

Monitoring the hemostasis with rotation thromboelastometry in patients with acute STEMI on dual antiplatelet therapy

First experiences

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Abstract

Rotation thromboelastometry (ROTEM) is a viscoelastometric point-of-care-test for the complex evaluation of changes in hemostasis, performed in whole blood. However, no prospective study evaluating the efficacy of the antiplatelet therapy using ROTEM was performed.

Fifty-six patients (34 men, 22 women, mean age 67.75 years, and age range 34–88 years) with acute ST-elevation myocardial infarction (STEMI), treated with dual antiplatelet therapy, undergoing urgent coronary angiography and percutaneous coronary intervention (PCI) of culprit coronary lesion were included. Three blood samples were taken (sample 1 taken before the urgent coronary angiography, sample 2 in 24 hours after the admission, and sample 3 in 30 days after acute STEMI). Twenty-one healthy blood donors (17 men, 4 women, mean age 50.38 years, and age range 40–74 years) were recruited as the control group. Blood samples were tested with ROTEM Gamma (Pentapharm GmbH, Munich, Germany) and light transmission aggregometry (LTA).

Clotting time (CT) was significantly prolonged and maximum clot firmness (MCF) was significantly higher in patients compared to controls. Mean platelet aggregation after the induction with arachidonic acid (33.2% vs 74.6% in sample 1 and 21.1% vs 74.6% in sample 2), as well as adenosine diphosphate (51.4% vs 72.7% in sample 1 and 37.1% vs 72.7% in sample 2), were significantly lower in patients with acute STEMI.

Significantly prolonged CT and increased MCF was found in patients with acute STEMI. This study confirmed the ability of ROTEM to identify changes in hemostasis in ACS patients on antithrombotic therapy.

Abbreviations: AA = arachidonic acid, ACS = acute coronary syndrome, ADP = adenosinediphosphate, ADPRB = ADP receptor blocker, CFT = clot formation time, CLI = clot lysis index, CT = clotting time, DAPT = dual antiplatelet therapy, LTA = light transmission aggregometry, MA = maximum amplitude, MCF = maximum clot firmness, PCI = percutaneous coronary intervention, PRP = platelet rich plasma, ROTEM = rotation thromboelastometry, STEMI = ST-elevation myocardial infarction, TEG = thromboelastography.

Keywords: acute coronary syndrome, dual antiplatelet therapy, light transmission aggregometry, rotation thromboelastometry

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The authors have no conflict of interest to disclose.

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1. Introduction

Primary percutaneous coronary intervention (PCI) is the principal treatment of choice for patients with acute ST-elevation myocardial infarction (STEMI). Additionally, antithrombotic (mostly dual antiplatelet therapy [DAPT] with aspirin and P2Y12 adenosinediphosphate [ADP] receptor blocker [ADPRB]) therapy forms the basis of pharmacological treatment in these patients.^[1] Nevertheless, not all of the patients achieve the desired clinical outcome despite DAPT. The phenomenon of so-called high on-treatment platelet reactivity was repeatedly connected with the risk for future cardiovascular events, including stent thrombosis.^[2,3] In addition, recently there is an effort to identify patients with high on-treatment platelet reactivity using various laboratory tests of hemostasis.^[4]

On the other hand, bleeding is another serious side effect of intensive antithrombotic therapy and severe bleeding represents the most important limitation of antithrombotic therapy in clinical practice. Previously, in a study performed by Laine et al,^[5] monitoring the hemostasis was able to identify patients with higher risk of noncoronary artery bypass graft-related bleeding on ADPRB therapy. Therefore, monitoring of hemostasis in patients on antithrombotic therapy is intensively studied in order to ensure sufficient on-treatment response and prevent adverse ischemic, as well as bleeding events.

There are many ways for such testing, which vary according to the method of detection, agonists used, and sample material for the analysis. A wide scale of the assays for the monitoring of antiplatelet therapy including turbidimetric light transmission aggregometry (LTA), whole blood aggregometry, assessment of platelet reactivity index or bleeding time, platelet function analyzer (100), the VerifyNow system, Multiplate impedance platelet aggregometry, flow cytometric analysis of the phosphorylation state of the vasodilator stimulated phosphoprotein, flow cytometric analysis of platelet functions in general, Ichor-Plateletworks, HemoStatus device, Impact cone and plate(let) analyzer, or thromboelastography (TEG) are recently available in clinical practice.^[6] Rotation thromboelastometry (ROTEM) is a new viscoelastometric point-of-care-test for the complex evaluation of changes in hemostasis recently introduced to clinical practice.^[7] This assay allows quick complex testing of hemostasis in one blood sample.

In this article, we report our first experiences with the use of ROTEM in laboratory monitoring the hemostasis in patients with acute STEMI on DAPT. We have focused mainly on the testing of clinical usefulness of this method. Last but not least, we provide a review of platelet function tests used for antiplatelet therapy monitoring with the main focus on the LTA and ROTEM-methods used in our study.

2. Study design, patients, and methods

2.1. Study design

A single center preliminary prospective observational study was performed. This study enrolled patients with acute STEMI admitted in order to perform urgent coronary angiography. All patients were treated with DAPT (200–400 mg aspirin loading dose, followed by a maintenance dose of 100 mg/daily and 600 mg clopidogrel loading dose followed by a maintenance dose of 75 mg/daily or 60 mg prasugrel loading dose followed by a maintenance dose of 10 mg/daily or 180 mg ticagrelor loading dose followed by a maintenance dose of 90 mg/twice daily) and weight-adjusted unfractionated heparin (100 IU/kg) administered prior urgent coronary angiography. No other antiplatelet or anticoagulant therapy (including oral anticoagulants) was administered. All patients subsequently underwent urgent coronary angiography together with primary PCI of culprit coronary lesion. Exclusion criteria for patient enrollment included insufficient initial dosage of antiplatelet therapy, “rescue” PCI after thrombolysis, unrealized PCI, primary PCI failure, cardiac arrest with the need of resuscitation, severe cardiac failure (Killip class IV), abnormal blood count (thrombocytopenia, platelet count less than $100 \times 10^9/L$), active bleeding, hemorrhagic stroke in the patient past history, creatinine clearance less than 25 mL/minute, and the history of noncompliance.

The control group was enrolled from healthy blood donors. Exclusion criteria for the control group were following: history of previous PCI, heart failure, anticoagulant or antiplatelet therapy, abnormal blood count (thrombocytopenia), smoking, active bleeding, or history of hemorrhagic stroke.

All included persons agreed with study participation and signed written informed consent prior to blood sampling. This prospective study was approved by the local ethical committee.

Blood samples were taken before the urgent coronary angiography (for the monitoring of the loading doses given in the prehospital setting, sample 1), 1 day after primary PCI (for the

monitoring of the maintenance doses given during the in-patient stay, sample 2) and 30 days after urgent coronary angiography (for the monitoring of the maintenance doses given in the outpatient setting, sample 3). LTA with the use of adenosine-diphosphate/ADP/(concentration 10 $\mu\text{mol/L}$) and arachidonic acid/arachidonic acid AA/(concentration 0.5 mmol/L) as the agonists of platelet aggregation and ROTEM using ex-TEM and fib-TEM reagent were chosen for the laboratory monitoring of hemostasis. Reference range for the use of ADP in inhibition of platelet aggregation was less than 50% of aggregation and for the use of AA less than 20% of aggregation.

2.2. Patients

Fifty-six patients (34 men, 22 women, mean age 67.75 years, and age range 34–88 years) with acute STEMI were enrolled. All patients were treated with DAPT. Clopidogrel was used in 30 patients, prasugrel in 21 patients, and ticagrelor in 5 patients, respectively. Patients underwent urgent coronary angiography and primary PCI of culprit coronary lesion. Average length of the hospitalization was 3.96 days. The average height was 170.43 cm, weight 122 kg, so average calculated body mass index was 42.2 kg/m². Patients reported positive family history of cardiovascular events in 12 cases, smoking in 11 cases at the time of the event, 16 patients were taking proton pump inhibitors (pantoprazole). In 40 of the patients, there was a history of arterial hypertension, 17 of them had type 2 diabetes mellitus, and 31 had dyslipidemia. The demographic data and concomitant medication used in the studied population is given in Table 1.

Twenty-one healthy individuals (17 men, 4 women, mean age 50.38 years, and age range 40–74 years), all enrolled in blood donor program, were recruited as the control group (Table 1). Exclusion criteria for the control group are reported in study design. In this group, 28.5% of individuals (6 individuals) had mild dyslipidemia controlled with dietary regimen (no pharmacotherapy was needed). None of these patients were on antiplatelet or anticoagulant therapy at the time of blood examination.

2.3. Methods

2.3.1. ROTEM testing. ROTEM is a viscoelastometric point-of-care-test for the analysis of changes in hemostasis, performed in whole blood. ROTEM enables rapid and complex evaluation of interactions of clotting factors, inhibitors, and cellular components in the exact stages of blood coagulation and lysis. The measuring module is mobile and can be used to test blood at the bedside of the patient. With the use of specialized reagents activating blood coagulation in vitro it shortens the diagnostic procedure to 15 minutes.

2.3.2. Assay principle. ROTEM was performed with ROTEM Gamma (Pentapharm GmbH, Munich, Germany). Citrated plasma samples (300 μL) were used for the examination. The measuring part comprises a cylindrical cup, in which a whole blood sample was placed. A pin was then immersed into the cup with the pin connected to a detector. The cup and the pin make an oscillation of each other at angle of 4.75°. Between pin and cup, the previously present gap of 1 mm, bridged by the blood, was subsequently formed. It was not able to test the blood viscosity or detect the initiation of blood clotting, when the first signals occurred after pin was connected by the first fibrin fibers filling the entire distance to the cup wall.^[8] This kinetics were detected mechanically and calculated by the computer to the curves and parameters.

Table 1
Demographic data, concomitant medication and baseline (pre-PCI) ROTEM, and LTA parameters in studied acute STEMI patients.

	Studied patient population		Significance
	Patients	Controls	
Number of patients (men/women)	56 (34/22)	21 (17/4)	N/A
Age	67.75 (38–88)	50.38 (40–74)	P=0.12
Arterial hypertension	71.4%	0.0%	P<0.001
Type 2 diabetes (T2D)	30.3%	0.0%	P<0.001
Dyslipidemia	55.4%	28.5%	P=0.09
Family history of cardiovascular diseases	21.4%	9.5%	P<0.05
Smoking	19.6%	0.0%	P<0.001
Beta blockers	88.9%	0.0%	P<0.001
ACE inhibitors or AT1R blockers	66.7%	0.0%	P<0.001
Statins	98.2%	0.0%	P<0.001
Diuretics	37.0%	0.0%	P<0.001
Clopidogrel	53.6%	0.0%	P<0.001
Prasugrel	37.5%	0.0%	P<0.001
Ticagrelor	8.9%	0.0%	P<0.001
Pantoprazole	28.6%	0.0%	P<0.001
Calcium channel blockers	7.4%	0.0%	P<0.001
Clotting time (EXTEM)	62 (57–70) seconds	55 (50–58) seconds	P<0.01
Clotting time (FIBTEM)	58 (51.5–68) seconds	49 (48–55) seconds	P<0.05
Maximum clot firmness (EXTEM)	66 (55–73) mm	63.5 (53–69) mm	P=0.15
Maximum clot firmness (FIBTEM)	19 (15–25) mm	14 (13–17) mm	P<0.05
Clot formation time (EXTEM)	80.0±23.8 seconds	71.6±32.0 seconds	P=0.21
Clot formation time (FIBTEM)	253.6±60.4 seconds	221.0±54.7 seconds	P=0.32
LTA – arachidonic acid induction	33.2±26.1%	74.6±18.6%	P<0.001
LTA – ADP induction	51.4±18.3%	72.7±13.7%	P<0.001

ACE=angiotensin-converting enzyme, ADP=adenosine diphosphate, AT1R=angiotensin 1 receptor, LTA=light transmission aggregometry, ROTEM=rotational thromboelastometry, N/A=not applicable.

2.3.3. Reagents. The assays used in our study were ex-TEM and fib-TEM assay. Blood samples were first recalcified with star-TEM reagent (20 µL, 0.2 mol/L CaCl₂) and subsequently activated by ex-TEM (extrinsic activator/tissue factor/not influenced by aprotinin, sensitive to heparin) or fib-TEM reagent (informing about fibrin clot strength without the influence of platelets inhibited by cytochalasin D). Tests were performed according to the instructions of the manufacturer. The measures, recorded from 2 channels, performing EXTEM and FIBTEM tests simultaneously were: clotting time (CT), clot formation time (CFT), maximum clot firmness (MCF), amplitude representing the clot firmness at various time intervals of the measurement, expressed in minutes (Ax), α angle, and clot lysis index (CLI).

Example of ROTEM analysis using mentioned parameters can be seen in Fig. 1.

CT may be regarded as a standard coagulation time, CFT is defined as the time required for the clot to reach a fixed firmness, MCF represents the maximal amplitude of the tracing and CLI is the residual clot firmness, expressed in percentage of MCF × minute after CT.^[9,10]

2.3.4. Light transmission aggregometry (LTA) testing. LTA was developed in 1962 by Born and O'Brien. The method is still regarded to be the gold standard for platelet function testing, providing the information needed for the diagnosis of platelet function defects.^[11] On the other hand, it is comprehensive, time-consuming, and technically challenging test. Despite these

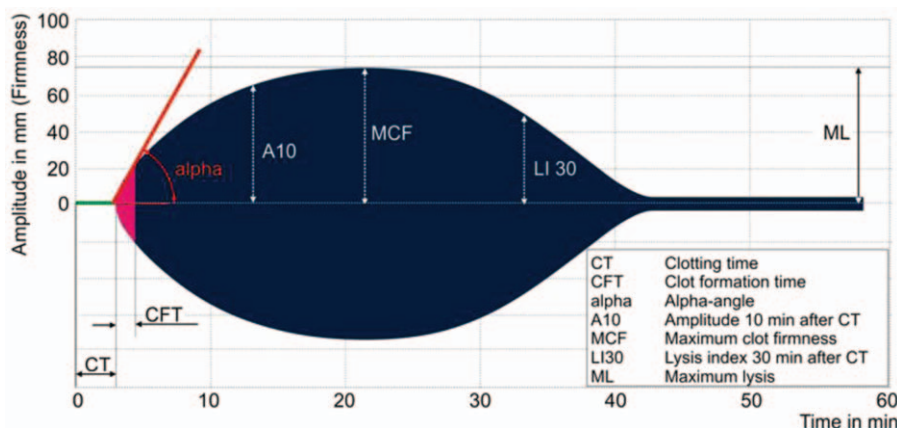


Figure 1. Graphic representation of rotation thromboelastometry (ROTEM) parameters (Pentapharm GmbH, Munich, Germany).

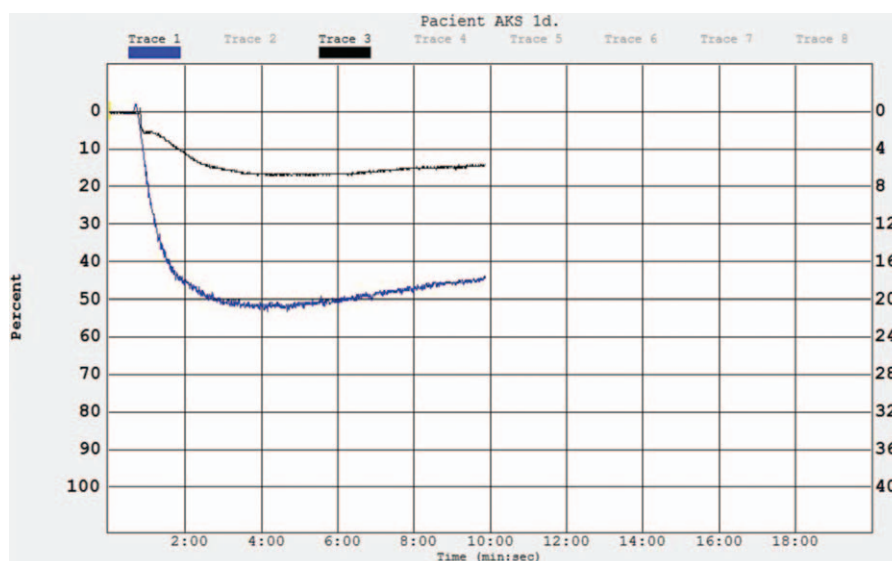


Figure 2. The aggregation curve of the patient after dual antiplatelet therapy loading doses administration.

cons, LTA remains to be widely used method with significant clinical use.

2.3.5. Assay principle and reagents. LTA detects the transmission of light through a sample of platelets in suspension (platelet-rich plasma [PRP], washed or gel-filtered platelets), increasing after platelet aggregation by an agonist. In contrast, a preexisting loose of platelet aggregation in solution may lead to the turbidity reduction. Platelet agonists, such as ADP, epinephrine, collagen, thrombin receptor activating peptide, the thromboxane A2 mimetic U46619, AA, or ristocetin are available.^[11]

We performed LTA with Chrono-log Model 700 Whole Blood/Optical Lumi-Aggregometer (Chronolog Corp., Havertown, PA) with the use of PRP. First we prepared PRP by the centrifugation of patients' plasma for 12 minutes at the speed of 0.9 rotations per minute. For the induction of platelet aggregation, the specific inducers ADP CHRONO-PAR in the concentration 10 $\mu\text{mol/L}$ and Helena Arachidonic Acid Reagent in the concentration 0.5 mmol/L were added, each to 2 plasma samples for the calculation of the final average percentage of platelet aggregability. Meanwhile, the preparation of platelet poor plasma by the centrifugation of patients' plasma for 10 minutes at the speed of 4.4 rotations per minute was necessary. The extent of induced aggregation was defined by the slope of the aggregation curve obtained from the change in light transmission over time. Light transmission was measured in PRP at the start and at the time of the maximum aggregation and compared with platelet poor plasma. Subsequently, we obtained the aggregation curves as illustrated in Fig. 2.

2.4. Statistical analysis

Data were in the 1st step tested for normality with the Shapiro–Walk test. Results are expressed as a number or a percentage (%) of cases, normally distributed continuous or interval-scaled variables are presented as mean \pm standard deviation (SD); otherwise median (M) and quartile ranges from the lower quartile to the upper quartile were used. Data were tested with *t* test or ANOVA in the case of normally distributed

data or with Mann–Whitney *U* test or Kruskal–Wallis test when data distribution was asymmetrical. Differences between proportions were tested with binominal tests. Categorical variables grouped in 2-way contingency tables were analyzed using chi-square tests. The significance of $P < 0.05$ was considered as a criterion for comparison between datasets with equal and unequal variances. The statistical analysis was performed with Statistical v. 7.0 (Stat Soft Inc., Dell Software, and Tulsa, OK).

3. Results

The CT (EXTEM) shortened from the day of income to the 30th day after PCI on treatment by the maintenance dose of DAPT: median 62 seconds (57–70) for the sample 1, median 54.5 seconds (50–62.25) for the sample 2, and 51 seconds (48.25–54.25) for the sample 3, respectively. In control individuals, a CT median of 55 seconds (50–58) was found. CT in controls was significantly shortened in comparison with sample 1 in patients ($P < 0.01$) and the difference in CT between sample 1 and sample 3 in patients (Fig. 3) was also statistically significant ($P < 0.001$). On the other hand, we did not observe a significant difference in other variables,

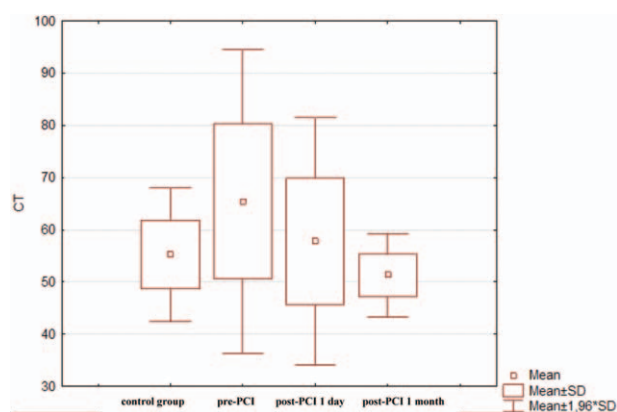


Figure 3. Results of the clotting time (CT) in sample 1 to 3 in the comparison with the control group (EXTEM test).

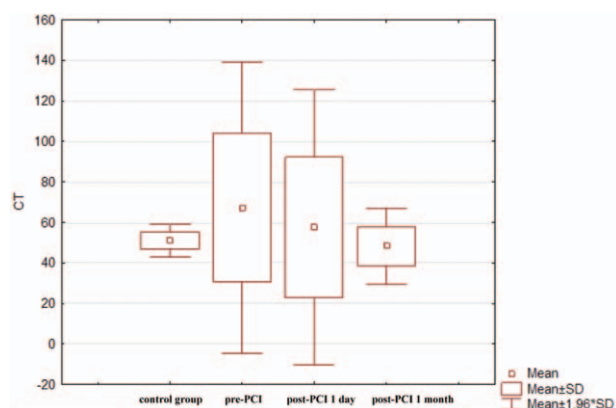


Figure 4. Results of the clotting time (CT) in sample 1 to 3 in the comparison with the control group (FIBTEM test).

such as A5, A10, A15, A20, A25, A30, CFT, MCF, α angle, or CLI30.

The CT (FIBTEM) in the patients with acute STEMI treated with DAPT from the day of income to the 30th day after PCI has also gradually shortened, when compared with control group. Median of CT was 58 seconds (51.5–68 seconds) for the sample 1, 48 seconds (43–55.5 seconds) for the sample 2, and 45 seconds (43–54.5 seconds) for the sample 3, respectively. In control group a CT median of 49 seconds (48–55 seconds) was obtained. In addition, significant differences between the patients with acute STEMI and controls in the amplitudes of the clot firmness measured at various time points were also detected. The median of amplitude A10, detected 10 minutes after CT in patients, examined at sample 1 was 17 mm (14–22 mm), at sample 2 was 17 mm (14.5–24 mm), and at sample 3 was 17.5 mm (15–21.5 mm), respectively. Kruskal–Walis test (Fig. 4) showed a significant difference at the level of $P < 0.05$ comparing A10 in patients with the median of A10 in controls (13 mm, 12–15 mm, respectively).

The median of amplitude A15 (measured 15 minutes after CT) in patients with acute STEMI was significantly different at sample 1 (18 mm [15–23 mm] vs 14 mm [12–16 mm], $P < 0.05$) and at sample 2 (17 mm [14.5–25 mm] vs 14 mm [12–16 mm], $P < 0.05$), when compared with controls. The median of amplitude A20 (detected 20 minutes after CT) in patients with acute STEMI was also significantly different in both samples compared to control individuals (sample 1: 18 mm [15–24 mm] vs 14 mm [13–16 mm], $P < 0.05$; sample 2: 18 mm [15.5–25 mm] vs 14 mm [13–16 mm], $P < 0.05$). Similar differences with increased clot firmness in patients with acute STEMI compared to controls were obtained 25 minutes after CT at sample 1 (median 19 mm [15–24.5 mm] vs 14 mm [13–17 mm], $P < 0.05$) and also at sample 2 (18 mm [15.5–26 mm] vs 14 mm [13–17 mm], $P < 0.05$), respectively. Evaluating the median of amplitude A30 (obtained 30 minutes after CT), we found significant differences ($P < 0.05$) at sample 1 (19 mm [16–25 mm] vs 14 mm [13–17 mm]), at sample 2 (18 mm [15.5–25 mm] vs 14 mm [13–17 mm]) and at sample 3 (20 mm [16–23.5 mm] vs 14 mm [13–17 mm]), respectively. Additionally, when evaluating the MCF in FIBTEM test, median of values obtained at sample 1 was 19 mm (15–25 mm) and at sample 2 was 19 mm (15.5–26 mm), while in the control individuals the median of MCF was significantly lower: 14 mm (13–17 mm), $P = 0.042$ (Fig. 5). However, other variables such as A5, CFT, α angle, and CLI30 were not significantly different.

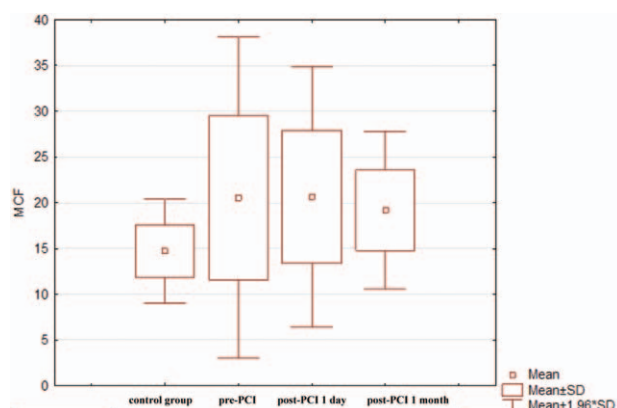


Figure 5. Results of the maximum clot firmness (MCF) in sample 1 to 3 in the comparison with the control group (FIBTEM test).

When testing the on treatment platelet reactivity with LTA, patients with STEMI showed decreased platelet aggregation after the use of both inducers (AA: 33.2% vs 74.6% in sample 1 and 21.1% vs 74.6% in sample 2, respectively; ADP: 51.4% vs 72.7% in sample 1 and 37.1% vs 72.7% in sample 2, respectively).

4. Discussion

As outlined in the introduction, several methods for the evaluation of the efficacy of antithrombotic therapy are currently available. ROTEM represents the dynamic and global method for the evaluation of hemostasis in different groups of the patients.^[12] Its forerunner, TEG has an important role in hepatobiliary and cardiac surgery. It is frequently used in obstetrics and traumatology to identify the causes of postoperative hemorrhage. TEG, method very similar to ROTEM,^[7] is regarded to be a quick and reliable test for the assessment of the effects of antiplatelet therapy on blood coagulation with the use of a novel parameter of area under curve, which could have the role predominantly in patients with acute coronary syndrome (ACS) and PCI.^[13] Modified TEG may be an objective method to assess platelet activity and platelet inhibition during all therapeutic phases in patients with ACS, underscoring the need to improve current therapeutic possibilities. Method provides an advantage in tailoring the therapy, as confirmed not only in the study of patients with unstable angina or non-STEMI, treated with clopidogrel, but also in those with ACS using combined triple antiplatelet therapy.^[14,15]

Many further studies were performed with the TEG^[15–18] or to our knowledge only 1 study using ROTEM with controversial results^[19] in patients with ACS to assess the efficacy of antiplatelet therapy. Despite the fact that in cardiology these methods have been shown to predict thrombotic episodes after the surgical intervention and PCI representing potentially helpful tool to assess the individual reaction of the patients to antiplatelet therapy and even to detect the influence of the tiny dose of aspirin, neither TEG nor ROTEM are still not routinely used in the diagnosis or treatment of thrombosis.^[20] Nevertheless, these tests may provide prognostic data; reduce morbidity and mortality due to thrombotic or hemorrhagic events.^[21]

Traditionally, the maximum amplitude (MA) of the TEG expressing the clot strength has been used to detect the effect of antiplatelet therapy. Previous studies have shown that TEG MA is a predictive parameter for ischemic episodes after PCI in

patients on antiplatelet agents.^[22,23] In the light of these initial presumptions, the results of modified TEG (expressed as clot strength – MA) correlate closely with the historical standard method – LTA.^[24] The study of Ren et al^[15] found that for acute MI patients, loading doses of antiplatelet agents achieve in some cases efficient platelet inhibition very difficultly and despite antiplatelet therapy the platelets remain in these patients in a high activation state (the average MA was 60.87 ± 5.42 mm).

According to our results of LTA using both inducers (AA and ADP), on-treatment platelet aggregation was in acute STEMI patients significantly decreased in the comparison with controls ($P < 0.001$), what may indicate sufficient efficacy of DAPT. Similarly, in ROTEM, the parameter CT was proved to be significantly prolonged in patients after recent STEMI (sample 1) in comparison with controls in both tests (EXTEM and also FIBTEM). This points out to potentially sufficient antiplatelet response to the loading doses of antiplatelet therapy.

On the contrary, clot firmness was significantly increased in patients with STEMI in all 3 examinations, as indicated by the parameters of A10 and A30 compared to controls and did not changed significantly in the course of the treatment. Previously, in the study performed by Ren et al,^[15] MA (in ROTEM MCF as a comparable parameter) more than 60 mm indicated platelet hyperreactivity. In our study, the maximal MCF measured in sample 3 was 68 mm. In fact, the finding of higher MCF in DAPT group might be counter-intuitive, because this parameter is usually connected with hypercoagulation.^[25] MCF represents the maximal amplitude of the tracing and it is possible that DAPT might change the clot formation and therefore affect this parameter. Another possible explanation of this finding is a suggestion that not all the patients achieve sufficient on-treatment response on DAPT maintenance doses (especially given in out-patient settings). However, no other studies examining changes of MCF on DAPT are available, and this indicates that recently there is no satisfactory explanation for this observation. On the other hand, FIBTEM test assesses the hemostasis with the exclusion of the platelet role in the formation of the clot. Therefore, the changes in hemostasis detected with FIBTEM could indicate to the fibrinogen disorder or the fibrin polymerization defect, rather than to the insufficient on-treatment response. These presumptions, however, need to be confirmed by further larger studies.

We decided to test the on-treatment platelet reactivity in 3 different time intervals: prior PCI (to test the efficacy of DAPT loading doses), 1 day after the PCI (to test the efficacy of in-patient DAPT maintenance doses) and 1 month after PCI (to test the efficacy of out-patient DAPT loading doses). Testing the on treatment platelet reactivity with LTA showed more potent platelet inhibition in post-PCI sample after both AA and ADP induction compared to pre-PCI sample. This indicates that more prolonged antiplatelet therapy achieves better platelet inhibition, which corresponds with previously published studies.^[3–4,26] Similar trends were found in CT (EXTEM) and CT (FIBTEM); on the other hand, we did not observe such differences in other ROTEM parameters. Right now, there is no satisfactory explanation for this observation. Therefore, these findings would have to be confirmed and explained in future studies.

In fact, standard parameters of ROTEM do not directly examine platelet function.^[7] Now, specific “platelet mapping assay” for ROTEM had been introduced to practice. This assay measures cloth strength, reflecting maximal platelet function, and detects the reduction in platelet function by both aspirin and clopidogrel.^[27,28]

However, currently there are only limited data about the utility of this assay for the monitoring of DAPT; especially in patients with ACS. This assay was previously tested in healthy volunteers,^[27–29] in non-ACS patients with or without antiplatelet therapy,^[29] in small samples of aspirin and clopidogrel-treated patients requiring acute surgical therapy,^[30,31] or coronary artery bypass surgery,^[32–34] and to predict bleeding in larger sample of acute STEMI patients undergoing primary PCI.^[35] For the detection of DAPT “resistance” there is only a single case report^[36] in patient with acute myocardial infarction; and 1 nonrandomized clinical study^[37] in which authors tried to guide the antiplatelet therapy with this assay (although with negative results) is also available. Moreover, no larger study examining the ability of platelet mapping assay to detect DAPT nonresponsiveness in patients with acute STEMI was performed. To summarize, although the results of so far published studies with platelet mapping assay for ROTEM are generally promising, more research would be definitely needed for the determination of its role in monitoring the efficacy of DAPT in ACS patients.

There were some important limitations of our analysis: 1st, cytochrome P450 2C19 polymorphism may be connected with the phenomenon of “ADP receptor blockers resistance.”^[38] Therefore, cytochrome P450 2C19 genetic polymorphism testing would be definitely useful in our patients and this testing would probably give interesting additional information about the mechanism of DAPT nonresponsiveness in our patients. However, we were not able to do this testing in our studied population due to technical matters. Finally, the drug compliance was not proven by a laboratory testing (measurement of ADPRBs metabolite, etc.) and therefore the exact confirmation of drug compliance with laboratory assessment is missing.

5. Conclusion

Examining acute STEMI patients treated with DAPT using ROTEM we were able to verify significant changes in hemostasis. However, based on current level of evidence, there is no definite answer to the question how does TEG help to adjust the DAPT in patients undergoing primary PCI. The use of ROTEM, including the use of platelet mapping assay for this test, in monitoring the antithrombotic therapy in ACS patients therefore should be studied more extensively.

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