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THE INFLUENCE OF OPEN SURGICAL AND ENDOVASCULAR ANEURYSM REPAIR OF AN ABDOMINAL AORTIC ANEURYSM ON HAEMOSTATIC SYSTEM ASSESSED BY ROTEM® TEST

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Abstract

Introduction. The disturbances in hemostasis system in open surgical repair (OR) and endovascular repair (EVAR) of an abdominal aortic aneurysm (AAA), may influence on the perioperative and early postoperative period by inducing serious complications. The aim of this study was to compare the impact of OR of AAA and EVAR on hemostatic system assessed by rotational thromboelastometry (ROTEM®) test.
Methods: The study included 60 patients who underwent elective AAA surgery, divided into two groups (OR and EVAR group - 30 patients in each group). The ROTEM® test was performed in 4 points. Three ROTEM® tests were performed: extrinsically activated assay with tissue factor (EXTEM), intrinsically activated test using kaolin (INTEM), and extrinsically activated test with tissue factor and the platelet inhibitor cytochalasin D (FIBTEM).
Results: No significant difference in age, gender and diameter of AAA between groups was found. The time required for the procedure was significantly longer in OR group and loss of blood was greater in OR group than in EVAR group ($p<0.001$). Extem CT, Extem CFT and Extem angle alpha, show significant differences between groups during the measuring time.
Conclusion: The disorders of hemostatic parameters assessed by ROTEM® test are present in both OR and EVAR, which are more pronounced in OR of AAA. Vigilant monitoring of hemostatic parameters evaluated by ROTEM® can help in administration of adequate and target therapy in patients undergo EVAR and OR of AAA.

Key words: hemostasis; coagulation, factors; endovascular; open surgery repair; abdominal aorta, aneurysm; rotational thromboelastometry; bleeding; complication;

Introduction

Aneurysm of abdominal aorta with its morphological properties leads to disorders of hemostatic system of patient. These disorders could be significantly worsened during and after surgical reconstruction of AAA. Elevated levels of individual coagulation factors, D dimer, and impaired platelet function were noticed pre-operatively very often.[1]

Elective open surgical repair of infrarenal abdominal aortic aneurysm (AAA) is associated with an operative mortality rate of 3% to 10%.[2] Bleeding during operation, cooling the patient, using of anesthetics, as ishaemia reperfusion injury results in a systemic inflammatory response with microvascular and macrovascular thrombosis that may cause myocardial injury, thromboembolism, and multiple organ failure thereby accounting for the great operative mortality. [3,4]

Compared to an open reconstruction, endovascular aneurysm repair (EVAR) of an AAA is safer alternative procedure in anatomically suitable patients. Thus, the EVAR-1, EVAR-2, and Dutch Randomized Endovascular Aneurysm Management trials

reported a 60% reduction in perioperative mortality with EVAR when compared to open surgical repair, but without the differences in late postoperative mortality. [5,6]

Inflammatory response can lead to haemostasis disorders if not more than at least the same as open reconstruction of AAA.[7,8] This is partly explained by the using of intrartery implant - stent graft [9,10] as well as manipulation with radiological introducers and catheter manipulation inside the blood vessel.[11,12] Complication of EVAR- endolaek can lead to functional disorder of hemostatic system, even to development of disseminated intravascular coagulation (DIC) syndrome.[13]

The aim of this study was to compare the impact of OR of AAA and EVAR on hemostasis, assessed by quality of blood clot measured by rotational thromboelastometry – ROTEM® (ROTEM® delta, TEM® International GmbH, Munich, Germany) parameters.

Materials and methods:

The study included 60 patients underwent elective AAA surgery, divided into two groups (OR and EVAR group - 30 patients in each group). The ROTEM® test was performed in 4 points. Three ROTEM® tests were performed: extrinsically activated assay with tissue factor (EXTEM), intrinsically activated test using kaolin (INTEM), and extrinsically activated test with tissue factor and the platelet inhibitor cytochalasin D (FIBTEM).

Written informed consent was obtained from all patients, after a detailed description of the procedure. Criteria for inclusion in the study were: asimptomatic AAA 5,5 cm and higher confirmed by multidetected computerized tomography (MDCT), the technical feasibility of performing the EVAR procedure – EVAR group. The study excluded patients who were known to suffer from any significant disorders in preoperative coagulation, who used oral anticoagulant drugs or antiplatelet drugs last 7 days, than patients with renal function failure, (serum creatinine greater than 200 μmol/L), hepatic disease, active inflammatory diseases and patients with malignancy.

1. Anesthesia
2. The procedure was performed under general anesthesia for all patients. All patients received a heparin at a dose of 100 IU / kg TT 15 minutes before point 2, and in the OR group after withdrawal of the vascular clam, the patients received protamine at a dose of 1 mg / kg. TT for the neutralization of Heparin - 10 minutes before point 3.

EVAR tehnique

On the basis of most-favorable angiographic morphology, we surgically exposed both femoral arteries for EVAR patients. Exclusion of the aneurysm or closing of the access tear was confirmed by angiography immediately following the surgery. Primary success criteria were intraoperative survival, the absence of open surgical conversion, the exclusion of aneurysmal sac and of any transected or dissected tract, the absence of type I orIII endoleaks. We used one or more GORE® EXCLUDER® AAA Endoprosthesis (W. L. Gore & Associates, Inc. Arizona,USA) in all patients: we always implanted a bifurcated prosthesis.

Open repair technique

Surgical approach in all patients in OR group was medial laparotomy with transperitoneal approach to abdominal aorta and iliac vessels. If we would do aortobifemoral reconstruction, femoral vessels would access in inguinal regions. The patient received Systemic Heparin at the dose of 100 IU/kg, and after 5 minutes, the proximal and distal clamping of AAA was initiated. After aortothomy, reconstruction was done in a typical manner, proximal anastomosis between the aorta and graft according to the type of end to end anastomosis endoaneurysmatic, and distal anastomosis was performed depending on the type of reconstruction as end-to-end (tubular graft) or end-to-end with iliac arteries or end-to-side anastomosis with femoral blood vessels (bifurcation graft). After completing the reconstruction and removal of vascular clamps, the patient received Protamine intravenously at an appropriate dose in relation to Heparin (100 IJ Heparin: 1 mg of Protamine). After established circulation and control of haemostasis, the surgery of the surgical wound was made in layers in a typical manner.

Coagulation was monitored by ROTEM®.

Three ROTEM® tests were performed: extrinsically activated assay with tissue factor (EXTEM), intrinsically activated test using kaolin (INTEM), and extrinsically activated test with tissue factor and the platelet inhibitor cytochalasin D (FIBTEM) (Figure 1.)

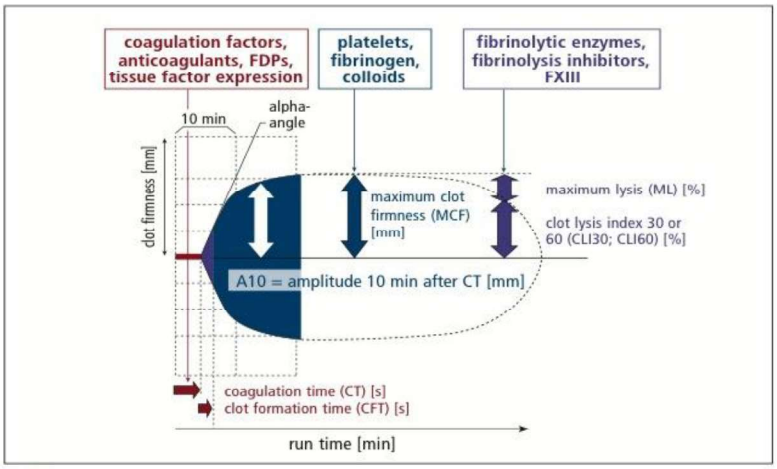

Fig. 1 ROTEM-tracing, parameters and influences: every square is 10 min on the horizontal axis. α-angle: slope of tangent at 20 mm amplitude; CT (coagulation time): time until start of clot formation (detection of a clot firmness of 2 mm); CFT (clot formation time): increasing polymerisation of fibrin and beginning interaction between fibin(-ogen) and platelets (time between detection of a clot firmness of 2 and 20 mm); MCF (maximum clot firmness): interaction between fibin(-ogen) and platelets; CLI (clot lysis index): physiological lysis within 60 min < 15% of MCF

Reference ranges for the tests parameters have been previously determined in a multi-centre investigation [14]

ROTEM tests were performed 10 minutes before starting anesthesia for both groups- point 1, and 10 minutes after placement of aortic clamps for OR group, 10 minutes after the placement of introducer for the road of SG-EVAR group-point 2, and 10 minutes after the release of vascular clamps- OR group, 10 minutes after the finished SG placement end release of femoral clamps- EVAR group- point 3, and 1 h after of finished operation-point 4.

ROTEM tests were performed according to the manufacturer's recommendations, and the analyses were started within five minutes of blood sampling. For prompt assessment of the patient's coagulation status, preliminary test results were obtained as early as five minutes after starting the analysis; the full results followed 10 to 20 minutes after starting the analysis.

Statistics

Continuous variables are presented as mean standard deviation and categorical variables as absolute number and percent value. Differences between groups were assessed using univariate ANOVA for continuous variables, post hoc analysis performed by Bonferroni test, or a chi-square test with the Fisher exact test and odds ratio with 95% confidence intervals for categorical variables; *P*-0.05 was considered significant. The computer program used was SPSS 11.0 (SPSS Inc., Chicago, IL).

Results:

There was no statistically significant difference in response to sex, age and size of AAA. Demographic and clinical characteristics are shown in Table 1.

Patients	Open (n=20)	EVAR (n = 20)	P-value
Age (years)	66.2+ 7,4	68.8+11,01	p=0,253
Sex M/F	27/3 (11.1%)	29/1 (3.48%)	p=0,630
Diameter of aneurysm (cm)	6,6+ 2,02	7,03 + 1.23	p=0,093
Operation time (min)	167.0 + 58.1	102.9 + 34.8	p<0,001
Bleeding volume (ml)	1058.21 + 722.9	389.6+ 161,6	p<0,001
ASA class III or IV	56.5 %	93,1 %	p<0,001

Table 1. Demographic and clinical characteristics

The time required for the procedure was significantly greater for AAA group than EVAR group. Loss of blood was contained for all groups, as shown in Table 1, with a significant difference between AAA and EVAR group (p<0,001), 1 EVAR patient required transfusion of erythrocyte concentrate. Regarding the ASA criteria, there were almost twofold many patients in the II and III categories in the EVAR group. (p<0,001)

Ex-tem CT between groups

The first Ex-tem CT analysis was done between groups. Descriptive statistic examined parameter **Extem CT** is shown in table 2.

Measure	Group				*p*value
	EVAR		OR		
	Arithmetic mean	SD	Arithmetic mean	SD	
A	66.87	12.78	70.38	19.21	0.456
B	79.13	16.10	81.08	24.15	0.768
C	80.69	17.28	94.10	27.93	0.081
D	74.73	13.18	77.08	21.21	0.774

Table 2. Ex-tem CT between groups

From the table it can be seen that in both groups there is an increase in average values and then a decrease in the last measurement. Also, there are no significant differences between groups in any of the four times (time points).Based on the results of the MIX model, it was found that there was a statistically significant difference in the change of the tested parameter in all patients together (F=18,837; p<0,001), there was no statistically significant difference between groups (F=1,069; p=0,306), and there was no statistically significant influence of the group on the change of the tested parameter in time (F=1,613; p=0,197).Distribution of patients compared to Extem CT in these four measurements is also shown graphically (Figure 1).

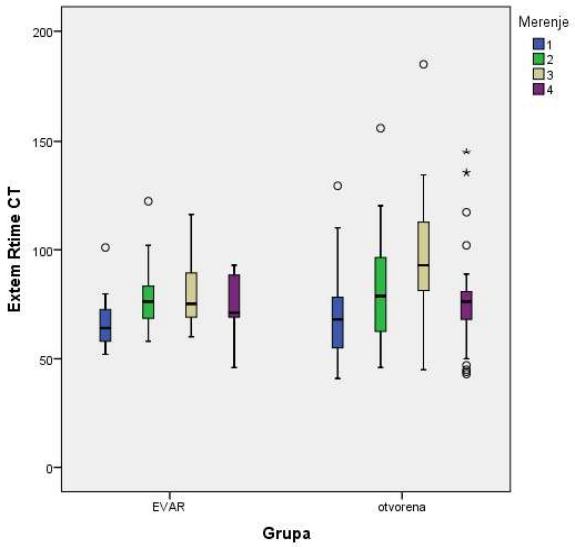

Figure 2. Extem CT between groups

Extem CFT between groups

After CT, CFT was analyzed. Unlike the previous parameter, the distribution here is not conventional, so the logarithmic data transformation was performed for the needs of the analysis, in order to obtain data that are adequate for parametric analysis. Descriptive statistic is shown in table 3 and refers to the original data.

Measure	Group				*p* value
	EVAR		OR		
	Arithmetic mean	SD	Arithmetic mean	SD	
A	70.27	22.330	73.97	25.560	0.572
B	86.88	67.723	85.06	31.997	0.627
C	88.67	47.250	127.23	53.627	0.006
D	99.08	57.456	88.32	31.430	0.944

Table 3. Ex-tem CFT between groups

It is evident that the average value of the tested parameter is jumped at the specified time point, and that jump is much higher in the OR group compared to the EVAR group. Based on the results of the MIX model, it was found that there was a statistically significant difference in the change of the tested parameter in all patients together (F=8,715; p<0,001), there was no statistically significant difference between groups (F=1,925; p=0,171), but there was a statistically significant influence of the group on the change of the tested parameter in time (F=3,350; p=0,026).
Distribution of patients compared to Extem CFT in these four measurements is also shown graphically (Figure2).

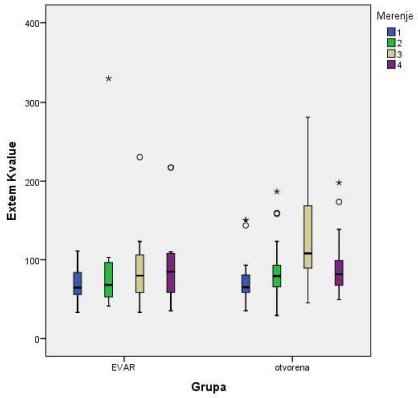

Figure 2. Extem CFT between groups

Extem angle alpha between groups

As in previous analyses, descriptive statistic of the Extem angle Alpha is shown in table 4.

Measure	Group				*p* value
	EVAR		OR		
	Arithmetic mean	SD	Arithmetic mean	SD	
A	76.53	3.87	74.36	6.44	0.208
B	74.81	8.62	74.59	5.30	0.907
C	73.73	7.87	70.13	6.36	0.071
D	72.57	8.81	73.23	5.04	0.804

Table 4. Extem angle alpha between groups

The average values of both groups show a similar trend in time. The only difference is the average difference in the C time point, which is also near the conventional level of significance of 0.05.Based on the results of the MIX model, it was found that there was a statistically significant difference in the change of the tested parameter in all patients together (F=8,541; p<0,001), there was no statistically significant difference between groups (F=0,999; p=0,322), and there was no statistically significant influence of the group on the change of the tested parameter in time (F=2,072; p=0,116).
The distribution of patients in relation to the Extem angle Alpha in these four measurements is also graphically presented on Figure 3.

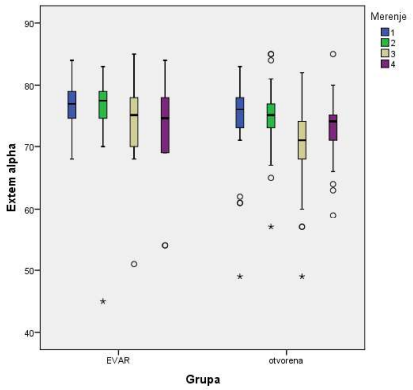

Figure 3. Ex-tem angle alpha between groups

Extem MCF between groups

Descriptive statistic of the Extem MCF is shown in table 5. Due to the non-conventional distribution of data, the logarithmic transformation was made and the data analysis was done on the transformed data. Descriptive statistic is shown on the source data (non-transformed) in table 5.

Measure	Group				*p* value
	EVAR		OR		
	Arithmetic mean	SD	Arithmetic mean	SD	
A	66.93	5.98	64.54	10.82	0.448
B	63.81	9.11	62.56	7.05	0.731
C	58.50	16.40	41.77	12.31	0.037
D	58.71	17.71	53.77	9.20	0.915

Table 5. Extem MCF between groups.

From the table it can be seen that in both cases there is a drop in value to C time point, in order to start the rise in value. Also, the average values are similar in both groups of patients, except at the C time point where there is a far greater fall in average values in the OR group of patients. Based on the results of the MIX model, it was found that there was a statistically significant difference in the change in the tested parameter in all patients together($F=8,541$; $p<0,001$), there was no statistically significant difference between groups ($F=3,166$; $p=0,081$), and there was no statistically significant influence of the group on the change of the tested parameter in time ($F=1,433$; $p=0,243$).The distribution of patients in relation to the Extem MCF in these four measurements is also graphically presented on Figure 4.

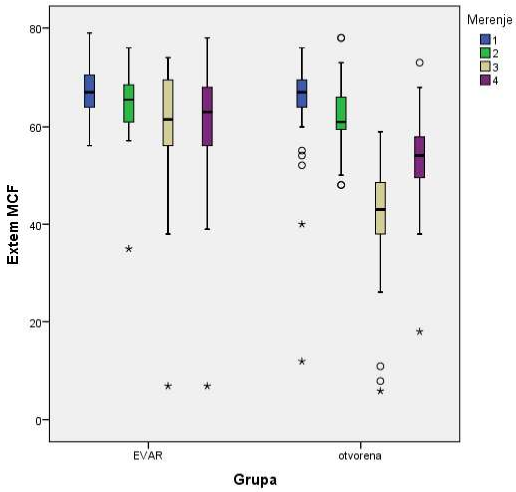

Figure 4. Extem MCF between groups.

Discussion

A very small number of studies have investigated the haemostasis disorder during the intervention itself and in the early postoperative course in the sense of detecting the causes of perioperative and postoperative bleeding, blood and blood products compensation in these two procedures. The goals of patient blood management are adequate preoperative evaluation and optimization of haemoglobin and bleeding parameters, techniques to minimize blood loss, blood conservation technologies and use of transfusion guidelines with targeted therapy.[15]

Hemostatic disorders (bleeding and thrombosis) and their consequences (multiorgan dysfunction, myocardial infarction, cerebrovascular insult and thromboembolism) represent the main cause of morbidity and mortality in surgery of AAA. Intraoperative blood loss can be the result of a technical error or the very bad technique (so-called "surgical bleeding"), but bleeding is often a cause of hemorrhagic diathesis. In a large number of patients, surgical bleeding and coagulopathy together cause a vicious circle in blood loss, which in the end can lead to an immediate life-threatening condition. There are several mechanisms that affect and lead to a disorder of balance between haemostasis and fibrinolysis in the perioperative period of surgical treatment of AAA. Haemostatic disorders, i.e. thrombosis and fibrinolysis can occur as a result of the presence of the AAA, as previously mentioned. Namely, there is often a sub-clinical activation of the hemostasis system due to the existence of a chronic inflammatory condition, but without significant clinical manifestations. In one study, it was described that in nearly 40% of patients with aneurysmal disease levels of fibrin degradation products in serum were elevated, indicating compensated coagulopathy.[16,17] It is widely known that large surgery, in particular vascular surgery, causes a systemic inflammatory response leading to activation of the haemostasis system with changes in process of coagulation and fibrinolysis. The balance is moved to the procoagulant state usually, and blood has a greater tendency to create a clot, causing organ ischemia. However, if there is a disbalance in the coagulation systems, normal mechanisms for inhibiting activated procoagulant proteins are insufficient, and a condition similar to disseminated intravascular coagulation can be created. This is a life-threatening condition and a significant cause of mortality after surgical treatment of AAA. We investigated the changes of ROTEM parameters between groups. The parameters mere analyzed in 4 points intraoperatively (A, B, CandD).

Extem CT was analyzed in both groups and there was a statistically significant difference between the groups at the measuring point C, with significantly higher values in the OR than in the EVAR group. There was a statistically significant difference in the variation of Extem in all patients, statistically significant influence of the group on the change of the tested parameter on time, but without statistically significant differences between groups. This jump of Extem CFT values in point C represents an extension of the clot forming time. The value of this parameter has been increased in both groups in point B also, which is associated with bleeding and a decrease in the concentration of coagulation and platelet factors. The last parameter we examined in Extem was MCF, which measures the firmness and stability of the clot, which depends of the polymerization and fibrinogen, presence of platelets and degree of fibrinolysis. There was a decrease in the strength and stability of the clot in point C, with statistically significant lower values in the OR.This can be explained by the fact that the firmness and stability of the clot is significantly lower in point C in the OR due to a significant blood loss, and therefore the loss of coagulation factors above all of fibrinogen and platelets. The cause of this instability of the clot can result in additional postoperative bleeding.

Conclusion

In this study, the parameters of „Point of Care“ tests were analyzed in patients operated AAA with classical and endovascular techniques. Considering classical hemostatic tests can measure individual aspects of the haemostasis system, and not hemostasis as a whole, we used ROTEM® tests as tests that examined hemostasis as a whole. Using these tests we were able to measure the dynamics of haemostasis in the intraoperative and postoperative period of our patients. During the intervention, but also postoperatively, significant changes occurred in the values of most of the parameters tested, not only at the OR, but also with the EVAR group. In the group of patients with significant bleeding, we found significant changes in the parameters of haemostasis. However, by analyzing the parameters of ROTEM tests we found significant changes in them at the very beginning of the intervention, which told us about the possible risk of bleeding. This primarily relates to parameters: Extem CT, Extem MCF.

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