# The value of Sonoclot detection technology to guide the clinical medication of the perioperative anticoagulation and antiplatelet therapy in patients with acute myocardial infarction undergoing emergent PCI

WU-XIAO YANG, CHUN-LIN LAI, FU-HENG CHEN, JI-RONG WANG, YOU-RUI JI and DONG-XIA WANG

Department of Cardiology, People's Hospital of Shaanxi Province, Taiyuan, Shaanxi 030012, P.R. China

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**Abstract.** The value of Sonoclot detection technology to guide the clinical medication of the perioperative anticoagulation and antiplatelet therapy in patients with acute myocardial infarction (AMI) undergoing emergent percutaneous coronary intervention (PCI) was estimated. One hundred and twenty-eight patients were randomly divided into control group and observation group with 64 cases in each group. Control group adopted routine blood coagulation indexes, including prothrombin time, activated partial thromboplastin time, fibrinogen and plasma thrombin time, platelet count and platelet aggregation turbidity analysis; observation group adopted Sonoclot detection technology, including activated clotting time, coagulation rate and platelet function. Anticoagulant therapy selected was of low molecular weight heparin calcium perioperatively, intraoperative unfractionated heparin, and clopidogrel (75 mg) combined with aspirin enteric-coated tablets (100 mg) as antiplatelet drugs. The therapy was administered in accordance with blood coagulation results. The blood coagulation time, postoperative creatine kinase isoenzyme MB, cardiac troponin I and B-type natriuretic peptide levels in the observation group are significantly lower than those in the control group ($P<0.05$) though the operating time and specifications of the stenting did not show any significant difference ($P>0.05$). The incidence of recurrent myocardial infarction, microembolism, acute and subacute thrombosis and bleeding events in the observation group are significantly lower than those in the control group ($P<0.05$). In the control group, there is no difference in the coagulation indexes of the patients with thrombosis events or bleeding events or no event ($P>0.05$). Whereas, in the observation group, there is significant difference in coagulation indexes of the patients with thrombosis events or bleeding events or no event ($P<0.05$). In conclusion, Sonoclot detection technology instructs emergent PCI treatment in AMI patients to shorten the detection time of blood coagulation, reduce the degree of myocardial injury, reduce the incidence of perioperative thrombosis and bleeding events. Furthermore, it has great value in guiding the clinical medication of anticoagulation and antiplatelet therapy.

*Correspondence to:* Dr Wu-Xiao Yang, Department of Cardiology, People's Hospital of Shaanxi Province, 29 Shuangtasi Road, Taiyuan, Shaanxi 030012, P.R. China
E-mail: 65987026@qq.com

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## Introduction

Acute myocardial infarction (AMI) is the most serious cardiovascular event, with high early mortality and disability rate as well as increased long-term acute and chronic heart failure (1). The application of percutaneous transluminal coronary angioplasty and stent implantation improves the survival rate of AMI in early stage. However, the occurrence of recurrent myocardial infarction, microthrombosis and bleeding events during perioperative period is an important factor that affects the treatment effect and long-term prognosis (2). The pathogenesis of AMI is related to the dysfunction of the endothelial cells of the coronary arteries and the balance disorder of coagulation and fibrinolysis system. Platelets, fibrin and various visible cellular components gather on the target lesions and cause acute thrombosis, as well as series of pathological processes such as the secondary thrombus rupture, hemorrhage, organization, and result in the acute ischemia-hypoxia injury of heart and other organs (3). Percutaneous coronary intervention (PCI) is an invasive procedure. Due to slow intraoperative blood flow, reperfusion injury and microinfarction the dysfunction coagulation mechanism in coronary arteries plays an important role in the recurrence, development, treatment, and prognosis of AMI (4). Research confirms (5) that the incidence of perioperative thrombosis and bleeding is 25-40% related to routine blood coagulation indexes, which include prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen (FIB) and plasma thrombin time (TT), platelet count and platelet (PLT) aggregation turbidity analysis. Sonoclot analyzer reflects on the whole process of the coagulation cascade and coagulation with intuitive signal curve as well as faster results (6). It has been successfully used

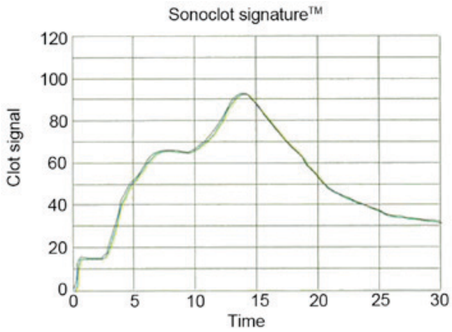


Figure 1. The normal curve of Sonoclot detection.

in blood transfusion management in extracorporeal circulation of cardiac surgery, ICU and various tumor therapy, early diagnosis of disseminated intravascular coagulation (DIC), blood coagulation monitoring during liver transplantation and monitoring for heparin and antiplatelet drug therapy (7,8). At present, there are few studies on the effect of Sonoclot detection technology on recent thrombosis and bleeding events for using as a guide for perioperative anticoagulation and antiplatelet therapy in patients with AMI undergoing emergent PCI. The present study summarizes the application experience of our center, in order to provide it as a reference for clinical rational use of anticoagulation and antiplatelet drugs.

## Patients and methods

*Patient data*. The study was conducted on 128 cases of AMI admitted to People's Hospital of Shaanxi between January 2013 and January 2016 who were diagnosed and treated with emergent PCI. Inclusion criteria: i) Primary AMI, the longest time from the onset to emergent PCI is 72 h; ii) did not receive thrombolytic therapy; iii) the operation predicted to be successful, the survival period is longer than 12 months; and iv) high treatment compliance and complete clinical data.

Patients with previous history of chronic angina, no anticoagulation and antiplatelet drug application history, other cardiac diseases (atrial fibrillation radiofrequency ablation treatment or long-term warfarin anticoagulation history, primary cardiomyopathy, chronic heart failure), other underlying diseases, such as chronic pulmonary disease, history of stroke, malignant tumor, lower limb varices or thrombosis, autoimmune diseases and pregnant or breast-feeding women were excluded from the study.

The study was approved by the Ethics Committee of People's Hospital of Shaanxi. Written informed consent was obtained from patients or their family members.

Patients were divided into control and observation groups, 64 cases in each group according to the order of admission. The control group had 42 males and 22 females, aged 43-77 years (58.6±13.7), AMI onset time of 6-39 h, (median time, 24.5 h), 46 cases were of ST-segment elevation myocardial infarction (STEMI) and 18 cases of non-STEMI (NSTEMI) confirmed by coronary angiography. There were 30 cases with target lesions in the left anterior descending (LAD), 14 cases are the left circumflex artery (LCX), and 20 cases are the right coronary artery (RCA). Percentage of lumen diameter stenosis is 85-100% (96.7±3.3). The observation group had 40 cases of male and 24 cases of female, aged 45-79 years (58.5±14.8), AMI onset time of 8-44 h (median time, 26.3 h), 43 cases were of STEMI and 21 cases of NSTEMI. There were 32 cases of LAD, 13 cases of LCX and 19 cases of RCA. The degree of lumen diameter stenosis is 90-100% (98.5±3.2). Baseline data of the two groups are comparable.

*Research methods*. The two groups of patients were treated according to the standard medical procedure by the same intervention operation and nursing team. The main stent

Table I. Comparison among operation time, stent diameter, length and number.

| Groups | Operation time (min) | Diameter of stent (mm) | Length of stent (mm) | No. of stent |
|---|---|---|---|---|
| Control | 82.4±10.2 | 3.5±1.2 | 18.2±3.5 | 1.2±0.4 |
| Observation | 76.5±12.3 | 3.6±1.4 | 17.4±3.3 | 1.3±0.5 |
| t-test | 0.324 | 0.152 | 0.225 | 0.096 |
| P-value | 0.639 | 0.856 | 0.754 | 0.925 |

Table II. Comparison among blood coagulation detection time, level of CK-MB, cTnI and BNP.

| Groups | Blood coagulation time (min) | Preoperative CK-MB (U/l) | Postoperative CK-MB | Preoperative cTnI (U/l) | Postoperative cTnI | Preoperative BNP (pg/ml) | Postoperative BNP |
|---|---|---|---|---|---|---|---|
| Control | 38.2±10.6 | 156.3±46.2 | 75.6±24.7 | 11.7±5.6 | 8.2±4.3 | 743.2±125.4 | 465.9±163.2 |
| Observation | 15.6±5.7 | 162.4±52.3 | 35.8±12.2 | 12.3±6.3 | 2.6±0.9 | 756.2±182.9 | 265.4±86.5 |
| t-test | 7.632 | 0.125 | 7.252 | 0.163 | 6.539 | 0.245 | 6.234 |
| P-value | 0.001[a] | 0.862 | 0.001[a] | 0.759 | 0.001[a] | 0.723 | 0.001[a] |

[a]P<0.05 statistically significant. CK-MB, creatine kinase isoenzyme MB; cTnI, cardiac troponin I; BNP, B-type natriuretic peptide.

types (Barui Medical Instrument Co., Ltd., Beijing, China) used were drug-coated Excel stent in majority of the cases, others were Endeavor and Xience V stent. Suction technique according to the thrombus load, adenosine to fully dilate coronary artery, and maximum heparin was applied. Pre-dilation was performed with a balloon, angiography confirmed that the stent expansion is good with thrombolysis in myocardial infarction (TIMI) flow. Patients in the control group were treated based on blood coagulation indexes, including PT, APTT, FIB and plasma TT, platelet count and PLT aggregation turbidity analysis. Among them, PT was prolonged by 3 sec (15-17 sec), APTT >45 sec, FIB <2 g/l, TT extended 3 sec (19-21 sec), platelet count <100x$10^9$/l, aggregation inhibition rate of PLT up to 80-90%.

The observation group used Sonoclot coagulation and platelet function analyzer (Sienco, Inc., Morrison, CO, USA), including the activated clotting time (ACT), coagulation rate (CR) and platelet function (PF). The normal curve of Sonoclot is shown in Fig. 1, in which the first step is the interaction of coagulation factors, blood viscosity changes, at this time the curve remains level, the sample present is in liquid state, normal ACT is 115-195 sec then the second step is formation of fibrin, the sample changes from the liquid gradually into a gel. CR as the rate of the formation of fibrin gel from the FIB in unit time, this is the first increase of the curve with the normal value of 11-35/min finally the third step is clot retraction wherein both platelets and fibrin play a role, the clot strength is increased, the curve rises and reaches its peak, then the contraction continues, the curve falls, normal value of PF <30 min.

*Observation index*. Comparison of operative time, the diameter, length and number of stent, coagulation test time, creatine kinase isoenzyme MB (CK-MB), cardiac troponin I (cTnI) and B-type natriuretic peptide (BNP), postoperative recurrent myocardial infarction, micro-emboli, acute and subacute thrombosis formation and bleeding events was carried out.

*Statistical analysis*. Analysis was performed using software SPSS 20.0 (IBM SPSS, Armonk, NY, USA). Data was presented as the mean ± standard deviation. To compare between the two groups independent samples t-test was used. Comparison among the three groups used single factor ANOVA analysis. Least significant difference (LSD)-t method was used to test pairwise comparison. Paired t-test was used to compare pre- and post-treatment. Categorical data were reported as the proportion and percentage. $\chi^2$ test was used between groups. The statistical significance was defined as P<0.05.

## Results

*Comparison among operation time, diameter, length and number of stents*. The operation time of the two groups, the diameter, length and number of stents implanted had no difference (P>0.05) as shown in Table I.

*Comparison among blood coagulation detection time, level of CK-MB, cTnI and BNP*. Blood coagulation detection time, postoperative CK-MB, level of cTnI and BNP in observation group were significantly lower than the control group, and the difference was statistically significant (P<0.05) as shown in Table II.

Table III. Comparison of perioperative and postoperative thrombotic events (%).

| Groups | Cases | Recurrent MI | Microembolism | Microembolism | Subacute thrombus | Incidence of thrombus | Gums, skin, mucosal bleeding | Gastrointestinal bleeding | Intracranial hemorrhage | Bleeding incidence |
|---|---|---|---|---|---|---|---|---|---|---|
| Control | 64 | 3 | 5 | 2 | 4 | 14 (21.88) | 6 | 3 | 1 | 10 (15.63) |
| Observation | 64 | 1 | 2 | 1 | 1 | 5 (7.81) | 2 | 1 | 0 | 3 (4.69) |
| $\chi^2$ | | | | | | 5.006 | | | | 4.195 |
| P-value | | | | | | 0.025[a] | | | | 0.041[a] |

[a]P<0.05 statistically significant. MI, myocardial infarction.

Table IV. Comparison of coagulation indexes in control group.

| Control group | Cases | PT (sec) | APTT (sec) | FIB (g/l) | TT (sec) | PLT ($100x10^9$/l) | PLT aggregation inhibition rate (%) |
|---|---|---|---|---|---|---|---|
| Patients with thrombotic events | 14 | 15.0±2.2 | 42.8±3.5 | 2.7±0.8 | 22.4±1.6 | 1.8±0.5 | 85.9±9.2 |
| Patients with bleeding events | 10 | 15.2±2.3 | 43.2±3.4 | 2.5±0.7 | 20.5±1.8 | 1.5±0.6 | 85.3±9.3 |
| Patients with no event | 40 | 14.9±2.4 | 44.3±3.6 | 2.4±0.9 | 21.2±1.9 | 1.7±0.4 | 86.4±9.5 |
| F-value | | 0.156 | 0.163 | 0.094 | 0.086 | 0.072 | 0.234 |
| P-value | | 0.862 | 0.759 | 0.853 | 0.896 | 0.963 | 0.639 |

PT, prothrombin time; APTT, activated partial thromboplastin time; FIB, fibrinogen; TT, thrombin time; PLT, platelet.

Table V. Comparison of coagulation indexes in the observation group.

| Observation group | Cases | ACT (sec) | CR (/min) | PF (min) |
|---|---|---|---|---|
| Patients with thrombotic events | 5 | 107.4±25.5 | 8.6±3.5 | 12.8±4.8 |
| Patients with bleeding events | 3 | 223.6±42.6 | 46.4±9.3 | 36.5±15.6 |
| Patients with no event | 56 | 165.8±34.2 | 18.9±7.2 | 22.4±10.5 |
| F-value | | 7.526 | 6.532 | 6.629 |
| P-value | | 0.001[a] | 0.001[a] | 0.001[a] |

[a]P<0.05 statistically significant. ACT, activated clotting time; CR, coagulation rate; PF, platelet function.

*Comparison of incidence of thrombosis and hemorrhage events during perioperative period*. The recurrent myocardial infarction, microembolism, acute and subacute thrombosis and bleeding events in the observation group were significantly lower than those in the control group, the difference was statistically significant (P<0.05) as shown in Table III.

*Comparison of coagulation indexes in control group*. In the control group, there was no difference (P>0.05) in the occurrence of thrombosis events, bleeding events and no event as shown in Table IV.

*Comparison of coagulation indexes in the observation group*. In the observation group, there was a significant difference in coagulation parameters (P<0.05) among patients with thrombosis events, bleeding events and no event as shown in Table V.

## Discussion

ACT mainly reflects the activity of endogenous blood coagulation system, CR reflects the level of FIB indirectly, and PF reflects PF. In more than 1,000 tests, abnormal results accounted for 27%, of these the main reason was low PF, which accounted for 64%; followed by heparin residual effect, accounting for 25%; decreased FIB level accounted for 9%; simple decrease of clotting factor was ~2%, no fibrinolytic hyperthyroidism (9). Different parts of Sonoclot graphics reflect blood coagulation cascade at different stages, according to the curve, we can determine the reason for coagulopathy, and infuse specific blood products targeting the affected stage. Supplementing, monitoring and correcting at the same time, we can also assess the effects timely in order to improve the prognosis of patients. This allows us to give appropriate blood products to patients at appropriate time, thus avoiding unnecessary empiric blood infusion. Routine blood clotting indices, such as, PT, APTT, FIB and TT reflect single stage of information in the process of coagulation cascade (10). The platelet count gives a quantitative but no qualitative information on the function of platelet. Although PLT aggregation turbidity analysis is a standard way to detect the PLT function clinically, it is time-consuming, laborious and relies on the operation of skilled professionals. *In vitro* plasma rich in PLT is under low shear stress condition which cannot accurately simulate the *in vivo* hemostatic state (11). In the heart-lung transplantation, Sonoclot index is better than traditional coagulation index in the forecast of bleeding (12); the ACT and CR value of patients with unstable angina are significantly higher than that of stable angina (13).

Perioperative anticoagulation and antiplatelet drugs not only affect the AMI thrombosis and progress of luminal stenosis, but also have great significance for the smooth operation of PCI. Based on the principle of Sonoclot detection theories, we applied it to the AMI thrombolytic therapy, which is of great value to the assessment of drug risk and reduction of bleeding events. This study concluded that, operation time, diameter, length or number of stent showed no significant difference in the groups. Interventional operation itself also has important influence on the function of blood coagulation system (14). Test time of blood coagulation, postoperative CK-MB, cTnI and BNP levels in observation group are significantly lower than that of control group. Sonoclot detection is more convenient and time-saving, and it has better effect in improving the efficiency of perioperative anticoagulation and antiplatelet drugs. Better coagulation control could also have more benefit in reducing myocardial injury (15). Recurrence of microembolism, myocardial infarction, acute and subacute thrombosis, as well as the incidence of bleeding in observation group are significantly lower than that of control group. Sonoclot index can reflex the body blood coagulation function more accurately and sensitively, for making more quickly reasonable adjustment in dose and types of anticoagulation and antiplatelet drugs (16). In control group, coagulation indexes of patients with blood clots, bleeding events and those with no incidents were not significantly different, however, coagulation indexes in the observation group had significant differences.

Based on the above, using Sonoclot detection technique to guide emergent PCI operation on AMI patients is a good choice, which can shorten the detection time of coagulation, reduce the degree of myocardial injury, perioperative thromboembolism and bleeding events, and it also has higher accuracy and sensitivity in guiding administration of anticoagulation and antiplatelet drugs.

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