Evaluations of Haemostatic Alterations in Coronary Artery Bypass Graft Patients Before and After Angiography Using Thrombelastography

Sermin Tetik1,2*, Emre Ermengu2, Koray AK3, Nilgün Tekkesin4, Sarfraz Ahmad5 and K. Turay Yardimci1

1Department of Biochemistry & Molecular Biology, Faculty of Pharmacy, Cyprus International University, Mersin Yolu, Nicosia, Cyprus
2Department of Biochemistry, Faculty of Pharmacy, Marmara University, Istanbul
3Department of Heart Surgery, School of Medicine, Marmara University, Istanbul
4Department of Clinical Biochemistry, Memorial Hospital Group, Istanbul, Turkey
5Florida Hospital Medical Center, Orlando, FL 32804, USA

*For Correspondence - stetik@ciu.edu.tr

Abstract
The Thrombelastograph™ (TEG) provides a global assessment of blood coagulation. The study aim was to evaluate the dynamic haemostatic parameters utilizing TEG in blood specimens of hyperlipidemic patients (n=22) and healthy donors (n=15) before and 30 min after the angiography. Such TEG parameters as: reaction time (R, min), clot formation time (K, min), fibrinogen activity (Angle, degree), clotting maximum amplitude (MA, mm), and clotting index (CI) were quantitated. The patients’ values before vs. after the angioplasty were: R = 4.74±1.59 vs. 3.36±0.89 min (5.48±1.39 min for control), K = 2.77±2.45 vs. 1.75±0.95 min (1.57±0.24 min for control), Angle = 64.38±11.21 vs. 69.72±8.22 degree (67.13±6.67 degree for control), MA = 52.2±16.94 vs. 57.84±9.46 mm (59.97±4.73 mm for control), and CI = 0.31±2.59 vs. 1.71±2.07 (0.22±2.14 for control). It is clear that the risk ratio was lowered in patients after the angiography where increased haemostatic defects were detected before the angiography.

Key words: Haemostatic system, Angiography, Thrombelastography, Coronary artery bypass graft.

Introduction
Peripheral artery disease, aside from heart and brain, represents all of the blood arterial diseases (1); however, peripheral endothelial disease definition is used generally for expression of the peripheral artery disease. In contrast, atherosclerosis, which refers to the blood flow through the arms and legs (2,3). Generally, there is no sign of the disease among half of the individuals with peripheric (vein) damar disease. The most common signs of the disease are: intermittent claudication (the intermittent leg ache) with walking and the advanced cases legache when at rest. Angiography is the standard method used for the diagnosis of arterial disease (4), which shows the location and extent of the decrease in passage size or complete blockage of coronary arteries. By detecting the extent of shrinkage or blockage of the vein, the therapy protocol is directed (2).

Haemostasis is the process of dynamic continuous events in human body, which directs as to where and when fibrin formation is needed. It could be analyzed by dividing into two situations, viz., primary and secondary haemostasis. While the primary hemostasis impairment is dependent on platelets and vascular cases, the secondary haemostasis diseases causes coagulation system abnormalities (5). The history and physical examination occupy important places in patients’ identification. For example, the primary haemostasis tests for platelet abnormalities are: platelet count, peripheric smear, and bleeding...
time. For the examination of secondary peripheral impairment, the prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin time (TT), and fibrinogen analysis are commonly used. Of course, depending upon these primary tests, the other advanced tests could be performed accordingly (6).

The Thrombelastograph™ (TEG) provides a global assessment of blood coagulation, taking into account platelet number and function, coagulation factors and natural clotting inhibitors. It is a dynamic and essential test that provides specific results in which whole blood is used, where coagulation is evaluated as a whole and various (multitude) results could be quantitated (7,8). In this study, we sought to determine the stress effect of angiography in the secondary haemostasis system (the haemostatic alterations) in whole blood of coronary artery bypass graft (CABG) patients before and after the angiography utilizing the TEG system, and the data are compared with the normal healthy volunteers.

**Materials and Methods**

After the approval from the primary institution’s Ethics Committee for human subjects use, the written informed consent from all participants of this study were obtained. Twenty-two patients (5 female, 17 male) between the age of 53-75 years, who enrolled to the Marmara University School of Medicine (Department of Heart & Vein Surgery), underwent peripheral arterial angiography procedure because of coronary arterial impairment, formed the basis of this study. Normal healthy volunteers (n=15) that had not taken any anticoagulant / aspirin for 10 days or before and were non-smokers, served as the control group.

Whole blood (10 mL) was drawn from the healthy volunteers as well as from the angioplasty patients (before and after the angiography) in sodium citrate as the anticoagulant (9:1) under vacuum. Blood analyses were performed within 1-2 h after the blood collection in the TEG Analyzer System (Haemostatics Corp., Niles, IL), located in the biochemistry laboratory of the Memorial Hospital, Istanbul, Turkey. Such TEG parameters as reaction time (R, min), clot formation time (K, min), fibrinogen activity (Angle, degree), clotting maximum amplitude (MA, mm), and clotting index (CI) were quantitated for each subject.

The SPSS 11.5 program was used for the statistical analysis. For the data analyses, in addition to the standard statistical methods which give mean ± standard error (SE), one-way ANOVA test was used for the comparisons between the groups with normal variations, and Tukey / standard deviation (SD) test was used for the detection of the group that causes variations. The Kruskal Wallis test was used for comparison of the groups sharing abnormal variations in parameters and Mann-Whitney U-test was used in detecting the groups causing differences. The results are evaluated in 95% dependence and \( p<0.05 \) value was considered statistically significant.

**Results**

The demographics and baseline/clinical characteristics of the patients and the control groups are shown in Table 1. While a majority of subjects in this study were male, about a quarter of them were females in both groups. The mean value for patients’ LDL was higher compared to the control group (168±16.4 vs. 89±6 mg/dL), the HDL level was 47±4.3 mg/dL and triglyseride was 240±25.7 mg/mL that were comparable to the control group. Also, the platelet counts were within the normal range for both group of subjects.

Fig. 1A show TEG results on Reaction Time (R), which was decreased after angiography (3.36±0.89 min) as compared to the control group (5.48±1.39 min, \( p<0.05 \)) and the value before angiography was 4.74±1.59 min (\( p>0.05 \)). The R time of CABG patients on individual case basis before and after the angiography are presented in Fig. 1B.

The mean clot formation time (K) for the control group was determined to be 1.57±0.24 min, which was not significantly different for the patients group (before angioplasty = 2.77±2.45 min, \( p>0.05 \)).
The results obtained on the TEG analyses for the fibrinogen activity (Angle) are shown in Fig. 3. Compared to the control group (67.13±6.67 degree), the mean values for fibrinogen activity was not significantly different as compared to the

\[ \text{min, after angioplasty} = 1.75\pm0.95 \text{ min (p>0.05)} \].

Wide variations in the values were noted throughout the experiment (Fig. 2A). Fig. 2B shows the data on individual patients’ K values for before and after the angioplasty.

**Fig. 1** (A) The Reaction Time (R) of controls and the GABG patient groups before and after the angiography as determined by TEG analyzer. (B) Data shows the individual R values determined for each patients before and after the angiography.

**Fig. 2** (A) Clot formation time (K) of the control and the CABG patient groups before and after the angiography as determined by TEG analyzer. (B) Data shows the individual K values for each patients determined before and after the angiography.

**Fig. 3** (A) The fibrinogen activity (Angle) of the controls and the CABG patient groups before and after the angiography as determined by TEG analyzer. (B) Data on the fibrinogen activity (Angle) for individual patient as determined before and after the angiography.

Haemastatic System and Angioplasty
patients group (before angioplasty 64.38±11.21 vs. 69.72±8.22 degree after angioplasty, p>0.05) (Fig. 3A). Again, wide variations were noted. The actual data on the individual patient’s fibrinogen activity before and after the angioplasty is shown in Fig. 3B.

Fig. 4 shows the TEG data obtained for the clot maximum amplitude (MA) values. As shown in Fig. 4A, increase in MA of the clot formation was detected before and after the angiography in CABG patients [before angioplasty = 52.20±16.94 mm, and after angioplasty = 57.84±9.46 (n=22)], which was not significantly different from the control group values [59.97±4.73 mm (n=15)]. The MA values are relative to the blood fibrinogen concentration in the patient group. The MA of clot values for individual patients before and after angiography are shown in Fig. 4B.

The results on the clot index (CI) determination by TEG analyzer are shown in Fig. 5. There was significant increase in the CI values, particularly after the angiography. As compared to the CI values for the control group [0.22±2.14 (n=15)], the CABG patients CI values were 0.31±2.59 (before angioplasty) and 1.71±2.07 (after angioplasty; p<0.05, n=22). The individual patients’ results thus obtained in reference to angiography are presented in Fig. 5B.
Discussion

The haemostatic system can be altered in relation to impairment of the equilibrium between the activation of clot forming factors and the anticoagulant system. It is well known that the important parameters related to atherosclerosis, viz., high blood lipid profile, hypertension or diabetes are highly relevant where these patients have high myocardial infarction ratio (9). The haemostasis is governed by complex mechanisms where related systems are in interplay with each other, having synergistic effects, including the stimulation of the opposite mechanisms. Also, individual body’s immune system and associated mechanisms as a whole play multifunctional roles (10-12). The haemostasis is analyzed according to its structural and functional entities, i.e., as primary and secondary systems. While the primary haemostasis is related to the platelet plug development in the damaged area of the vein, secondary haemostasis includes the plasma coagulation system reactions (13). Thus, haemostatic system works in relation with blood arteries, vein surfaces, endothelial system, platelets, coagulation factors, coagulation inhibitors, and fibrinolytic systems.

The TEG technique is an alternative method to conventional coagulation tests used in evaluation of the haemostatic system in general (9,14). The TEG is easily performed, with a relatively shorter turn-around-time and could evaluate the clot with its mechanical and visco-elastic specifications in the haemostatic system as a whole (15). The TEG generates several parameters during the clotting process. In patients where heart surgery is performed, the accurate evaluation of the serious haemostatic changes which play important role(s) in decreasing the transfusion quantity that causes the complications of the surgery is needed.

In this study, we demonstrate significant decrease in the reaction time after angiography utilizing TEG parameters analyses. In this patient group, the decrease in reaction time could have been one of the risk factors caused by angiography. While analyzing to angiography on the individual case basis for the increased reaction time (especially after the angiography), the decrease in reaction time becomes more significant/obvious. Notably, the clot formation time, fibrinogen activity, and maximum amplitude (before and after angiography) did not show much

<table>
<thead>
<tr>
<th>Factors</th>
<th>Patients (n=22)</th>
<th>Control (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>65 ± 12</td>
<td>52 ± 16</td>
</tr>
<tr>
<td>Gender (Female/Male)</td>
<td>5/17</td>
<td>4/11</td>
</tr>
<tr>
<td>Hypertension</td>
<td>13</td>
<td>N/A</td>
</tr>
<tr>
<td>Renal Pathology</td>
<td>5</td>
<td>N/A</td>
</tr>
<tr>
<td>On Statin, β-3-Blocker, ACE Inhibitor</td>
<td>6</td>
<td>N/A</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td>168.0 ± 16.4</td>
<td>89.0 ± 6.0</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)</td>
<td>47.0 ± 4.3</td>
<td>45.0 ± 8.7</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>N/A</td>
<td>175.0 ± 20.0</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>240.0 ± 25.7</td>
<td>210.0 ± 21.4</td>
</tr>
<tr>
<td>Platelet Count (x10⁹/L)</td>
<td>248.4 ± 27.8</td>
<td>210.0 ± 14.6</td>
</tr>
</tbody>
</table>

Data are shown as mean ± standard deviation values

Abbreviations: N/A = not applicable; ACE = angiotensin-converting enzyme; LDL = low-density lipoprotein; HDL = high-density lipoprotein;
variations. Also, the clot index in the patients (after angiography) was not significantly different as compared to the control group’s index.

Based on the individual case for the CI analysis, four patients (before angioplasty) showed hypercoagulation, and three patients (after angioplasty) showed hypercoagulation tendency. The specific observations in clot formation time, fibrinogen activity, clot maximum amplitude showed in the patients with coagulation risk, their haemostatic balance is taken under control by angiographic performances (18). Literature suggests that in patients where heart surgery is performed, the TEG analysis is highly recommended as one of the blood protective methods (9).

In recent years, thrombolytic treatments have been widely used in the clinical situations where abnormal thrombosis is also present (16). These thrombolytic treatments, not only used in acute myocardial infarction, but also in pulmonary emboli, arterial emboli and deep-vein thrombosis cases, where morbidity and mortality is high and serves as superior treatment options. In such cases during angiography, the treatment method selection may cause decrease in systematic side effects (16,17). Hence, in decreasing the microvascular bleeding and selection of effective anti-fibrinolytic agent during the surgery/treatment regimen, the use of TEG serves as a quick directive method (15). For example, while evaluating the TEG parameters, elongation in R time and decrease in MA resulting regimens due to aprotinin treatment regimen may draw attention to clinicians (15).

Frequently seen defective haemostatic system should be followed in high number of heart surgery patients analyzed with conventional comparative analysis. In this work, increased coagulation in the patients at the end of angiography, the risk ratio was lowered. With the TEG method, the use of anticoagulant and antifibrinolytic agents were effective factors that could be appropriately evaluated in light of these TEG analyses. Thus, we demonstrate that the risk ratio is lowered in the patients after angiography where increased coagulation were detected before the angiography.

References


