrstinu ugruška, koja zavisi od funkcije i broja trombocita i njihove interakcije sa fibrinom (Slike 3 i 4). Ovaj parametar se koristi kao

(CT), i.e. the interval between the moment of test initiation and the moment when fibrin starts forming. The K value represents the kinetics of clot formation, i.e. the speed of clotting at which a certain level of clot firmness is achieved (time elapsed from the beginning of clot formation until the moment when the amplitude reaches 20 mm). The α angle is the angle formed by the tangent when the amplitude is 2 mm. It represents the speed of fibrin formation (clot strengthening). The maximum amplitude (MA) represents clot firmness, which depends on the function and number of platelets as well as on their interaction with fibrin (Figures 3 and 4). This parameter



Slika 4. Primeri različitih poremećaja prikazanih tromboelastogramom

Preuzeto iz: Dimić N i dr. Procena obima intraoperativnog krvarenja i strategije za smanjenje rizika i nadoknadu volumena, u: Kalezić N. Perioperativna medicina 1. Medicinski fakultet, Beograd; 2020; 303-324.

Figure 4. Examples of different disorders shown on a thromboelastogram

From: Dimić N, et al. Procena obima intraoperativnog krvarenja i strategije za smanjenje rizika i nadoknadu volumena, in: Kalezić N. Perioperativna medicina 1. Medicinski fakultet, Beograd; 2020; 303-324.

marker za otkrivanje poremećaja funkcije trombocita. Ograničenje *TEG* metode ogleda se u nemogućnosti detektovanja poremećaja funkcije trombocita nastalih usled dejstva antitrombocitnih lekova, ali je ovaj nedostatak prevaziđen agregometrijskim testovima [11,14]. Modifikacija *TEG* metode, korišćenjem tkivnog faktora ili kaolina kao aktivatora, nazvana je brza *TEG* metoda (engl. *rapid TEG - rTEG*). Rezultati ovog testa su dostupnu u roku od oko 15 minuta i mogu se koristiti u proceni potrebe za ranom transfuzijom produkata krvi [15]. Spiess je sa svojim kolegama analizirao 1.079 pacijenata, pre i nakon uvođenja *TEG* metode, koja je predstavljala važan faktor pri donošenju odluka o nadoknadi krvi i krvnih produkata. Zaključeno je da nakon uvođenja *TEG* metode dolazi do značajnog smanjenja nadoknade krvi i svih krvnih produkata (osim krioprecipitata) zbog ranog otkrivanja poremećaja koagulacije i blagovremenog delovanja [16]. Četiri godine kasnije do istog zaključka došao je i Shore-Lesserson [17-19].

Rotaciona tromboelastometrija (*ROTEM*) je viskoelastična *POC* metoda kod koje se senzor fiksiran na rotacionoj osovini uranja u kivetu koja sadrži uzorak krvi. Gubitak elastičnosti tokom zgrušavanja krvi detektuje se kao refleksija svetla na malom ogledalu pričvršćenom za osovinu, a prikazuje se u vidu tromboelastograma [20].

Primenom *ROTEM* metode prate se sledeći parametri:

- vreme zgrušavanja (*CT*) jeste vreme od trenutka početka testa do trenutka kad maksimalna amplituda iznosi 2 mm. Ova vrednost pruža informacije o početku formiranja ugruška;
- vreme formiranja ugruška (engl. *clot formation time – CFT*) jeste vreme za koje maksimalna amplituda poraste sa 2 mm na 20 mm. Ova vrednost pruža informacije o polimerizaciji fibrina i stabilizaciji ugruška trombocitima i faktorom XIII;
- maksimalna čvrstina ugruška (engl. *maximum clot firmness – MCF*) jeste maksimalna amplituda koja je registrovana u testu i zavisi od broja i funkcije trombocita i koncentracije fibrinogena;
- ugao α jeste ugao koji formira tangenta kada je amplituda 2 mm;
- maksimalna razgradnja ugruška (engl. *maximum lysis – ML*) je odnos najniže amplitude nakon postizanja maksimalne čvrstine ugruška i maksimalne amplitude;
- stabilnost ugruška tokom maksimalne razgradnje ili indeks razgradnje ugruška (engl. *clot lysis index – CLI*);
- maksimalna brzina zgrušavanja (engl. *maximum velocity – maxVel*);
- vreme do maksimalne brzine (engl. *time to maximum velocity – t-maxVel*) [21].

is used as a marker for discovering platelet function disorder. The limitation of the TEG method is reflected in its inability to detect platelet function disorders resulting from the influence of antiplatelet drugs. This shortcoming has been overcome with aggregometry tests [11,14]. A modification of the TEG method, whereby the tissue factor or kaolin is used as an activator, has been named the rapid TEG method (rTEG). The results of this test are available within 15 minutes and can be used in assessing the need for early transfusion of blood products [15]. With his colleagues, Spiess analyzed 1,079 patients, before and after introducing the TEG method, which was an important factor when deciding on blood and blood product replacement. They concluded that, due to early detection of coagulation disorder and timely intervention, a significant decrease in blood and all blood product replacement occurred, after the introduction of the TEG method [16]. Shore-Lesserson reached the same conclusion four years later [17-19].

Rotational thromboelastometry (ROTEM) is a viscoelastic POC method whereby a sensor fixed on a rotational axis is immersed in a cuvette containing the blood sample. The loss of elasticity during blood coagulation is detected as the reflection of light on a small mirror fixed to the axis, and it is represented in the form of a thromboelastogram [20].

The following parameters are monitored with the ROTEM method:

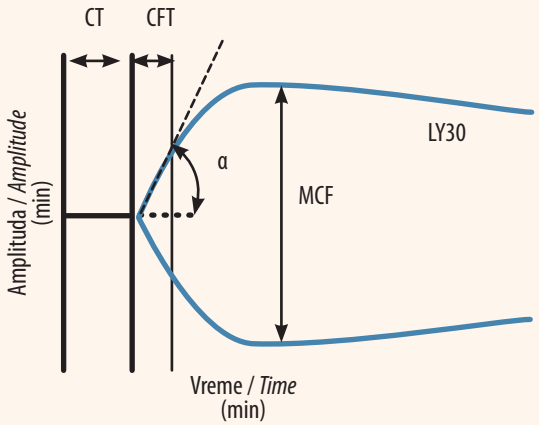
- clotting time (CT) is the time measured from the moment when the test begins until the moment when the maximum amplitude reaches 2 mm. This value provides information on the beginning of clot formation;
- clot formation time (CFT) is the time necessary for the maximum amplitude to increase from 2 mm to 20 mm. This value provides information on fibrin polymerization and the stabilization of the clot with thrombocytes and factor XIII;
- maximum clot firmness (*MCF*) is the maximum amplitude registered in the test and it depends on the platelet number and function and on fibrinogen concentration;
- the α angle is the angle formed by the tangent when the amplitude is 2 mm;
- maximum clot lysis (ML) is the ratio between the minimum amplitude after achieving maximum clot firmness and the maximum amplitude;
- clot stability during maximum lysis or clot lysis index (CLI);
- maximum clotting velocity, i.e. maximum velocity (maxVel);
- time to maximum velocity (t-maxVel) [21].

U okviru *ROTEM* metode koagulacija može biti aktivirana tkivnim faktorom (*EXTEM*) ili elaginskom kiselinom (*INTEM*) u cilju ubrzavanja analize. Aktivatori unutrašnjeg puta koagulacije (*INTEM* – fosfolipid i elaginska kiselina) i spoljašnjeg puta koagulacije (*EXTEM* – tkivni faktor) koriste se da bi pružili informacije slične onima koje pružaju *aPTT* (*INTEM*) i *PT* (*EXTEM*). Osim osnovnih skrining testova (*INTEM* i *EXTEM*) postavljanje diferencijalne dijagnoze je moguće dodatkom specifičnih reagenasa. Kombinovanjem i poređenjem rezultata različitih *ROTEM* testova moguće je detektovati nedostatak jednog ili više faktora koagulacije, i na osnovu toga u pravo vreme započeti sa adekvatnom terapijom (nadoknadom) [22,23]. Vreme izvođenja i analiziranja *ROTEM* testa iznosi oko 10-20 minuta i može se ponoviti za oko 10 minuta od administriranja određenog faktora koagulacije ili produkta krvi sa ciljem usmeravanja dalje terapije, odnosno praćenja efekta primenjene terapije [24].

ROTEM se ne koristi za dijagnostikovanje poremećaja funkcije trombocita, iako indirektno može ukazati na poremećaj njihovog broja ili funkcije [25]. Takođe, ne može se detektovati poremećaj hemostaze usled fon Vilebrandove bolesti ili korišćenja antitrombocitnih lekova primenom samo *ROTEM* metode, već kombinacijom *ROTEM* metode i agregometrijskih testova [26]. Terapijski algoritmi bazirani na *ROTEM* metodi, zasnovani na nadoknadi koncentrata fibrinogena i protrombinskog kompleksa (*PCC*), ali i primeni antifibrinolitika u traumi, transplantaciji jetre, kardiohirurgiji i drugim granama hirurgije, redukuju transfuziju alogene krvi [27]. Anderson je u svojoj kliničkoj studiji pokazao da je, usled uvođenja *ROTEM* metode, kod značajno manjeg broja pacijenata izvršena transfuzija eritrocita, SZP i trombocita [28]. *ROTEM* metoda nije pokazala uticaj na smanjenje mortaliteta, ali jeste

For the purpose of expediting the analysis within the ROTEM method, coagulation can be activated with the tissue factor (EXTEM) or with ellagic acid (INTEM). Intrinsic coagulation pathway activators (INTEM – phospholipid and ellagic acid) and extrinsic coagulation pathway activators are used to provide information similar to that provided by aPTT (INTEM) and PT (EXTEM). In addition to performing basic screening tests (INTEM and EXTEM) it is possible to establish a differential diagnosis by adding specific reagents. By combining and comparing the results of different ROTEM tests, it is possible to detect a deficiency in one or more coagulation factors, and based on this finding, start with appropriate and timely replacement therapy [22,23]. The time needed to perform and analyze the ROTEM test is around 10 to 20 minutes and the test can be repeated around 10 minutes after the administration of a particular coagulation factor or blood product, whereby further therapy is directed, i.e. the effect of the applied therapy is monitored [24].

ROTEM is not used for diagnosing platelet function disorder, although it can indirectly point to a disruption in the platelet number or function [25]. Also, it is not possible to detect hemostasis disorder resulting from von Willebrand disease or the use of antiplatelet drugs by applying only the ROTEM method; rather it is necessary to combine the ROTEM method and aggregometry tests [26]. Therapeutic algorithms, which are based on the ROTEM method and founded on the replacement of the fibrinogen concentrate and the prothrombin complex concentrate (PCC), but also on the application of antifibrinolytics in trauma, liver transplantation, cardiac surgery, and other branches of medicine, reduce the transfusion of allogenic blood [27]. In his clinical study, Anderson showed that, because of the introduction of the ROTEM method, the transfusion of erythrocytes, FFP, and thrombocytes was performed in a significantly



Slika 5. ROTEM – parametri praćenja

Preuzeto iz: Dimić N i dr. Procena obima intraoperativnog krvarenja i strategije za smanjenje rizika i nadoknadu volumena, u: Kalezić N. Perioperativna medicina 1. Medicinski fakultet, Beograd; 2020; 303-324.

Figure 5. ROTEM – Monitored parameters

From: Dimić N, et al. Procena obima intraoperativnog krvarenja i strategije za smanjenje rizika i nadoknadu volumena, in: Kalezić N. Perioperativna medicina 1. Medicinski fakultet, Beograd; 2020; 303-324.

EXTEM & INTEM

- Normalan CT / *Normal CT*
- Normalna A / *Normal A10*
- Nema hiperfibrinolize / *Without hiperfibrinolysis*

FIBTEM : normalna A / *Normal A10*

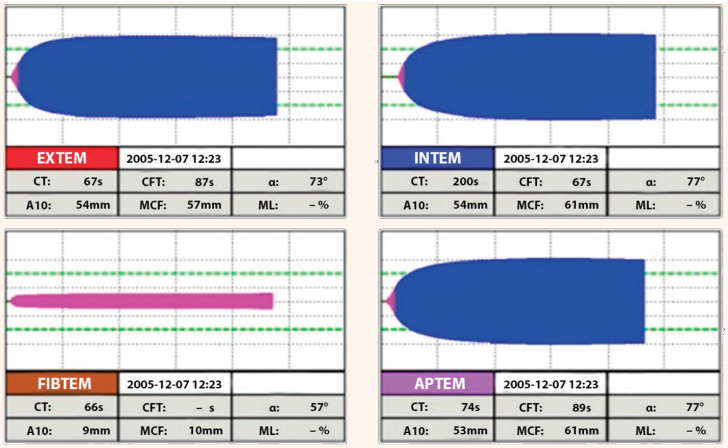
= > dovoljan nivo Fb / sufficient fibrinogen level

&

EXTEM : normalna / *Normal value*

= > normalni Tr / *Normal platelet value*

APTEM = EXTEM = > nema hiperfibrinolize / *Without hiperfibrinolysis*



Slika 6. ROTEM – normalan nalaz

Preuzeto iz: Dimić N i dr. Procena obima intraoperativnog krvarenja i strategije za smanjenje rizika i nadoknadu volumena, u: Kalezić N. Perioperativna medicina 1. Medicinski fakultet, Beograd; 2020; 303-324.

Figure 6. ROTEM – Normal finding

From: Dimić N, et al. Procena obima intraoperativnog krvarenja i strategije za smanjenje rizika i nadoknadu volumena, in: Kalezić N. Perioperativna medicina 1. Medicinski fakultet, Beograd; 2020; 303-324.

na smanjenje perioperativnog gubitka krvi i nadoknade krvi i krvnih produkata [29]. Larsen je ispitivao dijagnostička svojstva *TEG* metode (aktivirane kaolinom) i *ROTEM* metode, i zaključio je da *ROTEM* obezbeđuje preciznije informacije o svim ispitivanim koagulopatijama, te omogućava bržu dijagnostiku, dok *TEG* metoda nije pokazala zadovoljavajuće rezultate u razlikovanju dilucione koagulopatije i koagulopatije izazavane trombocitopenijom, što može dovesti do nepotrebne transfuzije trombocita (Slike 5 i 6) [11,30].

PREDNOSTI I NEDOSTACI *POC* METODA

Za razliku od standardnih laboratorijskih testova, za izvođenje *POC* metoda potrebna je veoma mala količina krvi (do 5 ml) bez dodatne obrade i preanalitičkog vremenskog odlaganja. Ovo posebno ima značaja kod dugoležećih bolesnika u jedinicama intenzivnog lečenja, koji zahtevaju svakodnevnu (ponekad i češću) procenu koagulacionog statusa, pri čemu standardni laboratorijski testovi (koji ponekad zahtevaju uzimanje i do 20 ml krvi) mogu pogoršati hemostazni potencijal pacijenta. Uzorak krvi potreban za izvođenje *POC* metoda može se nositi u laboratoriju ili se *POC* metode mogu izvoditi u neposrednoj blizini pacijenata (engl. *near-patient*), u operacionoj sali ili jedinici intenzivne nege, pa čak i u terenskim uslovima [31]. Ipak, njihova glavna prednost jeste brza dostupnost rezultata [32]. U poređenju sa standardnim laboratorijskim koagulacionim testovima, za čije izvođenje je potrebno između 40 i 90 minuta, što je neprihvatljivo u situacijama akutnog krvarenja, jer ne reflektuje trenutno stanje koagulacionog sistema, *POC* testovi mogu pružiti informacije o koagulacionom statusu pacijenta u roku od oko 15 minuta. Na taj način, *POC* testovi predstavljaju gotovo trenutni klinički prikaz

reduced number of patients [28]. The ROTEM method did not demonstrate any influence on the reduction in mortality, but it did influence the reduction in perioperative blood loss, as well as blood and blood product replacement [29]. Larsen studied the diagnostic properties of the TEG method (kaolin activated) and the ROTEM method, and concluded that ROTEM provided more precise information on all the investigated coagulopathies and enabled swifter diagnostics, while the TEG method failed to show satisfactory results in differentiating between dilutional coagulopathy and thrombocytopenia induced coagulopathy, which could lead to unnecessary platelet transfusion (Figures 5 and 6) [11,30].

ADVANTAGES AND SHORTCOMINS OF THE POC METHODS

As opposed to standard laboratory tests, only a very small amount of blood (up to 5 ml) is necessary for performing the POC methods, without additional processing or preanalytical delay. This is especially important in patients who have been bedridden for a longer period of time in intensive care units, and who require daily (sometimes even more frequent) coagulation status assessment. At the same time, standard laboratory tests, which sometimes require taking up to 20 ml of blood, may worsen the hemostasis potential of the patient. The blood sample needed for performing POC methods can be taken to the laboratory; POC methods can be carried out in the immediate proximity of the patient (near-patient); they can be performed in the operating theatre, in intensive care units, or even in the field [31]. However, their main advantage is quick availability of results [32]. In comparison with standard laboratory coagulation tests, which can take from 40 up to 90 minutes, which is unacceptable in situations of acute bleeding, since the

koagulacionog stanja pacijenta [33]. Zbog toga je nepisano pravilo da se u slučaju nemogućnosti izvođenja *POC* dijagnostičkih metoda, čija upotreba može nadomestiti nedostatke i ograničenja standardnih koagulacionih testova, odluke o nadoknadi krvi i krvnih derivata, u toku operacije, donose na osnovu kliničkih znakova [13,34].

Viskoelastični testovi omogućavaju ranu procenu potrebe za masivnom transfuzijom i usmerenom terapijom specifičnim hemostatskim lekovima, koncentratima faktora koagulacije, kao i produktima krvi [35]. Nekoliko kohortnih studija pokazalo je da je hemostatska terapija bazirana na *POC* testiranju povezana sa smanjenjem potrebe za transfuzijom (nadoknadom) krvi, smanjenom incidencom neželjenih događaja uzrokovanih transfuzijom, kao i sa boljim krajnjim ishodom [36]. Ovi testovi pomažu lekarima da prepoznaju pacijente koji su pod povećanim rizikom od krvarenja, a koji mogu imati veliku korist od tzv. *cell-saver* metode, kao i one koji bi imali koristi od profilaktičke primene antifibrinolitika [37].

Pacijentima sa akutnim koronarnim sindromom se često preporučuje prestanak uzimanja antitrombocitne terapije nekoliko dana pre kardiohirurške intervencije. Ipak, prestanak uzimanja ovih lekova značajno povećava rizik od rane tromboze grafta ili stenta nakon kardiohirurške intervencije, pa se antitrombocitni lekovi ipak primenjuju do dana operacije, iako se time povećava rizik od perioperativnog i postoperativnog krvarenja [38]. Upotreba dvojne antitrombocitne terapije (aspirin i klopidogrel) može dovesti do poremećaja agregacije trombocita, a povezana je i sa povećanjem gubitka krvi, povećanim rizikom za hiruršku reintervenciju i produžavanjem vremena oporavka u jedinici intenzivne nege, u kojoj *POC* metode igraju značajnu ulogu [39].

Perioperativna procena funkcije trombocita u kardiohirurgiji, ali i u drugim granama hirurgije, može se izvršiti pomoću multiplejt testa ili *TEG* testa, Ovako vođena hemostatska terapija povezana je sa: smanjenjem postoperativnog krvarenja, smanjenjem potrebe za nadoknadom krvnih produkata, poboljšanjem ishoda operacije, smanjenjem finansijskih troškova, i značajnim smanjenjem mortaliteta [40]. Upotreba transfuzijskih algoritama, zasnovanih na *POC* metodama, pokazala je smanjenje potrebe za nadoknadom krvnih produkata i smanjenje gubitka krvi u kardiohirurgiji [41]. U skorašnjoj kohortnoj studiji, koja je obuhvatila 3.865 kardiohirurških pacijenata, prva linija terapije zasnovana na transfuziji koncentrata fibrinogena i protrombinskog kompleksa, i vođena primenom *POC* metoda (*ROTEM* i *Multiplate*) usko je povezana sa značajnim smanjenjem potrebe za transfuzijom alogene krvi,

results do not reflect the current state of the coagulation system, POC tests can provide information on the patient's coagulation status within 15 minutes. Thus, POC tests are an almost immediate clinical representation of the patient's coagulation status [33]. This is why it is an unwritten rule that, when it is not possible to perform POC diagnostic methods, whose application can make up for the shortcomings and limitations of standard coagulation tests, decisions on blood and blood product replacement during an operation, are made on the basis of clinical signs [13,34].

Viscoelastic tests enable early assessment of the need for massive transfusion and for guided therapy with specific hemostatic drugs, coagulation factor concentrates, and blood products [35]. Several cohort studies have shown that hemostatic therapy based on POC testing is connected with a reduced need for blood transfusion (replacement), a reduced incidence of adverse effects caused by transfusion, as well as with a better final outcome [36]. These tests help doctors recognize patients who are at increased risk of bleeding, and who can greatly benefit from the cell-saver method, as well as patients who would benefit from prophylactic antifibrinolytic application [37].

Patients with acute coronary syndrome are often recommended to stop antiplatelet therapy several days prior to cardiac surgery. However, discontinuing these drugs significantly increases the risk of early graft or stent thrombosis after cardiac surgery, which is why antiplatelet drugs are, nevertheless, applied until the day of the surgery, even though this increases the risk of perioperative and postoperative bleeding [38]. Application of dual antiplatelet therapy (aspirin and clopidogrel) can lead to platelet aggregation disorder, and it is also connected to increased blood loss, increased risk of surgical reintervention, and prolonged recovery time in an intensive care unit, where POC methods play a significant role [39].

Perioperative platelet function assessment in cardiac surgery, and in other branches of surgery as well, can be performed with the aid of the Multiplate or the TEG test. Hemostatic therapy guided in this way is linked to a decrease in postoperative bleeding, a decreased need for blood product replacement, improved surgery outcomes, decreased financial costs, and a significant decrease in mortality [40]. The use of transfusion algorithms based on POC methods has demonstrated a decrease in the need for blood product replacement and a decrease in blood loss in cardiac surgery [41]. In a recent cohort study, which included 3,865 cardiac surgery patients, first-line therapy based on the transfusion of the fibrinogen concentrate and the prothrombin complex concentrate, and guided by the application of POC methods (ROTEM

redukcijom incidence masivne transfuzije, reoperacije i tromboembolijskih komplikacija, kao i sa ekonomskom uštedom [27,42]. Pacijenti sa hirurškim krvarenjem, koji zahtevaju hitnu re-eksploraciju, lakše se identifikuju uz pomoć *POC* metoda nego standardnim laboratorijskim testovima, koji mogu pokazivati abnormalne vrednosti i do nekoliko sati nakon kardiohirurške operacije [43].

Kod velikih operacija, u slučaju intraoperativnog krvarenja, odluka o nadoknadi krvnih produkata se donosi na osnovu kliničke procene stanja pacijenta. Intraoperativno krvarenje je dinamički proces sa potencijalno životno ugrožavajućim posledicama, koji, zajedno sa primenom kristaloidnih rastvora, dovodi do hemodilucije i potrošnje faktora koagulacije [44]. Dok se koncentracija hemoglobina i broj trombocita određuju u roku od 15 minuta, za dobijanje rezultata SLT potrebno je od 45 do 90 minuta [31]. *POC* metodama je potrebno značajno manje vremena za procenu koagulacionog statusa [45]. Odluka o nadoknadi krvnih produkata na osnovu *POC* metoda tokom intraoperativnog krvarenja doprinosi značajnom smanjenju nadoknade krvnih produkata, svih eventualnih posledica i rizika koje ova nadoknada nosi, kao i značajnom poboljšanju ishoda same operacije [46]. Iskustva pokazuju da, kod ozbiljnog akutnog krvarenja, terapijski algoritmi treba da budu usmereni ka povećanju vrednosti parametara *ROTEM* analize, iznad normalnih referentnih granica [47].

POC metode imaju sve veću ulogu u dijagnostikovanju septičnih stanja. Imajući u vidu da biomarkeri sepse, kao što su prokalcitonin i interleukin-6, mogu biti povišeni i kod traumatizovanih pacijenata ili pacijenata podvrgnutih operativnim zahvatima, kada nema infekcije, parametri *POC* metoda mogu imati ulogu kao biomarkeri u ranom otkrivanju sepse kod kritično obolelih pacijenata. Naime, u svojoj studiji, koja je obuhvatila 56 pacijenata sa ozbiljnom sepsom i 52 pacijenta podvrgnuta operativnim zahvatima, Adamzik je pokazao da je tromboelastometrijski parametar - indeks razgradnje, pouzdaniji biomarker sepse od prokalcitonina, interleukina-6 i C-reaktivnog protein (CRP) [48].

Trenutna saznanja o patologiji koagulopatije uzrokovane traumom govore o velikom značaju hiperfibrinolize [49]. Fibrinogen je prvi faktor čije se vrednosti kod krvarenja snižavaju ispod referentnih [50]. Glavni uzrok smanjene čvrstine ugruška kod traumatizovanih pacijenata je upravo oštećenje polimerizacije fibrina, čiji je uzrok smanjena koncentracija fibrinogena [51]. Ozbiljna deficijencija fibrinogena kod traumatizovanih pacijenata je upozoravajući znak na moguću hiperfibrinolizu [52]. *ROTEM* je brza i pouzdana metoda detekcije perioperativne fibrinolize [53]. U maloj

and Multiplate) was closely connected with a significant decrease in the need for allogenic blood transfusion, a reduction of massive transfusion incidence, reoperation and thromboembolic complications, as well as with economic savings [27,42]. Patients with surgical bleeding who require urgent re-exploration are identified more easily with the aid of POC methods than with standard laboratory tests, which can show abnormal values up to several hours after cardiac surgery [43].

In major surgery procedures, in case of intraoperative bleeding, the decision on blood product replacement is made based on the clinical assessment of the patient's status. Intraoperative bleeding is a dynamic process with potentially life-threatening consequences, which, together with the administration of crystalloid fluids, results in the hemodilution and depletion of coagulation factors [44]. While the hemoglobin concentration and platelet count are determined within 15 minutes, obtaining standard laboratory test results takes from 45 to 90 minutes [31]. POC methods need significantly less time for coagulation status assessment [45]. Basing the decision on blood product replacement during intraoperative bleeding on POC methods contributes to a significant reduction in blood product replacement, a reduction in all the possible consequences and risks which this method entails, as well as to a significant improvement in the outcomes of the surgical procedure [46]. Experience has shown that, in serious acute bleeding, therapeutic algorithms need to be directed towards increasing the value of the ROTEM analysis parameters, above the normal reference range [47].

POC methods have an increasing role in diagnosing septic conditions. Bearing in mind that sepsis biomarkers, such as procalcitonin and interleukin-6, can be elevated in traumatized patients or patients undergoing surgical procedures, when there is no infection, the parameters of POC methods may play a role as biomarkers in early detection of sepsis in critically ill patients. Namely, in a study involving 56 patients with serious sepsis and 52 patients who had undergone surgical procedures, Adamzik demonstrated that the thromboelastometry parameter – the lysis index, was a more reliable biomarker of sepsis than procalcitonin, interleukin-6 and C-reactive protein (CRP) [48].

Current knowledge on the pathology of trauma-induced coagulopathy speaks to the great significance of hyperfibrinolysis [49]. In bleeding, fibrinogen is the first factor whose values drop below reference values [50]. The main cause of reduced clot firmness in trauma patients is, in fact, damage in fibrin polymerization, caused by a reduced concentration of fibrinogen [51]. Serious fibrinogen deficiency in trauma patients is a warning sign for possible hyperfibrinolysis [52]. ROTEM is a swift and

retrospektivnoj studiji, u kojoj je 36 traumatizovanih pacijenata podeljeno u dve grupe, izvršeno je poređenje terapijskog algoritma zasnovanog na transfuziji SZP bez primene *ROTEM* metode i terapijskog algoritma zasnovanog na *ROTEM* testiranju i ordiniranju faktora koagulacije bez transfuzije SZP. Uočena je značajna razlika između dve pomenute grupe, u smislu redukcije transfuzije i neželjenih događaja transfuzije u grupi u kojoj je izvršeno *ROTEM* testiranje [54]. Prospektivna studija, koja je uključivala 517 traumatizovanih pacijenata, pokazala je da tromboelastografija omogućava brzu procenu koagulacionog statusa traumatizovanih pacijenata, brzu detekciju hipofibrinogenemije i rano ordiniranje koncentrata fibrinogena, što je povezano sa značajno boljim preživljavanjem [55]. Takođe, upotrebom *POC* metoda značajno se smanjuje gubitak krvi i potreba za nadoknadom krvi i njenih derivata kod traumatizovanih pacijenata, ali se ne smanjuje mortalitet [56].

Naravno, i *POC* metode imaju svoja ograničenja, a to su, pre svega, problem standardizacije (koji prati i SLT) i cena. Standardizovana temperatura od 37^{0}C, na kojoj se *POC* testovi izvode, može ometati detektovanje koagulopatija koje nastaju u stanjima hipo/hipertermije. Takođe se ne mogu detektovati koagulopatije koje nastaju usled poremećaja normalnog fiziološkog stanja pacijenta, npr. poremećaj vrednosti pH krvi, koncentracije jona kalcijuma, ili hematokrita [57]. Cena izvođenja *POC* testova (aparatura, reagensi, rastvori, održavanje) prevazilazi cenu izvođenja SLT. Kombinovano izvođenje agregometrijskih i viskoelastičnih testova košta od 25 do 35 evra, dok je cena izvođenja standardnih koagulacionih testova manja od 10 evra. Ipak, ova razlika u ceni može se kompenzovati odlukama o racionalnijoj nadoknadi krvi i njenih derivata i primeni drugih lekova, koje se donose na osnovu rezultata *POC* metoda [58]. U svojoj studiji, Nuttal je pokazao da primena *POC* metoda dovodi do manjeg postoperativnog gubitka krvi, samim tim i manje nadoknade krvi i krvnih derivata [46]. U studiji koja je obuhvatila 1.422 pacijenta, podvrgnutih kardiohirurškim operacijama, Spalding je zaključio da upotreba *POC* metoda dovodi do finansijske uštede od 50 odsto, usled smanjene nadoknade krvi, njenih derivata i drugih hemoterapijskih agenasa [20]. Gorlinger je, u retrospektivnoj studiji koja je obuhvatila 3.865 kardiohirurških pacijenata, poredio finansijski efekat prilikom primene koagulacione terapije jedne godine pre (2004.) i jedne godine nakon (2009.) uvođenja *ROTEM* metode i formiranja terapijskih algoritama na osnovu njenih rezultata kod kardiohirurških pacijenata. Ustanovljena je finansijska ušteda od 34,3 procenta nakon upotrebe *POC* metoda, te je zaključeno da je 2009.

reliable method for detecting perioperative fibrinolysis [53]. In a small retrospective study, involving 36 trauma patients, divided into two groups, the therapeutic algorithm based on FFP transfusion without the application of the ROTEM method was compared to the therapeutic algorithm based on ROTEM testing and administering the coagulation factor without FFP transfusion. A significant difference was found, with the group which was tested with the ROTEM method showing a reduction in transfusion and adverse transfusion events [54]. A prospective study, including 517 trauma patients, showed that thromboelastography enabled quick coagulation status assessment in trauma patients, swift detection of hyperfibrinogenemia, and early administration of the fibrinogen concentrate, which is linked to a much higher survival rate [55]. Additionally, the application of POC methods significantly reduces blood loss and the need for blood and blood product replacement in trauma patients. However, it does not reduce mortality [56].

Naturally, POC methods have their limitations. These are, primarily, the problem of standardization (which is an issue with standard laboratory tests as well) and the cost. The standard temperature for performing POC tests is 37^{0}C, which may impede the detection of coagulopathies occurring in states of hypo- or hyperthermia. Also, coagulopathies resulting from normal physiological state disruption cannot be detected; for instance, abnormal blood pH value, abnormal calcium ion concentrations in the blood, or abnormal hematocrit values [57]. The cost of performing POC tests (equipment, reagents, solutions, maintenance) exceeds the cost of standard laboratory tests. Combined aggregometry and viscoelastic testing costs between 25 and 35 euros, while standard laboratory testing costs less than 10 euros. However, this difference in cost can be compensated by more rational decisions on blood and blood product replacement and application of other therapy, which are made based on POC test results [58]. In his study, Nuttal demonstrated that POC method application resulted in lesser postoperative blood loss, thereby necessitating less blood and blood product replacement [46]. In a study involving 1,422 patients, who had undergone cardiac surgery procedures, Spalding concluded that the application of POC methods led to a financial saving of 50 percent, which was the result of decreased blood and blood product replacement and a decrease in the application of other therapeutic agents [20]. In a retrospective study involving 3,865 cardiac surgery patients, Görlinger compared the financial effect of coagulation therapy application, a year before (2004) and a year after (2009) the introduction of the ROTEM method and the formation of therapeutic algorithms based on ROTEM test results in cardiac surgery patients. A saving of 34.3 percent was found after POC methods application,

godine bolnica zbog upotrebe terapijskih algoritama vođenih *ROTEM* metodom ostvarila uštedu od oko 50.000 dolara. Ekonomska ušteda usled smanjenja nadoknade krvi i njenih derivata može kompenzovati ili prevazići povećanje nastalo utroškom koncentrata faktora koagulacije [42].

ZAKLJUČAK

Istraživanje literature pokazalo je da je *POC* testiranje brže i sveobuhvatnije od standardnog laboratorijskog testiranja i da omogućava efikasniji i ekonomičniji pristup u lečenju. SLT nisu pogodni za brzo i precizno perioperativno identifikovanje poremećaja i nedostataka faktora koagulacije. S druge strane, *POC* metode obezbeđuju brzo postavljanje diferencijalne dijagnoze poremećaja i nedostataka faktora koagulacije, kod postojeće ili novonastale koagulopatije. Samim tim, opravdano je preporučiti upotrebu *POC* metoda u kreiranju terapijskih algoritama u lečenju pacijenata sa specifičnim perioperativnim poremećajima koagulacije. Pored ovoga, *POC* metode imaju ulogu u postavljanju dijagnoze septičnog stanja, a mogu čak biti od značaja u predviđanju mortaliteta kod septičnih pacijenata, iako nije definitivno potvrđen uticaj ovih testova na snižavanje postoperativnog umiranja. S obzirom da nijedna *POC* metoda samostalno ne pokriva celokupni spektar hemostaze, preporučuje se kombinacija agregometrijskih i viskoelastičnih metoda. Terapija koagulopatija i poremećaja nastalih perioperativnim gubitkom krvi treba da bude zasnovana na algoritmima postavljenim na osnovu *POC* metoda.

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and it was concluded that the hospital had saved 50,000 dollars due to the application of therapeutic algorithms guided by the ROTEM method. The economic saving resulting from the reduction in blood and blood product replacement can compensate or even exceed the increase in costs resulting from coagulation factor concentrate expenditure [42].

CONCLUSION

Reference literature analysis has shown that POC testing is faster and more comprehensive than standard laboratory testing and it provides for a more efficient and cost-effective approach to treatment. Standard laboratory tests are not suitable for quick and precise perioperative identification of disorder and deficiency in coagulation factors. On the other hand, POC methods enable a quick differential diagnosis of disorder and deficiency in coagulation factors, in preexisting and newly developed coagulopathy. Therefore, it is justified to recommend the use of POC methods in creating therapeutic algorithms for the treatment of patients with specific perioperative coagulation disorders. Additionally, POC methods play a role in diagnosing sepsis, and may even be important in predicting mortality in septic patients, although the influence of these tests on reducing postoperative mortality has not definitively been confirmed. Since no single POC method can cover the whole specter of hemostasis, it is recommended to combine aggregometry with viscoelastic methods. Treatment of coagulopathies and disorders resulting from perioperative blood loss should be founded on algorithms established on the basis of POC methods.

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