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## PRIMENA TRANSFUZIOLOŠKE KOMPONENTNE TERAPIJE NA OSNOVU ROTACIONE TROMBOELASTOMETRIJE

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**Sažetak: Uvod:** Rotaciona tromboelastometrija je ispitivanje koje ima široku primenu kod pacijenata sa visokim rizikom od krvarenja i to najčešće kod pacijenata sa traumom i u velikim hirurškim intervencijama. Osnovna karakteristika testa je dobijanje rezultata za kratko vreme kako bi se pravovremeno mogla doneti odluka o primeni individualne terapije transfuzijom krvnih komponenti što doprinosi njihovoj racionalnoj upotrebi. **Cilj rada:** Utvrditi zastupljenost komponentata krvi u transfuzijskom lečenju pacijenata u Urgentnom centru Univerzitetskog Kliničkog centra Srbije na osnovu dobijenih rezultata rotacione tromboelastometrije, analizirati učestalost njihove primene u ispitivanoj populaciji i ukazati na prednost ovakvog modaliteta lečenja pacijenata. **Materijal i metode:** Retrospektivnom studijom analizirani su povređeni pacijenti pod rizikom traumom indukovane koagulopatije (TIC), kojima je urađena rotaciona tromboelastometrija u Službi bolničke banke, Odeljenja za pretransfuzijsko testiranje Urgentnog centra Univerzitetskog Kliničkog centra Srbije, u periodu cele 2023. godine. Iz protokola Službe dobijeni su podaci o rezultatima rotacione tromboelastometrije i primenjene terapije komponentama krvi. **Rezultati:** Tokom perioda studije kod 776 pacijenata je izvršeno testiranje korišćenjem rotacione tromboelastometrije što je kod njih 358 (46,13%) zahtevalo terapiju komponentama krvi. Krioprecipitat je primenjen kod 48 (13,40%) pacijenata, koncentrat trombocita kod 69 (19,27%) a krioprecipitat i trombociti istovremeno kod 61 (17,03%) pacijenata. Ostali terapijski modaliteti uključivali su primenu trombocita, dezmopresina i transeksamične kiseline dok je najmanje zastupljena primena zamrznute sveže plazme i to kod svega 17 (4,74%) pacijenata. **Zaključak:** Analiza primenjene komponente krvi u terapijske svrhe u odnosu na rezultate testa rotacione tromboelastometrije je pokazala širok dijapazon terapijskih modaliteta u lečenju pacijenata. Test rotacione tromboelastometrije obezbeđuje primenu individualne terapije krvnim komponentama posledično smanjujući potrebu za transfuzijama, omogućava bolju dijagnostičku preciznost i smanjuje troškove dugotrajnog lečenja pacijenata.

**Ključne reči:** rotaciona tromboelastometrija, terapija, trauma, transfuzija, krvarenje

### UVOD

Rotaciona tromboelastometrija (ROTEM) je ispitivanje koje predstavlja sastavni deo „Point-of-Care“ testiranja. Karakteriše ga da se izvodi u kratkom vremenskom intervalu nakon uzimanja uzorka pacijenta kako bi se mogla doneti pravovremena odluka o transfuziološkom zbrinjavanju pacijenta. Rezultati testa se dobijaju brzo, što omogućava i brzu modifikaciju terapije ako za tim ima potrebe [1]. ROTEM testiranje se sve više uključuje u rutinski dijagnostički algoritam i lečenje krvarenja kod pacijenata koji su pod velikim rizikom od krvarenja kao što su pacijenti sa traumom. U Urgentnom centru Univerzitetskog Kliničkog centra Srbije najveći

broj pacijenata čine oni sa hitnim prijemom kao posledica traume. Brza klinička procena stanja povređenog pacijenta omogućava predikciju nastanka traumom indukovane koagulopatije (TIC) kao i potrebe za aktiviranjem protokola masivne transfuzije [2]. U ove svrhe moguće je koristiti više ROTEM testova koji omogućavaju uočavanje razlike između mehaničkog i hemostatskog krvarenja, identifikaciju poremećaja u različitim fazama hemostaznog procesa zahvaljujući čemu je moguća ciljana i racionalna upotreba krvi i krvnih komponenti. ROTEM predstavlja funkcionalni test koji grafički prikazuje stvaranje i razgradnju ugruška zahvaljujući čemu se može pratiti progresija ili razrešavanje koagulopatije nakon traume [3].

## ROTATIONAL THROMBOELASTOMETRY GUIDED BLOOD COMPONENT ADMINISTRATION

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**Abstract: Introduction:** Rotational thromboelastometry is a diagnostic tool extensively utilized for patients at high risk of bleeding, particularly those experiencing trauma or undergoing significant surgical procedures. This test is notable for providing rapid results, facilitating timely decisions regarding the application of individualized transfusion therapies, thereby optimizing the rational use of blood components. **Aim:** The objective of this study is to assess the utilization of blood components in the transfusion treatment of patients at the Emergency Center of the University Clinical Center of Serbia, based on the outcomes of rotational thromboelastometry. The analysis aims to evaluate the frequency of these interventions in the studied population and to highlight the advantages of this treatment modality.

**Material and methods:** This retrospective study analyzed trauma patients who underwent rotational thromboelastometry at the Hospital Blood Bank, Department of Pre-transfusion Testing, Emergency Center of the University Clinical Center of Serbia, from January 1st 2023, to December 31st 2023. Data regarding the results of the thromboelastometry tests and subsequent blood component therapies were extracted from the Service's protocols. **Results:** During the study period, 776 patients were evaluated by means of rotational thromboelastometry, of which 358 (46.13%) required blood component therapy. Cryoprecipitate was administered to 48 (13.40%) patients, platelet concentrate to 69 (19.27%), and a combination of cryoprecipitate and platelets to 61 (17.03%) patients. Additional therapeutic approaches included the administration of platelets, desmopressin, and tranexamic acid, while fresh frozen plasma was utilized the least, in only 17 (4.74%) patients. **Conclusion:** The analysis of blood components used for therapeutic purposes in relation to the rotational thromboelastometry demonstrated a wide range of therapeutic modalities in the treatment of patients. This testing method facilitates individualized therapy with blood components, subsequently diminishing the need for transfusions, enhancing allows for better diagnostic precision, and reduces costs associated with long-term management of patients.

**Key words:** rotational thromboelastometry, therapy, trauma, transfusion, bleeding

### INTRODUCTION

Rotational thromboelastometry (ROTEM) is a test which is an integral part of "Point-of-Care" testing. It is characterized by being performed within a short time frame after the patient's sample is taken, allowing timely decisions regarding the transfusion management of the patient. The results are obtained quickly, which enables a rapid modification of therapy if needed [1]. ROTEM testing is being increasingly integrated into the routine diagnostic algorithm and management of bleeding in patients at high risk of bleeding, such as trauma patients. At the Emergency Center of the University Clinical Center of Serbia, the majority of patients are those admitted urgently as a result of trauma. A rapid clinical assessment of the injured patient's

condition allows the prediction of trauma-induced coagulopathy (TIC) and the need to activate the massive transfusion protocol [2]. For these purposes, multiple ROTEM tests can be used to distinguish between mechanical and hemostatic bleeding, identify disorders in various stages of the hemostatic process, thereby enabling targeted and rational use of blood and blood components. ROTEM is a functional test that graphically displays the formation and breakdown of a clot, allowing monitoring of the progression or resolution of coagulopathy following a trauma [3].

#### *ROTEM screening tests*

The basic screening tests are the EXTEM and INTEM tests. These screening tests provide

### *Skrining ROTEM testovi*

Osnovni skrining testovi su EXTEM i INTEM test. Skrining testovi daju opštu informaciju o statusu sistema hemostaze. EXTEM test pokazuje senzitivnost za deficit faktora koagulacije iz spoljašnjeg puta dok INTEM test pokazuje senzitivnost za deficit faktora koagulacije iz unutrašnjeg puta i antikoagulaciono delovanje heparina i inhibitora trombina. Oba testa su senzitivna na učestvovanje trombocita u čvrstoći krvnog ugruška, na nivo fibrinogena i polimerizacije fibrina, deficit faktora XIII i hiperfibrinolizu [4,5].

### *Dodatni ROTEM testovi*

Ispitivanje sistema hemostaze proširuje se izvođenjem dodatnih testova: FIBTEM, APTEM i HEPTTEM.

- FIBTEM testu je EKSTEM test za fibrinski deo ugruška. FIBTEM eliminiše doprinos trombocita u formiranju ugruška i omogućava otkrivanje nedostatka fibrinogena ili poremećaja polimerizacije fibrina.
- APTEM test je test zasnovan na EKSTEM testu i omogućava otkrivanje fulminantne hiperfibrinolize. Test pomaže u identifikaciji neophodnosti davanja antifibrinolitičkih lekova. Omogućava procenu da li samo antifibrinolitička terapija normalizuje koagulaciju ili je potrebno preduzeti dodatne mere (npr. davanje fibrinogena ili trombocita)
- HEPTTEM test predstavlja INTEM test koji omogućava identifikaciju nedostataka hemostaze čak i u prisustvu heparina i predstavlja INTEM test bez interferencije heparina ili heparinskih antikoagulanasa [5,6].

### *Parametri ROTEM testiranja*

Primarni rezultat je reakciona kriva u vidu tromboelastograma koji opisuje dinamiku formiranja krvnog ugruška njegov obim, čvrstoću i elastičnost tokom svih faza procesa koagulacije. U rutinskoj kliničkoj praksi analiziraju se sledeći parametri tromboelastograma [6].

#### **1. Vreme koagulacije (eng. Clotting Time: CT)**

Vreme koagulacije (CT) odslikava vreme od aktivacije koagulacije do početnog stvaranja krvnog ugruška tj. do postizanja čvrstoće krvnog ugruška od 2mm. Produženo CT je posledica deficita faktora koagulacije, hiperfibrinolize, hipofibrinogenemije i prisustva heparina. Skraćen CT je posledica hiperkoagulabilnosti.

#### **2. Vreme formiranja krvnog ugruška (eng. Clot Formation Time: CFT)**

Vreme formiranja krvnog ugruška (CFT) odslikava vreme koje je potrebno za postizanje čvrstoće krvnog ugruška veličine 2mm. CFT oslikava inicijalnu polimerizaciju fibrina tj. interakciju između fibrinogena i trombocita.

#### **3. Ugao alfa ( $\alpha$ ugao)**

Ugao alfa predstavlja ugao između horizontalne srednje linije i tangente koja dodiruje koagulacijsku krivu u tački u kojoj je postignuta čvrstoća krvnog ugruška veličine 2mm. On reflektuje kvantitativni i kvalitativni odnos između fibrinogena i trombocita.

#### **4. Maksimalna čvrstoća krvnog ugruška (eng. Maximum Clot Firmness: MCF)**

Maksimalna čvrstoća krvnog ugruška (MCF) predstavlja maksimalnu amplitudu koja se postiže tokom testiranja i ukazuje na stabilnost fibrinskog ugruška. U EXTEM i INTEM testu, MCF oslikava nivo fibrinogena i trombocita dok u FIBTEM testu ukazuje na koncentraciju i funkcionalnost fibrinogena.

#### **5. Maksimalna liza koaguluma (eng. Maximum Lysis: ML)**

Maksimalna liza (ML) koaguluma predstavlja maksimalnu fibrinoliznu aktivnost koja se ispoljava u toku analize i predstavlja procenat lize krvnog ugruška.

### **CILJ RADA**

Cilj rada je utvrditi zastupljenost komponenta krvi u transfuzijskom lečenju povređenih pacijenata u Urgentnom centru Univerzitetskog Kliničkog centra Srbije na osnovu dobijenih rezultata rotacione tromboelastometrije, analizirati učestalost njihove primene u ispitivanoj populaciji i ukazati na prednost ovakvog modaliteta lečenja pacijenata.

### **MATERIJAL I METODE RADA**

Retrospektivna studija analizirala je povređene pacijente (sa traumom) kojima je rađeno ROTEM testiranje u Službi bolničke banke, Odeljenja za pretransfuzijsko testiranje Urgentnog centra Univerzitetskog Kliničkog

general information about the status of the hemostasis system. The EXTEM test is sensitive to the deficiency of coagulation factors in the extrinsic pathway, while the INTEM test is sensitive to the deficiency of coagulation factors in the intrinsic pathway, as well as to the anticoagulant effects of heparin and thrombin inhibitors. Both tests are sensitive to platelet participation in clot firmness, fibrinogen levels, fibrin polymerization, factor XIII deficiency, and hyperfibrinolysis [4,5].

#### *Additional ROTEM tests*

The analysis of the hemostasis system is expanded by performing additional tests: FIBTEM, APTEM and HEPTEM.

The FIBTEM test is an EXTEM test for the fibrin component of the clot. FIBTEM eliminates the contribution of platelets in clot formation and allows detection of fibrinogen deficiency or fibrin polymerization disorders.

The APTEM test is based on the EXTEM test and allows detection of fulminant hyperfibrinolysis. This test helps identify the need for administering antifibrinolytic therapy. It enables the assessment of whether antifibrinolytic therapy alone normalizes coagulation or if additional measures are required (e.g., administration of fibrinogen or platelets).

The HEPTEM test is an INTEM test that allows identification of hemostasis deficiencies even in the presence of heparin and represents an INTEM test without interference from heparin or heparin anticoagulants [5,6].

#### *The parameters of ROTEM analysis*

The primary result is a reaction curve in the form of a thromboelastogram, which describes the dynamics of blood clot formation, its size, firmness, and elasticity throughout all the phases of the coagulation process. In routine clinical practice, the following thromboelastogram parameters are analyzed [6].

#### 1. Clotting Time (CT)

CT reflects the time from the activation of coagulation to the initial formation of the blood clot, i.e., until the clot reaches a firmness of 2 mm. A prolonged CT is the result of coagulation factor deficiency, hyperfibrinolysis, hypofibrinogenemia, and the presence of heparin. A shortened CT is a result of hypercoagulability.

#### 2. Clot Formation Time (CFT)

CFT reflects the time required to achieve firmness of a 20 mm clot. CFT reflects the initial

polymerization of fibrin, specifically the interaction between fibrinogen and platelets.

#### 3. $\alpha$ -Angle

The alpha angle represents the angle between the horizontal baseline and the tangent that touches the coagulation curve at the point where the firmness of the blood clot of 2 mm is achieved. It reflects the quantitative and qualitative relation between fibrinogen and platelets.

#### 4. Maximum Clot Firmness (MCF)

MCF represents the maximum amplitude achieved during testing and indicates the stability of the fibrin clot. In the EXTEM and INTEM tests, MCF reflects the levels of fibrinogen and platelets, while in the FIBTEM test it indicates the concentration and functionality of fibrinogen.

#### 5. Maximum Lysis (ML)

ML represents the maximum fibrinolytic activity observed during the analysis and indicates the percentage of blood clot lysis.

### AIM

The aim of this study is to assess the utilization of blood components in the transfusion treatment of trauma patients at the Emergency Center of the University Clinical Center of Serbia, based on the outcomes of rotational thromboelastometry. The analysis aims to evaluate the frequency of these interventions in the studied population and to highlight the advantages of this type of treatment for patients.

### MATERIALS AND METHODS

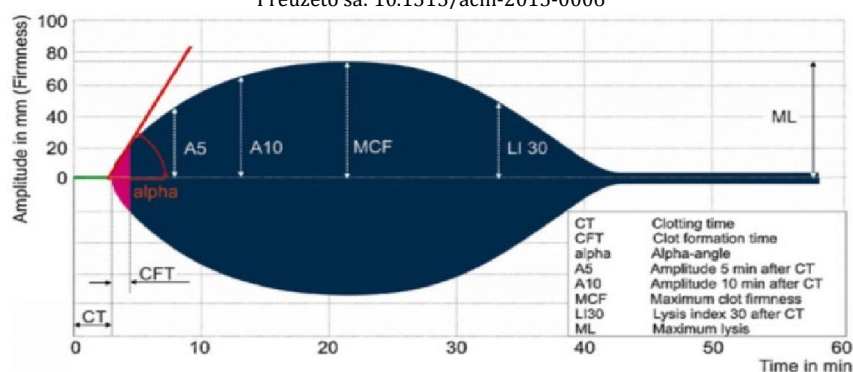
This retrospective study analyzed trauma patients who underwent ROTEM testing in the Hospital Blood Bank, Department of Pre-Transfusion Testing, at the Emergency Center of the University Clinical Center of Serbia, from January 1st 2023, to December 31st 2023. Based on the obtained results, therapy was administered to each patient. Testing on the ROTEM analyzer was conducted using a tube containing 3.2% sodium citrate as an anticoagulant (Vacutainer Brand, Belliver Industrial Estate, Plymouth, UK, 4.5 ml, 9 NC 0.129 M). A volume of 300  $\mu$ L of resuspended blood was taken from the tube for each of the two tests (EXTEM and FIBTEM) using a pipette with predefined aspiration and expiration time intervals, it was placed into the "cup & pin" chamber where specific activators for each test were added. Upon activation of each test, the

centra Srbije, u periodu od 1. januara 2023. do 31. decembra 2023. godine. Na osnovu dobijenih rezultata ordinirana je terapija svakom pacijentu. Testiranje na ROTEM analizatoru je rađeno iz epruvete sa 3,2% Na-citratom kao antikoagulansom (Vacutainer Brand, Belliver Industrial Estate, Plymouth, UK, 4.5 ml, 9 NC 0.129 M). Iz epruvete je uzimano po 300 $\mu$ L resuspendovane krvi za svaki od 2 testa (EXTEM i FIBTEM) i pipetom sa predefinisanim

vremenskim intervalima aspiracije i ekspiracije unošeno u „cup & pin“ čašicu gde su dodavani aktivatori koji su specifični za svaki od testova pojedinačno. Po aktiviranju svakog od testova, rezultati su praćeni na ekranu ROTEM analizatora (Slika 1) i posle dobijanja traženih vrednosti, rezultat je štampan, opisan i sa predloženom terapijom distribuiran ka odeljenima koja su ponela zahtev za navedenu proceduru.

**Slika 1.** Ilustracija ROTEM grafičkog zapisa koji prikazuje sve faze hemostaze.

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U Tabeli 1 su prikazane referentne vrednosti ROTEM-a na osnovu kojeg se ordinirala terapija pacijentima.

**Tabela 1.** ROTEM parametri, normalne vrednosti

|               | CT (s)  | CFT (s) | Alpha (°) | A10 (mm) | A20 (mm) | MCF (mm) | ML (%) |
|---------------|---------|---------|-----------|----------|----------|----------|--------|
| <b>EXTEM</b>  | 38-79   | 34-159  | 63-83     | 43-65    | 50-71    | 50-72    | 0-15   |
| <b>INTEM</b>  | 100-240 | 30-110  | 70-83     | 44-66    | 50-71    | 50-72    | 0-15   |
| <b>FIBTEM</b> | 38-62   | /       | /         | 7-23     | 8-24     | 9-25     | /      |

### REZULTATI

Tokom posmatranog perioda kod 776 pacijenata je izvršeno testiranje korišćenjem ROTEM-a. Na osnovu dobijenih rezultata kod

njih 358 (46,13%) bilo je neophodno da se primeni terapija komponentama krvi, dok kod 418 (53,87%) za takvim vidom terapije nije bilo potrebe (Tabela 2).

**Tabela 2.** Potreba za komponentnom terapijom na osnovu vrednosti parametara ROTEM-a

|                                                                  | N          | %             |
|------------------------------------------------------------------|------------|---------------|
| Pacijenti kod kojih je primenjena terapija krvnim komponentama   | 358        | 46,13         |
| Pacijenti kod kojih nije primenjena terapija krvnim komponentama | 418        | 53,87         |
| <b>Ukupno</b>                                                    | <b>776</b> | <b>100,00</b> |

Pojava znakova kliničkog krvarenja kod pacijenata u odnosu na pol prikazana je u Tabeli 3. Postoji statistički značajna razlika na osnovu

rezultata  $\chi^2$  testa u prisutnosti znakova kliničkog krvarenja u odnosu na pol ( $\chi^2 = 7.989$ ,  $p=0.005$ ). Kod pacijenata ženskog pola, 53,88%

results were monitored on the ROTEM analyzer screen (Figure 1), and once the values were obtained, the result was printed, described, and distributed along with the proposed therapy to

the departments that had requested the procedure.

**Figure 1.** Illustration of the ROTEM graphical record showing all phases of hemostasis. Sourced from: 10.1515/acm-2015-0006.

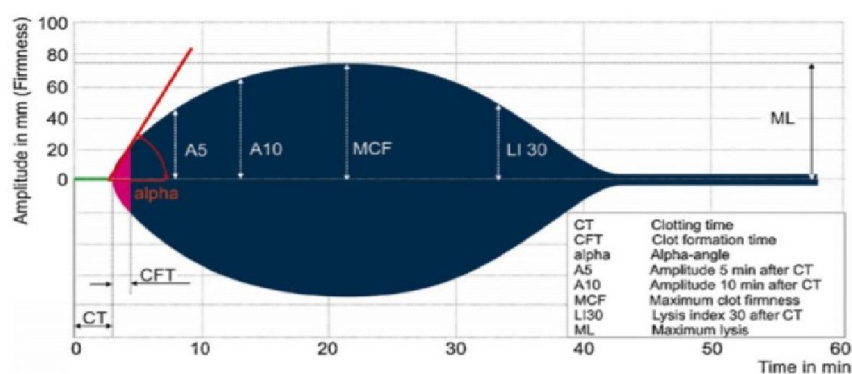


Table 1 presents the ROTEM reference values, on the basis of which the therapy was administered to patients.

**Table 1.** ROTEM parameters, normal values

|        | CT(s)   | CFT(s) | Alpha(°) | A10(mm) | A20(mm) | MCF(mm) | ML(%) |
|--------|---------|--------|----------|---------|---------|---------|-------|
| EXTEM  | 38-79   | 34-159 | 63-83    | 43-65   | 50-71   | 50-72   | 0-15  |
| INTEM  | 100-240 | 30-110 | 70-83    | 44-66   | 50-71   | 50-72   | 0-15  |
| FIBTEM | 38-62   | /      | /        | 7-23    | 8-24    | 9-25    | /     |

## RESULTS

During the observation period, ROTEM testing was performed on 776 patients. Based on the

obtained results, 358 of them (46.13%) required therapy with blood components, while 418 (53.87%) did not need such therapy (Table 2).

**Table 2.** Need for component therapy based on ROTEM parameter values

|                                                            | N   | %      |
|------------------------------------------------------------|-----|--------|
| Patients who received therapy with blood components        | 358 | 46.13% |
| Patients who did not receive therapy with blood components | 418 | 53.87% |
| Total                                                      | 776 | 100%   |

The occurrence of clinical bleeding in patients by gender is shown in Table 3. There is a statistically significant difference in the presence of clinical bleeding related to gender ( $\chi^2 = 7.989$ ,

$p=0.005$ ). Among female patients, 53.88% exhibit clinical bleeding, while 43.83% of male patients show signs of bleeding.

ima znakove kliničkog krvarenja, dok su kod 43,83% pacijenata muškog pola prisutni znaci krvarenja.

**Tabela 3.** Prisutnost znakova kliničkog krvarenja u odnosu na pol

| Pol    | Znaci kliničkog krvarenja |         |     |        | Ukupno % |      |
|--------|---------------------------|---------|-----|--------|----------|------|
|        | Da                        | %       | Ne  | %      |          |      |
| M      | 233                       | 42,83 % | 311 | 57,17% | 544      | 100% |
| Ž      | 125                       | 53,88%  | 107 | 46,12% | 232      | 100% |
| Ukupno | 358                       | 46,13%  | 418 | 53,87% | 776      | 100% |

Pojava znakova kliničkog krvarenja kod pacijenata u odnosu na starost prikazana je u Tabeli 4. Postoji statistički značajna razlika na osnovu rezultata  $X^2$  testa u prisutnosti znakova krvarenja u odnosu na starost ( $X^2 = 104.902$ ,

$p < 0.001$ ). Krvarenje je najviše bilo prisutno u starosnoj grupi od 75 do 84 godine (85,71%) a najmanje kod starosne kategorije od 35 do 44 godine (19,39%).

**Tabela 4.** Prisutnost znakova kliničkog krvarenja u odnosu na starost

| Starost (godine) |  | Znaci kliničkog krvarenja |        |     |        | Ukupno % |      |
|------------------|--|---------------------------|--------|-----|--------|----------|------|
|                  |  | Da                        | %      | Ne  | %      |          |      |
| 23-34            |  | 25                        | 31,65% | 54  | 68,35% | 79       | 100% |
| 35-44            |  | 38                        | 19,39% | 158 | 80,61% | 196      | 100% |
| 45-54            |  | 101                       | 52,33% | 92  | 47,67% | 193      | 100% |
| 55-64            |  | 139                       | 63,18% | 81  | 36,82% | 220      | 100% |
| 65-74            |  | 43                        | 58,11% | 31  | 41,89% | 74       | 100% |
| 75-84            |  | 12                        | 85,71% | 2   | 14,29% | 14       | 100% |
| Ukupno           |  | 358                       | 46,13% | 418 | 53,87% | 776      | 100% |

Distribucija primene krvnih komponenti kod pacijenata prikazana je na Grafikonu 1. Posmatrajući distribuciju krvnih komponenti krioprecipitat je primenjen kod 48 (13,40%) pacijenata, trombociti kod 69 (19,27%), krioprecipitat i trombociti istovremeno kod 61 (17,03%) pacijenta. Primena trombocita i dezmopresina (DDAVP) je bila neophodna kod

72 (20,11%) pacijenta. Upotreba zamrznute sveže plazme (ZSP) je primenjena kod samo 17 (4,74%) pacijenata. Trombociti, traneksamična kiselina (TXA), DDAVP i krioprecipitat su terapijski primenjeni kod 22 (6,14%) pacijenta dok su krioprecipitat, trombociti i DDAVP ordinirani kod 38 (10,6%).

| Table 3. Presence of signs of clinical bleeding by gender |                            |         |     |        |          |
|-----------------------------------------------------------|----------------------------|---------|-----|--------|----------|
|                                                           | Signs of clinical bleeding |         |     |        |          |
| Gender                                                    | Yes                        | %       | No  | %      | Total %  |
| M                                                         | 233                        | 42.83 % | 311 | 57.17% | 544 100% |
| F                                                         | 125                        | 53.88%  | 107 | 46.12% | 232 100% |
| Total                                                     | 358                        | 46.13%  | 418 | 53.87% | 776 100% |

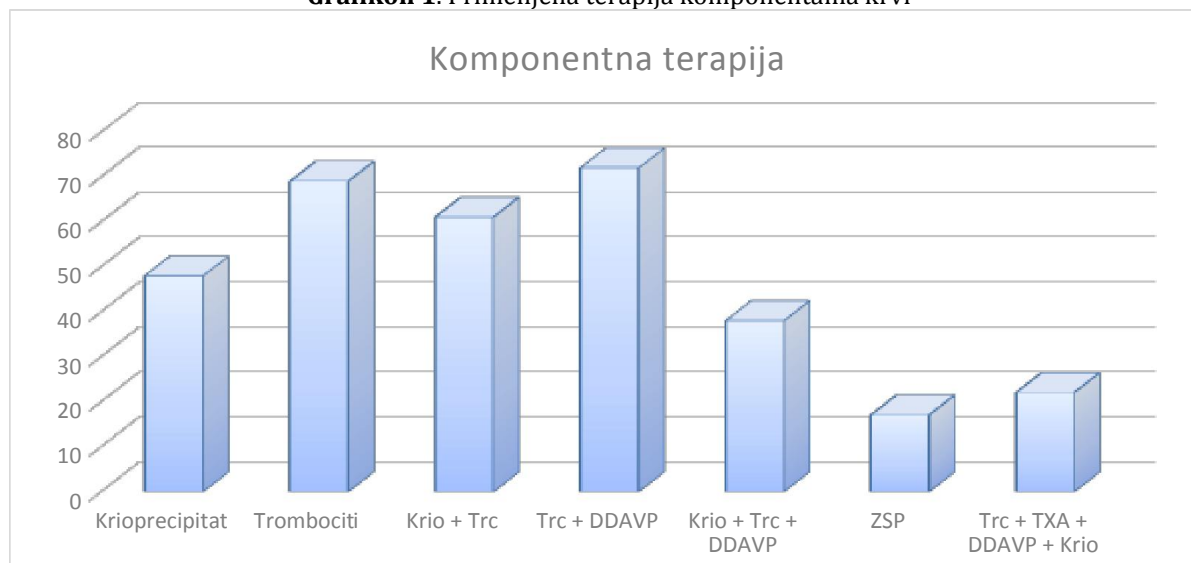
The occurrence of clinical bleeding in patients by age is shown in Table 4. There is a statistically significant difference in the presence of signs of bleeding based on the results of the  $X^2$

test ( $X^2 = 104.902$ ,  $p < 0.001$ ). Bleeding was most prevalent in the age group of 75 to 84 (85.71%) and least prevalent in the age group of 35 to 44 (19.39%).

| Table 4. Presence of signs of clinical bleeding by age |                            |        |     |        |          |
|--------------------------------------------------------|----------------------------|--------|-----|--------|----------|
|                                                        | Signs of clinical bleeding |        |     |        |          |
| Age (years)                                            | Yes                        | %      | No  | %      | Total %  |
| 23-34                                                  | 25                         | 31.65% | 54  | 68.35% | 79 100%  |
| 35-44                                                  | 38                         | 19.39% | 158 | 80.61% | 196 100% |
| 45-54                                                  | 101                        | 52.33% | 92  | 47.67% | 193 100% |
| 55-64                                                  | 139                        | 63.18% | 81  | 36.82% | 220 100% |
| 65-74                                                  | 43                         | 58.11% | 31  | 41.89% | 74 100%  |
| 75-84                                                  | 12                         | 85.71% | 2   | 14.29% | 14 100%  |
| Total                                                  | 358                        | 46.13% | 418 | 53.87% | 776 100% |

The distribution of blood component usage among patients is shown in **Figure 2**. Observing the distribution of blood components, we can see that cryoprecipitate was administered to 48 patients (13.40%), platelets to 69 patients (19.27%), and cryoprecipitate and platelets simultaneously to 61 patients (17.03%). The administration of platelets and desmopressin

(DDAVP) was necessary for 72 patients (20.11%). Fresh frozen plasma (FFP) was used in only 17 patients (4.74%). A combination of platelets, tranexamic acid (TXA), DDAVP, and cryoprecipitate was administered to 22 patients (6.14%), while cryoprecipitate, platelets, and DDAVP were given to 38 patients (10.6%).

**Grafikon 1.** Primenjena terapija komponentama krvi

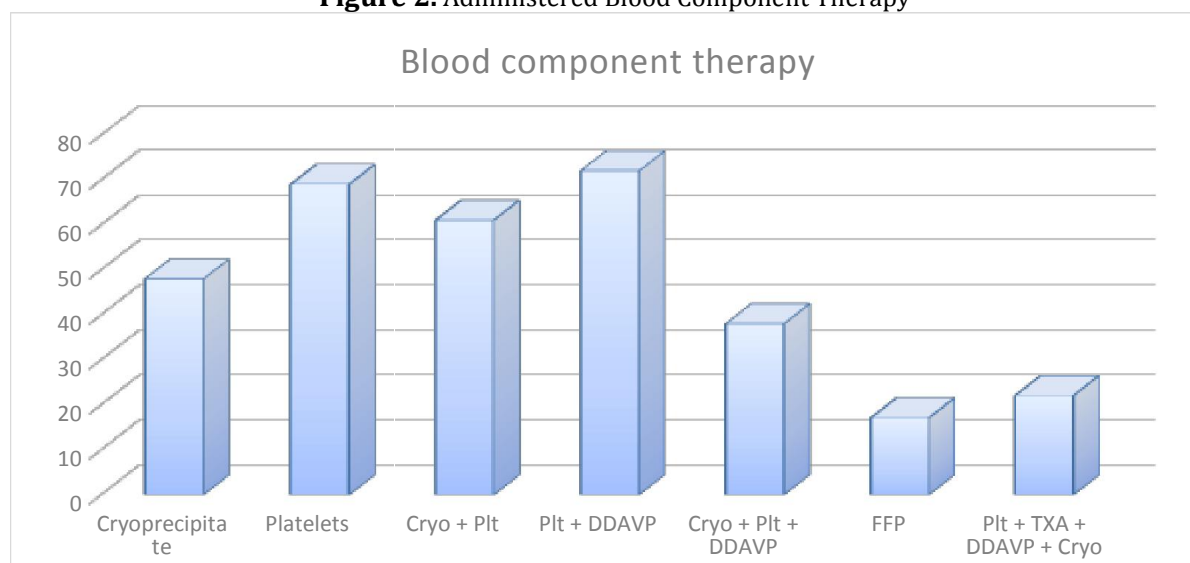
Kod 31 (8,65%) pacijenta potvrđena je tendencija ka hiperkoagulabilnosti od kojih je kod 11 (35,48%) pacijenata preporučena primena Kybernin P 500 kao supstitucija deficita antitrombina.

### DISKUSIJA

Cilj ove studije je bio da se proceni uticaj ROTEM-om vođenih transfuzija na primenu krvnih komponenti kod pacijenata sa traumom. Terapija krvnim komponentama navođena ROTEM-om povezana je sa poboljšanim ishodima pacijenata, posebno što posledično utiče i na smanjenje potrebe za alogenim transfuzijama krvi. Naša studija je imala značajno veći udeo pacijenata muškog pola (70,1%) u odnosu na žene. Razlike u polu kod pacijenata sa traumom su dobro dokumentovane kroz razna istraživanja i to u korist muškog pola. Naime, muškarci su češće zastupljeni kao pacijenti sa politraumom, čemu često doprinosi rizično ponašanje koje podrazumeva upotrebu alkohola kao i vožnju automobila pod uticajem alkohola [1]. Osim toga, najveći broj uzroka višestrukih povreda su svakako posledica saobraćajnih nesreća, povrede na radu, koje se često dešavaju kod mlađih populacija, muškog pola, sa dosta kretanja i teškim radom [1,2]. Takođe, traume se javljaju i kod starijih osoba kao posledica pada i preloma [1,3].

Studije su pokazale da ROTEM može značajno smanjiti zahteve za transfuzijom kod

kardiohirurških pacijenata, kod traume i transplantacije jetre [7,8]. Görlinger sa saradnicima je utvrdio da primena ROTEM-a kod kardiohirurških pacijenata smanjuje potrebu za eritrocitima, ZSP i trombocitima, čime se smanjuju rizici od komplikacija povezanih sa transfuzijom krvi [9]. Rezultati naše studije pokazuju da je ROTEM-om navođena transfuzija prvenstveno rezultirala povećanom primenom fibrinogena u vidu krioprecipitata, bilo kao jedina primenjena komponenta kod 13,40% pacijenata, bilo kroz primenu u kombinaciji sa drugim komponentama. Sprovedena istraživanja pokazuju da ROTEM identifikuje nedostatak funkcionalnog fibrinogena pouzdanije nego standardni testovi hemostaze. Više studija je dokazalo da pacijenti sa stečenim deficitom fibrinogena imaju povišen morbiditet i mortalitet prilikom trauma ili intervencija koje mogu dovesti do krvarenja [10,11]. Schochl sa saradnicima je dokazao da terapija vođena ROTEM-om omogućava brzu korekciju hipofibrinogenemije kod pacijenata sa teškom traumom, smanjujući potrebu za velikim volumenima ZSP i pratećim rizicima [12]. Prilikom javljanja TIC, stečena hipofibrinogenemija je najraniji nalaz koagulopatije [9,12]. Do sniženja koncentracije fibrinogena dolazi usled gubitka krvi, kao i zbog hemodilucije usled primene kristaloida. Već u prvom satu od nastanka krvarenja zapaža se pad fibrinogena [13]. Razlog je nemogućnost jetre da kompenzuje tako značajan gubitak u kratkom

**Figure 2.** Administered Blood Component Therapy

In 31 patients (8.65%), a tendency towards hypercoagulability was confirmed, and in 11 of these patients (35.48%), the administration of Kybernin P 500 was recommended as a substitution for antithrombin deficiency.

### DISCUSSION

The aim of this study was to assess the impact of ROTEM-guided transfusions on the use of blood components in traumapatients. ROTEM-guided therapy with blood components is associated with improved patient outcomes, particularly as it also reduces the need for allogeneic blood transfusions. Our study had a significantly higher proportion of male patients (70.1%) compared to females. Gender differences among trauma patients have been well documented in various studies, with a higher prevalence of males. Specifically, men are more frequently represented as polytrauma patients, often due to risky behaviors that include alcohol consumption and driving under the influence of alcohol [1]. Additionally, most causes for multiple injuries are indeed the result of traffic accidents and work-related injuries, which often occur in younger male populations who are more mobile and engaged in physically demanding jobs [1,2]. Moreover, traumas also occur among the elderly because of falls and fractures [1,3]. Studies have shown that ROTEM can significantly reduce transfusion requirements in cardiac surgery patients, trauma cases, and liver

transplantation [7,8]. Görlinger et al. found that the use of ROTEM in cardiac surgery patients decreases the need for red blood cells, FFP and platelets, thereby reducing the risks of complications associated with blood transfusions [9].

The results of our study show that ROTEM-guided transfusion primarily led to increased use of fibrinogen in the form of cryoprecipitate, either as the sole component administered in 13.40% of patients or in combination with other components. Research indicates that ROTEM identifies functional fibrinogen deficiency more reliably than standard hemostasis tests. Several studies have demonstrated that patients with acquired fibrinogen deficiency have increased morbidity and mortality during trauma or procedures that may cause bleeding [10,11]. Schochl et al. demonstrated that ROTEM-guided therapy enables rapid correction of hypofibrinogenemia in severely traumatized patients, reducing the need for large FFP transfusion volumes and associated risks [12]. In cases of trauma-induced coagulopathy (TIC), acquired hypofibrinogenemia is the earliest sign of coagulopathy [9,12]. Fibrinogen levels decrease due to blood loss and hemodilution from the use of crystalloids. A decline in fibrinogen can be observed within the first hour of bleeding as the liver is unable to compensate for such a rapid loss in a short period. [13]. Rapid identification of hypofibrinogenemia is crucial for the effective treatment of

vremenskom periodu. Brza identifikacija hipofibrinogenemije je ključna za efikasno lečenje koagulopatije. ROTEM takođe omogućava procenu nedostatka trombocita i usmerava na ciljanu terapiju trombocitima. Studija Collinsa i saradnika prikazala je da ROTEM može identifikovati nedostatak trombocita kod pacijenata sa masivnim krvarenjem, omogućavajući adekvatnu i pravovremenu terapiju trombocitima, čime se smanjuju rizici od trombocitopenije i povezanih komplikacija [14]. Trombocitopenija je jedan od faktora koji predviđaju rizik od smrti kod pacijenata sa traumom [9,15]. Primenom ROTEM-a može se za kratko vreme po prijemu pacijenta otkriti da li je neophodna transfuzija trombocita. Ruger sa saradnicima je sugerisao da se korišćenjem ROTEM-a i brzom detekcijom in vivo promena u koagulaciji nakon traume doprinosi u pravovremenoj primeni trombocita jer postoji dobra korelacija između ROTEM-a i standardnih parametara koagulacije i broja trombocita [16]. U grupi pacijenata koje smo analizirali trombociti su primenjivani u više terapijskih modaliteta, i kao pojedinačni oblik terapije kod 19,27% pacijenata, i kao vid terapije u kombinaciji sa krioprecipitatom, DDAVP i TXA. Primena TXA od 1000mg kod trauma pacijenata predstavlja deo protokola sa dokazanim smanjenim brojem intraoperativnog i postoperativnog hemoragijskog sindroma i primenjena je 6,14% pacijenata kao deo terapije koja je uključivala primenu trombocita, DDAVP i krioprecipitata [17]. Primena DDAVP je indikovana kod snižene aktivnosti trombocita i kod 20,11% pacijenata je primenjena u kombinaciji sa trombocitima a kod 6,14% pacijenata kao deo terapije sa trombocitima, krioprecipitima i TXA. Upotrebom ROTEM-a primetno je da je komponenta koja se najmanje primenjivala ZSP. Naime, pre implementacije ROTEM-a, na snazi su bili protokoli koji su se koristili kod pacijenata sa traumom a zasnivali su se na primeni unapred određenog odnosa eritrocita, trombocita i zamrznute sveže plazme (ZSP) i to u fiksnom odnosu 1:1:1. ROTEM

omogućava precizniju identifikaciju koagulacionih poremećaja, što vodi ka racionalnijoj upotrebi ZSP. Tradicionalni laboratorijski testovi, kao što su protrombinsko vreme (PT) i aktivirano parcijalno tromboplastinsko vreme (aPTT), često ne daju kompletnu sliku koagulacije, što može dovesti do prekomerne upotrebe ZSP [18]. Studija Webera sa saradnicima je prikazala da primena ROTEM-a vodi ka značajnom smanjenju upotrebe ZSP u kardiohirurgiji, dok individualna terapija krvnim komponentama vodi ka bržem zaustavljanju krvarenja kod pacijenata [19].

Analizirajući parametre ROTEM-a kod ispitivanih pacijenata vršila se supstitucija odgovarajućih komponenti ili primena hemostatskih lekova kroz ciljanu terapiju koja je usklađena sa individualnim karakteristikama i potrebama pacijenta. Takav način primene transfuzijskog lečenja je imao uticaj na smanjenje primene nepotrebnih transfuzija krvnih komponenti i rizika koje sa sobom nose a istovremeno se efikasnije zbrinjavalo krvarenje kod pacijenata.

### ZAKLJUČAK

Analiza primenjene transfuziološke komponentne terapije u odnosu na rezultate ROTEM testa pokazala je širok dijapazon terapijskih modaliteta u lečenju pacijenata. Kod 776 pacijenata je izvršeno testiranje korišćenjem ROTEM-a. i prema rezultatima ovog testa kod njih 358 pacijenata (46,13%) bilo je neophodno da se primeni terapija komponentama krvi dok kod ostalih 418 (53,87%) za takvim vidom terapije nije bilo potrebe. Rezultati testa obezbeđuju primenu individualne terapije krvnim komponentama posledično smanjujući potrebu za transfuzijama, omogućavaju bolju dijagnostičku preciznost i smanjuju troškove dugotrajnog lečenja pacijenata. Dodatna ispitivanja i integracija u rutinsku kliničku praksu će unaprediti njegovu ulogu u optimizaciji nege pacijenata i upravljanju koagulopatijama.

coagulopathy.

ROTEM also allows the assessment of platelet deficiency and guides to targeted platelet therapy. The study by Collins et al. demonstrated that ROTEM can identify platelet deficiency in patients with massive bleeding, enabling adequate and timely platelet therapy, thereby reducing the risks of thrombocytopenia and associated complications [14]. Thrombocytopenia is one of the factors predicting the risk of death in trauma patients [9,15]. By using ROTEM, the need for platelet transfusion can be determined shortly after the patient's admission. Ruger et al. suggested that the use of ROTEM and the rapid detection in vivo changes in coagulation following trauma contribute to the timely administration of platelets, as there is a good correlation between ROTEM, standard coagulation parameters and platelet count [16]. In the group of patients we analyzed, platelets were used in multiple therapeutic modalities, both as a sole therapy in 19.27% of patients and as a part of combined therapy with cryoprecipitate, DDAVP and TXA. The use of 1000 mg TXA in trauma patients is part of a protocol that has been shown to reduce the incidence of intraoperative and postoperative hemorrhagic syndrome and was administered to 6.14% of our patients as part of a therapy that included platelets, DDAVP and cryoprecipitate [17]. The use of DDAVP is indicated in cases of reduced platelet activity and was administered to 20.11% of patients in combination with platelets and to 6.14% of patients as part of a therapy including platelets, cryoprecipitate and TXA. With the use of ROTEM, it was observed that FFP was the least used component. Prior to the implementation of ROTEM, the protocols in place for trauma patients were based on the

application of a predetermined ratio of red blood cells, platelets, and FFP in a fixed 1:1:1 ratio. ROTEM allows for more precise identification of coagulation disorders, leading to a more rational use of FFP. Traditional laboratory tests, such as prothrombin time (PT) and activated partial thromboplastin time (aPTT) often do not provide a full perspective of coagulation, which can result in the overuse of FFP [18]. The study by Weber et al. showed that the use of ROTEM leads to a significant reduction in the use of FFP in cardiac surgery, while individualized therapy with blood components leads to faster stopping of bleeding in patients [19]. By analyzing ROTEM parameters in the studied patients, the substitution of appropriate blood components or the application of hemostatic medicine was performed through targeted individual therapy for the patient. In this way, ROTEM-guided transfusion therapy reduced the use of unnecessary blood component transfusions and associated risks, with more efficiency in managing bleeding in the patients.

## CONCLUSION

The analysis of blood components used for therapeutic purposes guided by the rotational thromboelastometry demonstrated a wide range of therapeutic modalities in patient treatment. This testing method facilitates individualized therapy with blood components, subsequently diminishing the necessity for transfusions, enabling better diagnostic precision, and reducing costs associated with long-term patient management. Further studies and integration into standard clinical practices are warranted to enhance its effectiveness in patient care optimization and coagulopathy management.

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