Original Article

The application of thromboelastogram in detection of indexes of antiplatelet therapy for coronary heart disease

Shu-Wu Zhao[1], Yu-Ping Wang[2], Lin-Dong Xu[1], Wei Gang[1]

[1]Department of Cardiology, Dagang Hospital of Binhai New Area, Tianjin 300270, China; [2]Department of Cardiology, Haibin People's Hospital of Tianjin City, Tianjin 300280, China

Contributions: (I) Conception and design: SW Zhao; (II) Administrative support: LD Xu; W Gang; (III) Provision of study materials or patients: LD Xu; W Gang; (IV) Collection and assembly of data: SW Zhao; (V) Data analysis and interpretation: SW Zhao; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Shu-Wu Zhao. Department of Cardiology, Dagang Hospital of Binhai New Area, No. 1200 of Nanhuan Road, Dagang District, Tianjin 300270, China. Email: shuwuzhaodoc@163.com.

Background: This study aims to explore the application value of thromboelastogram (TEG) in antiplatelet therapy in coronary artery intervention.

Methods: A retrospective analysis of 90 cases of coronary interventional treatment was conducted in our hospital from January 2010 to January 2012. Cases were divided into three groups, according to the kind of coronary heart disease: angina pectoris (AP) group (30 cases), unstable angina pectoris (UAP) group (30 cases) and acute myocardial infarction (AMI) group (30 cases). TEG changes in patients between the three groups were analyzed.

Results: The differences in international normalized ratio (INR) and activated partial thromboplastin time (APTT) indexes among the three groups of patients were statistically significant (P<0.05), but these indexes significantly decreased in the AMI group. Furthermore, D-D, Fgb, Angle and MA indexes significantly increased in the UAP and AMI groups, compared with the AP group; while TEG regular parameter K and R values were markedly reduced. Coagulation graphics were higher in the UAP and AMI groups than in the AP group (χ^2=4.261, 3.908; P<0.05), suggesting that the difference was statistically significant. In 11 cases of ischemic events, arachidonic acid (AA)-induced platelet inhibition rate was 63.63%, while adenosine diphosphate (ADP)-induced platelet inhibition rate was 36.37% (χ^2=5.026; P<0.05); suggesting that ADP-induced platelet inhibition rate was markedly reduced. This is the main risk of ischemic events within three months after percutaneous coronary intervention.

Conclusions: The detection of indexes of antiplatelet therapy in coronary artery intervention is helpful for antiplatelet medication, thus can effectively reduce the incidence of ischemic events.

Keywords: Thrombus elasticity; coronary intervention; antiplatelet therapy

Submitted Jul 15, 2016. Accepted for publication Dec 02, 2016.
doi: 10.21037/jtd.2016.12.77
View this article at: http://dx.doi.org/10.21037/jtd.2016.12.77

Introduction

Thromboelastogram (TEG) is an index that can comprehensively reflect dynamic changes of blood coagulation (1). The detection of TEG can help completely understand the whole process of the fibrin formation and dissolution in whole blood sample, which makes the analyis of platelet aggregation, fibrin cross connection and the blood clot dissolution process possible (2). Interventional therapy is one of the methods for the treatment for coronary heart disease. In order to inhibit the aggregation of platelets in the stent, and prevent thrombosis, anti-platelet therapy should be given before and after intervention (3). In order to investigate the index-detecting value of TEG in

Table 1 General data of the two groups were compared with [n (%)]

Group	Gender	N	Age (years)	Median age (years)
AP	Male 12 cases, female 18 cases	30	42–80	61±25.3
UAP	Male 19 cases, female 11 cases	30	45–78	61.5±27.8
AMI	Male 14 cases, female 16 cases	30	48–79	63.5±28.1

Note: the difference was statistically significant (P<0.05). AP, angina pectoris; UAP, unstable angina pectoris; AMI, acute myocardial infarction.

antiplatelet therapy in percutaneous coronary intervention (PCI), the author conducted a retrospective analysis of the clinical data of 90 patients who underwent PCI in our hospital from January, 2010 to January, 2012.

Methods

General information of 90 patients who underwent PCI from January 2010 to January 2012 at our hospital was included into the study. The diagnosis of coronary heart disease in all patients was in line with the criteria of World Health Organization (WHO), and TEG was monitored in patients during antiplatelet therapy. Exclusion criteria mainly included three aspects: first, patients who recently used drugs affecting coagulation function (such as Bloven, etc.); second, patients with histories of tumors, severe liver and kidney or blood system diseases; third, patients with severe infection history and clopidogrel- and aspirin-allergy histories. After admission, all 90 patients were given aspirin, clopidogrel, statins, beta blockers, calcium antagonists, angiotensin converting enzyme inhibitors, and so on. According to the clinical classification of coronary heart disease, the 90 patients were divided into three groups: stable angina pectoris (AP) group, unstable angina pectoris (UAP) group and acute myocardial infarction (AMI) group (n=30, each group). In the AP group, five cases had a history of hyperlipidemia, seven cases had a history of diabetes, eight cases had a history of hypertension, nine cases had a history of smoking, eight cases had a history of drinking; in the UAP group, seven cases had a history of hyperlipidemia, six cases had a history of diabetes, six cases had a history of hypertension, ten cases had a history of smoking, eight cases had a history of drinking; in the AMI group, eight cases had a history of hyperlipidemia, five cases had a history of diabetes, nine cases had a history of hypertension, eight cases had a history of smoking, nine cases had a history of drinking. The differences in gender (F=1.028; P=0.971), age (F=0.936; P=0.542), and basic diseases (F=1.443; P=0.870) among the three groups were not statistically significant. General information of the two groups of patients is listed in *Table 1*.

Apparatus and equipment

TEG 5000 thrombelastogram system and matching test cup and reagent [Haemoscope Corporation, States Food and Drug Administration (import) no. 2402231 2009] were used. The fully automatic blood coagulation analyzer (STAGO, France) was used to measure coagulation function (four indexes): prothrombin time (PT), thrombin time (TT), activated partial thromboplastin time (APTT), and fibrinogen (FIB).

Specimen collection and detection methods: one to three days after PCI fasting venous blood (2 mL) from the patients, for TEG detection. Anticoagulation was performed with 3.8% sodium citrate, and then the blood samples were analyzed within two hours by professional analyzer, according to the rules of operation, 4 mL of blood for coagulation testing and 2 mL for routine blood testing. The detection of platelets inhibition was detected by 0.5 g/L arachidonic acid (AA) and 1.0 μmol/L adenosine diphosphate (ADP).

Drug treatment methods: at preoperative 72 hours, clopidogrel (Produced by Hangzhou Sanofi Minsheng Pharmaceutical Co., Ltd.; National drug approval: No. H20056410) was administered. The initial dose was 300 mg, and from the second day the dose became 75 mg/time, 1 time/day, and aspirin (Produced by Bayer healthcare Co., Ltd.; National drug approval: No. J20080078) was given.

TEG graphic comparison method: according to the score of the index, the TEG graphics can be divided into two types, namely, normal graphics and hypercoagulability graphics. Commonly, normal graphics has eight indicators: the coagulation reaction time (4–8 minutes), blood clot forming time (1–4 minutes), the included angle between the tangent at the maximum curve and the horizontal line (47–74°), the maximum range of the graph (55–73 mm), the elastic force of thrombus (–3 to 3), LY30 (0–8%), and EPL

Table 2 TEG changes in the three groups of patients

Group	R (min)	K (min)	Angle (¢X)	MA (mm)	CI	LY30	TT	PT (s)	APTT (s)	Fgb (g/L)	PLT ($\times10^9$/L)	INR	D-D (mg/L)
AP [30]	6.25±1.50	3.14±0.76	56.51±5.02	29.52±15.04	−3.60±3.74	1.05±2.39	18.82±10.03	15.39±2.07	34.24±5.33	3.29±0.73	209.83±82.17	0.91±0.12	0.10±0.07
UAP [30]	5.88±2.69	2.61±0.82	62.65±5.22	29.52±15.04	−3.80±4.43	1.17±2.94	20.14±12.02	14.02±2.18	37.91±7.13	3.75±0.66	215.31±92.20	0.80±0.11	0.24±0.10
AMI [30]	5.42±4.53	2.47±0.60	65.27±17.34	37.61±13.29	−2.29±3.02	0.35±0.65	22.40±4.13	20.71±6.85	45.22±13.28	4.36±1.20	206.74±85.42	0.75±0.04	0.34±0.13
F value	0.0086	0.0139	0.0000	0.0000	0.0000	0.0000	0.0000	0.4203	0.0000	0.0097	0.9682	0.0000	0.0000
P value	0.0086	0.0139	0.0000	0.0000	0.0000	0.0000	0.0000	0.4203	0.0000	0.0097	0.9682	0.0000	0.0000

TEG, thromboelastogram; AP, angina pectoris; UAP, unstable angina pectoris; AMI, acute myocardial infarction; TT, thrombin time; PT, prothrombin time; APTT, activated partial thromboplastin time; INR, international normalized ratio.

(0–15%). When clotting time and blood clot forming time decreased, and the maximum range of the graph increased, the coagulation function of patients was disordered, hypercoagulability occurred

Observation index

Within three months after discharging from the hospital, patient's recovery situations, the presence of ischemic events, fatal and non-fatal myocardial infarction, heart failure and unstable angina pectoris were followed-up by outpatient review and phone-call inquiry, and the medication of antiplatelet drugs was analyzed.

Statistical data were processed by SPSS16.0 software

Measurement data were expressed as mean ± standard deviation ($\bar{x}$ ± SD), and count data were expressed as percentage. Intergroup comparison was conducted using F-test. P<0.05 was considered statistically significant.

Results

Comparison of changes in TEG among the three groups

Changes in TEG indices are listed in *Table 2*. The differences in PT and PLT among the three groups of patients were not statistically significant (P>0.05), and the differences in APTT and international normalized ratio (INR) among the three groups of patients were statistically significant (P<0.05), and the degrees of decrease in these indices were most significant in the AMI group. Compared with the AP group, D-D, Angle, TEG and MA indexes significantly increased in the UAP and AMI groups while P value and R value were significantly shortened (P<0.05).

Comparison of the TEG graphs among the three groups of patients

Results revealed that the proportion of hypercoagulability graphs in the AMI and UAP groups were higher than in the AP group (χ^2=4.261, 3.908; P<0.05), suggesting that the differences were statistically significant, as shown in *Table 3*.

Analysis of the inhibition rate of platelet aggregation in patients after PCI

Results of antiplatelet therapy in 90 patients revealed that

Table 3 Comparison of TEG in three groups

Project	AP [30] (%)	UAP [30] (%)	AMI [30] (%)	F value	P value
Normal graphics	28 (96.7)	20 (66.7)	13 (43.3)	4.042	0.0007
High setting figure	0	9 (30.0)	15 (50.0)	4.830	0.0006

TEG, thromboelastogram; AP, angina pectoris; UAP, unstable angina pectoris; AMI, acute myocardial infarction.

65 patients had normal antiplatelet drug reactions, and among these 65 patients ischemic events occurred in six patients (9.23%) within three months after discharge. Among these six patients, two patients had unstable angina pectoris, three patients had cerebral apoplexy, and one patient had acute myocardial infarction. Among the 25 patients with low antiplatelet drug reactions, 16 patients had low clopidogrel reactions, nine patients had low aspirin reactions, and among these patients ischemic events occurred in five patients within three months after discharge (20%). Among these five patients, one patient had unstable angina pectoris, two patients had cerebral apoplexy, and two patients had acute myocardial infarction (χ^2=4.347; P<0.05). This suggests that between patients with low antiplatelet drug reaction and normal antiplatelet drug reaction, the difference in the incidence of ischemic events within three months was statistically significant. In 11 patients with ischemic events, AA-induced platelet inhibition rate was 63.63%, while ADP-induced platelet inhibition rate was 36.37% (χ^2=5.026; P<0.05), suggesting that the ADP-induced platelet inhibition rate significantly decreased, which was a major risk factor for ischemic events within three months after PCI.

Discussion

Thromboelastometry is an analyzer which depicts the blood coagulation process through the high sensitive hanging thread, and obtains graphs of blood clot formation and related index values (4). Through the analysis of thrombelastogram, coagulation information can be obtained; providing data for clinical treatment with accuracy (5). Thromboelastometry can be used for the differential diagnosis of various causes of bleeding or hypercoagulable states. For surgical patients, it can screen out all kinds of coagulation abnormalities, determine the risk of bleeding, diagnose coagulation disorders, and guide in the pheresis transfusion and treatment. It has clinical efficacy (6) in the monitoring of various anticoagulants, as well as antifibrinolytics and pro-coagulation drugs. A blood sample can be used to monitor the formation of blood clots and the whole process of fibrinolysis. Coagulation factor is the index of detection and evaluation of whole blood coagulation function in the aspects of protein, platelet aggregation and fibrinolysis. The effect of heparin and low molecular weight heparin was not affected. For patients who need the long-term use of antiplatelet drugs, the effectiveness and safety of their medication can be guaranteed (7,8). Coronary heart disease is caused by atherosclerosis, which is a serious threat to the life safety of elderly patients. At present, PCI is one of the main treatment methods, in addition to the operation and drug treatment. Its advantage is minimal invasion, hence this approach has been widely used in the treatment of coronary heart disease (9). PCI requires preoperative determination of the body's blood coagulation function and condition. In order to prevent ischemic events, clopidogrel combined with aspirin should be administered; but this method remains controversial due to the medication time. In some patients, low antiplatelet drug reaction conditions occur, resulting in thrombosis and ischemic events (10). PCI restenosis is a major problem for physicians and patients, and it is not good for each patient to strengthen antiplatelet therapy. Several clinical studies in Japan and South Korea have suggested that clopidogrel has no response or has a low response rate of 4–40% (11,12). Furthermore, in some studies (13), the definition of "aspirin resistance" and "clopidogrel resistance" is similar to "antiplatelet drug resistance". This can only be shown as "aspirin resistance" or "clopidogrel resistance", or the existence of these two (14). However, the definition of antiplatelet drug resistance remains controversial; and some scholars choose to use the terms antiplatelet drugs with no response or low response, anti-platelet drug treatment failure, etc. However, its essence has not been significantly changed (13-16). A standard empirical definition has been mostly used in different studies, in which the aspirin and clopidogrel, as well as platelet aggregation rate were detected using TEG method, when AA-induced platelet inhibition rate is less than or equal to 50% (17). For aspirin resistance,

ADP-induced platelet inhibition rate is <30% in clopidogrel or ticagrelor resistance (18). In order to monitor the coagulation function of patients who undergo PCI and guide the clinical application of antiplatelet agents, the TEG can be used to monitor perioperative platelet inhibition (19). TEG can accurately display the coagulation status and platelet aggregation in digital form, guide the clinical treatment and provide early warning for ischemic events (20).

According to relevant research data, the TEG test mainly uses the basic mode of the cell in monitoring the continuous process of blood coagulation and the fibrinolysis, without the need for processing of blood and plasma. Computer software can be used to generate these results automatically with a preliminary diagnosis function; providing a reference for physicians to develop a treatment program. When the extension of the action time of anticoagulants and blood coagulation factor, R value increases with time, blood becomes hypercoagulable with a shortened coagulation time; suggesting that patients has acute coronary syndromes. The time of blood clot formation reflects the change of platelet function and level of fibrin in patients. In addition, the maximum range of the fibrin thrombus produced by the scan represents an absolute intensity, which can accurately determine the maximum dynamic properties of fibrin and platelet in patients. This index in the UAP, AMI and AP groups significantly improved in this study, which indicated that platelet coagulation function was strong. Angle represents the rate of thrombosis, which can reflect the functions of platelets and FIB, and has the same significance as the time of blood clot formation. Fgb represents the formation of thrombosis, showing changes in coagulation function. Thrombosis disorganize endothelial cells, leading to abnormal phenotype of cells; thus, resulting in arterial sclerosis. The results of this study revealed that indices in the UAP group and AMI group were higher than in the AP group, which indicated that the blood was in a certain state of hypercoagulability. This suggests that the use of TEG to monitor coagulation function and guide antiplatelet medication can significantly reduce the incidence of ischemic events after PCI, which has high application value for clinical treatment.

In order to explore the clinical application of the thrombus, the investigators of this study conducted a comparative study of 90 patients with coronary intervention in the hospital. Results after PCI TEG revealed three months of low reaction of antiplatelet drugs in patients with ischemic event rates, which were significantly higher than antiplatelet drug responsiveness in normal patients; and basic TEG monitoring of platelet aggregation inhibition rate was found and may be associated with the low reaction of clopidogrel and FGB. According to related literature, the low response of clopidogrel has five aspects: genetic variation, hyperinsulinemia, poor insulin resistance, the four basic platelets between the drug, and the role of the five degrees of angina pectoris and intestinal absorption. Through this data, clinical research found that diabetes is a key factor in the low response to antiplatelet drugs and hyperinsulinemia in patients with diabetes mellitus (DM), which directly affects the arsenic chlorides gray reaction. Therefore, this controls the patient's blood sugar in time, makes a reasonable adjustment to the drug use of platelets, and reduces the probability of antiplatelet drugs as low as possible. Furthermore, it is not clear how many patients were referred to surgery after failed percutaneous coronary interventions. A more clinically relevant analysis of preoperative platelet function testing might thus contribute to redefine the patients no more as responder/non-responder, but as prone/not prone to bleeding. This could certainly improve the clinical practice, suggesting a more efficient planning of the operative programmes to limit the use of blood products (21). Certainly, other preoperative patient features, such as age, body surface, renal function, along with specific comorbidities (e.g., liver disease), should be taken into account in this perspective, in order to minimize the risk of transfusion or the amount of transfusions required, as the negative impact on the postoperative outcome has been recently suggested to be dose-dependent.

To summarize, the use of a blood clot elastic graph can be employed to monitor the coagulation status of patients with coronary heart disease, reflect the situation of platelet aggregation, and develop a personalized treatment program; reducing the incidence of ischemic events. This is worthy of clinical promotion and application. However, lack of large randomized controlled platelet function monitoring in dual antiplatelet therapy of the PCI and BYPASS perioperative. The current guidelines do not recommend. This study by the perioperative period of liver transplantation, inspired by monitoring on blood coagulation function, hoping to explore individualized dual antiplatelet therapy strategy.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was approved by Ethics Committee of the Dagang Hospital of Binhai New Area, Tianjin.

References

1. Hao B, Cui H, Zhang L, et al. The detection of the value of the elasticity of the blood of patients with liver cancer. Henan Medical Research 2013;22:69-71.
2. Chen N, Yang C, Jing C. Thrombelastogram detection of 5 kinds of liquid for the effect of preoperative preload on blood coagulation function. Hebei Medicine 2013;35:1348-9.
3. Wang W, Lu S, Jiang Z, et al. The clinical application of the thrombus in the coronary heart disease (CHD). Practical Journal of Cardiovascular and Cerebrovascular Diseases 2012;20:1455-6.
4. Yan Z, Yang X, Zhou L. Effects of heparin concentration Thrombelastogram evaluation on coagulation function value. Shandong Medicine 2012;52:70-2.
5. Lou S, Zhang Y, He Y, et al. The application of the thrombus in patients with severe thrombocytopenia. Laboratory Medicine and Clinical 2011;8:1931-4.
6. Zhang H, Yang T. Application in the treatment of patients with antiplatelet therapy in patients with coronary artery interventional therapy. Chinese Journal of Cardiovascular Medicine 2013;5:46-7.
7. Reikvam H, Steien E, Hauge B, et al. Thrombelastography. Transfus Apher Sci 2009;40:119-23.
8. Cotton BA, Minei KM, Radwan ZA, et al. Admission rapid thrombelastography predicts development of pulmonary embolism in trauma patients. J Trauma Acute Care Surg 2012;72:1470-5; discussion 1475-7.
9. Anderson JL, Adams CD, Antman EM, et al. 2011 ACCF/AHA Focused Update Incorporated Into the ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2011;123:e426-579.
10. Feng L, Bai Y, Liu T, et al. Clinical study on the efficacy of the treatment of the elderly patients with oral anti platelet agents. Chinese and Foreign Health Digest 2012;10:527-8.
11. Hoshino K, Horiuchi H, Tada T, et al. Clopidogrel resistance in Japanese patients scheduled for percutaneous coronary intervention. Circ J 2009;73:336-42.
12. Shim CY, Yoon SJ, Park S, et al. The clopidogrel resistance can be attenuated with triple antiplatelet therapy in patients undergoing drug-eluting stents implantation. Int J Cardiol 2009;134:351-5.
13. Gorog DA, Sweeny JM, Fuster V. Antiplatelet drug 'resistance'. Part 2: laboratory resistance to antiplatelet drugs-fact or artifact? Nat Rev Cardiol 2009;6:365-73.
14. Cattaneo M. Resistance to anti-platelet agents. Thromb Res 2011;127 Suppl 3:S61-3.
15. Cattaneo M. Aspirin and clopidogrel: efficacy, safety, and the issue of drug resistance. Arterioscler Thromb Vasc Biol 2004;24:1980-7.
16. Patrono C, Coller B, Dalen JE, et al. Platelet-active drugs: the relationships among dose, effectiveness, and side effects. Chest 1998;114:470S-488S.
17. Tantry US, Bliden KP, Gurbel PA. Overestimation of platelet aspirin resistance detection by thrombelastograph platelet mapping and validation by conventional aggregometry using arachidonic acid stimulation. J Am Coll Cardiol 2005;46:1705-9.
18. Bliden KP, Tantry U, Zaman K, et al. High platelet reactivity is a risk factor for post-discharge ischemic complications following elective coronary stenting. J Am Coll Cardiol 2005;45:33A.
19. Zhao L, Wei X, Du F, et al. A study on the assessment of clopidogrel response in patients with acute coronary syndrome. Chemists 2013;30:105-8.
20. Tian W, Liu W. The application value of the thrombus in the cardiovascular disease. Int J Cardiol 2012;309:39-41.
21. Rubino AS, Della Corte A, Giordano R, et al. Impact of preoperative antiplatelet therapy on in-hospital outcomes after coronary artery bypass grafting. Eur J Cardiothorac Surg 2014;46:335.

Cite this article as: Zhao SW, Wang YP, Xu LD, Gang W. The application of thromboelastogram in detection of indexes of antiplatelet therapy for coronary heart disease. J Thorac Dis 2016;8(12):3515-3520. doi: 10.21037/jtd.2016.12.77

