Int J Clin Exp Med 2015;8(7):11360-11369
www.ijcem.com /ISSN:1940-5901/IJCEM0008669

Original Article

Efficacy and safety of different doses of tirofiban combined with ticagrelor on diabetic patients with AMI receiving in emergency percutaneous coronary intervention (PCI)

Yang Liu, Hengliang Liu, Zhenxuan Hao, Guoying Geng, Qi Chen, Wenjie Han, Kailong Jia, Yuxin Zhou

Department of Cardiology, People's Hospital of Zhengzhou, Southern Medical University, Zhengzhou 45002, Hean, China

Received April 1, 2015; Accepted June 2, 2015; Epub July 15, 2015; Published July 30, 2015

Abstract: Objective: The aim of this study was to investigate the efficacy and safety of dual antiplatelet drugs combined with different doses of tirofiban on diabetic patients with acute myocardial infarction (AMI) receiving emergency percutaneous coronary intervention (PCI). Methods: 158 diabetic patients with AMI undergone emergency PCI were randomly divided into three groups: Group A (53 cases) as the control group-dual anti-platelet agents (aspirin + ticagrelor); Group B (52 cases)-dual anti-platelet agents + conventional dose of tirofiban [10 μg/kg by PCI and 0.15 μg/(kg·min) by continue venous pump for 24 h]; Group C (53 cases)-dual antiplatelet agents + half-dose tirofiban [10 μg/kg by PCI and 0.075 μg/(kg·min) by continue venous pump for 24 h]. Results: Compared with group A, thrombolysis in myocardial infarction 3 (TIMI3) blood flow and TIMI myocardial perfusion grade 3 (TMPG3) myocardial perfusion of patients in group B and group C after PCI was significantly higher ($P < 0.05$), the average day of hospitalization was significantly shorter ($P < 0.05$), reinfarction during hospitalization, post-infarction angina, severe arrhythmia, the incidence of cardiac function above KillipIII level was significantly lower ($P < 0.05$). And the differences between group B and C was not statistically significant ($P > 0.05$). Severe bleeding and moderate incidence of bleeding in group B was significantly higher than that in group A and group C ($P < 0.05$). Conclusions: Based on combination of dual the anti-platelet agents and ticagrelor for diabetic patients with AMI receiving PCI, the combination of half-dose tirofiban can effectively improve TIMI flow and TMPG myocardial tissue perfusion, and reduce the incidence of major adverse cardiac events (MACE) and severe bleeding.

Keywords: Diabetes, acute myocardial infarction, primary percutaneous coronary intervention, anti-platelet, complications, bleeding

Introduction

Thrombus formation caused by unstable coronary plaque rupture, platelet activation, aggregation and adhesion was the pathological basis of acute myocardial infarction (AMI) [1, 2]. Early recovery of the infarct-related artery blood flow was the most important principle of treatment for AMI. Percutaneous coronary intervention (PCI) was the most effective treatment for the opening of the infarct-related artery [3-5]. After restoration of blood flow of infarct-related artery, slow blood flow or no-reflow was one of the major complications of emergency PCI. Acute or subacute thrombosis was the most serious complications and cardiovascular events (major adverse cardiac events, MACE) in emergency PCI for AMI [6, 7]. The incidence of slow flow or no-reflow and thrombotic event for diabetic patients after emergency PCI was significantly higher than that of general population [8, 9], dual anti-platelet therapy of thromboxane (TXA2) inhibitor (aspirin) and P2Y12 receptor inhibitors was the main therapeutic measures to prevent thrombosis.

However, there were still serious complications due to thrombosis in some patients, IIb/IIIa receptor inhibitors plus dual anti-platelet therapy can effectively reduce the incidence of slow flow or no-reflow, reduce acute and subacute thrombosis, reduce AMI complications and the

occurrence of MACE [10, 11], but the occurrence probability of the bleeding in the triple combination treatment of anti-platelet drugs significantly increased. How to weighed the risks of thrombotic events and bleeding complications was a serious problem that we must face [12]. This study was designed to investigate the short-term efficacy and safety of different doses of tirofiban combined with third-generation P2Y12 receptor inhibitor ticagrelor in the treatment for diabetic patients with AMI.

Materials and methods

Study subjects

158 diabetic ST elevated myocardial infarction (STEMI) cases diagnosed by emergency PCI and admitted to coronary care unit (CCU) in our hospital during January, 2013 and December, 2014 were selected, and randomly divided into three groups: Group A, the control group treated by dual anti-platelet agents (Aspirin + ticagrelor) without tirofiban (53 patients aged 50 to 79, mean age of 59.9 ± 7.9) years; Group B-dual anti-platelet agents + standard-dose tirofiban group including 52 patients, aged 52 to 77 (mean age of 60.6 ± 7.7) years; Group C-dual anti-platelet agents + half-dose tirofiban group including 53 patients, aged 51 to 78 (mean age of 59.9 ± 9.3) years. The AMI was diagnosed in accordance with guidelines for the ST-segment elevation myocardial infarction developed by ACC/AHA [4]. The diagnosis of diabetes was in accordance with diagnostic criteria of WHO in 1999 [13]. Inclusion criteria: 1) STEMI onset ≤ 12 h. 2) Has been diagnosed with diabetes. 3) Agreed with emergency PCI. Exclusion criteria: 1) STEMI onset ≥ 12 h. 2) Suspected to be aortic dissection. 3) Uncontrolled hypertension ≥ 180/110 mmHg (1 mmHg = 0.133 kpa). 4) Performed remedial PCI after thrombolytic therapy. 5) A history of cerebral hemorrhage and a history ischemic stroke within one year. 6) Severe liver and kidney dysfunction. 7) A history of bleeding disorders. The studies met the Declaration of Helsinki and were approved by the Ethics Committee of Zhengzhou People's Hospital.

Emergency PCI

After admission, patients were treated by electrocardiogram (ECG), oxygen inhalation, and immediately recorded 18-lead ECG tracings, checked blood glucose, lipids, enzymes, troponin, other related biochemical and routine testing programs by exsanguinate, while gave orally 300 mg aspirin (Bayer company, 100 mg/tablet) and 180 mg ticagrelor (tablets, AstraZeneca, 90 mg/tablet). The relevant preoperative examinations were completed, after the consent of patients and/or their families, the patients were sent to the cath lab to perform emergency surgery. The coronary angiography was developed with the US company GE DSA vascular development machine using judksin method, set the sheathed tube via the right radial artery (146 cases) or the right femoral artery (12 cases), gave 3000U heparin through the sheath. After defining the criminal vessels by vascular angiography, gave additional 7000U heparin through the sheath, sent guiding catheter to reach the coronary artery. If thrombus shadow was visible in angiography, thrombus was aspired using thrombus aspiration catheter (the cases in the three groups using the thrombus aspiration catheter were three cases, three cases and four cases, respectively). After guiding the wire through the occlusion of criminal vessels, performed intracoronary tirofiban hydrochloridethe (injection, China Wuhan Grand Pharmaceutical group Co. production company) to group B and group C with dose of 10 μg/kg in the mode of bolus injection, tirofiban was not given to group A. Performed repeat angiography to understand the situation of coronary blood flow, as well as PTCA + stenting or direct stenting according to the situation of target lesions, all patients used sirolimus-eluting stents (China Beijing Dunlop medical Devices Co., Ltd.). After PCI, performed continuous intravenous infusion of tirofiban hydrochloride to group B with 0.15 μg/(kg·min) and group C with 0.075 μg/(kg·min) for 24 h.

Emergency PCI only treated criminal vessels, if no criminal vessels needed for treatment, performed secondary PCI on selective day after 10-14 days. Reviewed cardiac enzymes, troponin, ECG, echocardiography, liver and kidney function, and continuously took 100 mg/d of aspirin, 180 mg/d of ticagrelor, took statins, angiotensin-converting enzyme inhibitors (ACEI), β-blockers and antidiabetic drugs twice in morning and evening.

Outcome observations

Based on the results of lesion characteristics by coronary angiography analysis, and the stenting diameter and length (for example, two

Table 1. General clinical data of patients in the three groups

Items	Dual anti-platelet group (Group A, 53 cases)	Standard-dose tirofiban group (Group B, 52 cases)	Half dose tirofiban group (Group C, 53 cases)
Age (years)	59.9 ± 7.9	60.6 ± 7.7	60.6 ± 7.7
Gender (Male/Female)	22/31	21/31	23/30
Hypertension [cases (%)]	33 (62.26)	35 (67.30)	36 (67.92)
Smoking history [cases (%)]	17 (32.08)	15 (28.85)	19 (35.85)
Fat lipids [cases (%)]	31 (58.49)	35 (67.30)	33 (62.26)
Serum creatinine (mmol/L)	89.6 ± 9.9	91.8 ± 10.8	88.3 ± 13.9
PCI history [cases (%)]	3 (5.67)	5 (9.62)	6 (11.32)
Pre-infarction angina [cases (%)]	2 (3.77)	7 (13.46)	4 (7.55)
Family history of coronary heart disease [cases (%)]	4 (7.55)	3 (5.77)	8 (15.09)

or more stents needed to be implanted for two or more criminal artery lesions, the addition of implanted stents was the stent length, for a longer serial implantation for target lesions, the length of the implanted two stents subtracted 4 mm was the total stent length, the diameter and length of the implanted stents for criminal vessels in the secondary surgery were not counted); the length of stay; the average balloon time after admission (min); the number of two or more stents in the emergency PCI; secondary PCI on elective day, post-infarction angina, reinfarction during hospitalization, acute and subacute thrombosis within stents, severe arrhythmias (sustained ventricular tachycardia, ventricular fibrillation, emerging hemodynamically unstable atrial fibrillation or atrial flutter, atrioventricular block, but no including intraoperative reperfusion arrhythmias in PCI), heart function with above KillipIII level, cardiogenic shock, mortality within 30 d and severe bleeding (intracranial hemorrhage, or gastrointestinal bleeding, hemoptysis caused circulatory instability, decreased hemoglobin ≥ 5 g/dl, hematocrit reduced ≥ 15%), moderate bleeding (hemoptysis, hematemesis amount ≥ 100 ml/d and melena, hematuria, etc.), mild bleeding (hemoptysis, hematemesis volume < 100 ml/d and puncture hematoma, skin bruising, mucosal and gums bleeding, hematuria) and other adverse events of the three groups were statistically analyzed. The thrombolysis in myocardial infarction (TIMI) flow grade of the infarct-related artery and myocardial perfusion grade (TIMI myocardial perfusion grade, TMPG) were recorded after PCI [14, 15]. TIMI flow grade standards were as follows. Grade 0 indicated no forward blood flow in the distal of occlusion; grade 1 represented portion of contrast agent entered through the occlusion site, but could not fill the distal vessels; grade 2 denoted contrast agents can completely fill the distal coronary artery, but the filling and removal speed of contrast agent was delayed compared with that of the normal coronary; grade 3 represented contrast agents completely and quickly fill the distal vessels and quickly removed. Grade TIMI0 and TIMI1 indicated no coronary recanalization; grade TIMI2 and TIMI3 denoted three coronary recanalization. TMPG grading standards: grade 0 for myocardial contrast injection and little or no staining dye during the emptying; grade 1 for slow myocardial staining, and only partially dyed or myocardial diffuse punctate staining in the secondary injection of contrast agent; grade 2 for myocardium stained, but the myocardium staining or fading was very slow, the myocardial staining even existed at the end of emptying; grade 3 for normal blood flow, myocardium was widely stained, the staining was only mild persistent or no staining at the end of emptying.

Statistical methods

SPSS16.0 statistical software was used. Data was denoted as x ± s. Count data was analyzed using X^2 test, and measurement data with the t test. $P < 0.05$ was considered to be statistically significant.

Results

Clinical data

The differences of age, sex, hypertension, smoking history, hyperlipidemia, renal function, previous PCI history and family history of coronary heart disease among the three groups was not statistically significant ($P > 0.05$, **Table 1**).

Table 2. Characteristic comparisons of coronary artery lesions for patients in the 3 groups [number of cases (%)]

Lesion characteristic	Dual antiplatelet group (Group A, 53 cases)	Standard-dose tirofiban group (Group B, 52 cases)	Half dose tirofiban group (Group C, 53 cases)
Single-vessel lesions	10 (18.87)	11 (21.15)	9 (16.98)
Double vessel lesions	19 (35.85)	13 (25.00)	16 (30.19)
Three branch lesions	24 (45.28)	28 (53.84)	28 (52.83)
Combined with left main lesions	3 (5.66)	4 (7.69)	4 (7.55)
Target vessel LAD In Emergency PCI	27 (50.94)	29 (55.77)	31 (58.49)
Left circumflex artery	10 (18.87)	8 (15.38)	9 (16.98)
Right coronary artery	16 (30.19)	15 (28.85)	13 (24.52)
Stent diameter (mm, x ± s)	2.69 ± 0.33	2.67 ± 0.31	2.70 ± 0.39
Stent length (mm, x ± s)	24.52 ± 3.74	25.03 ± 4.77	26.39 ± 4.29
Preoperative TIMI grade			
0	49 (92.45)	50 (96.15)	51 (96.23)
1~2	4 (8.55)	2 (3.85)	2 (3.77)
3	0	0	0
Postoperative TIMI grade			
0	5 (9.43)[c]	1 (1.92)[c]	0 (0.00)[c]
1~2	8 (15.09)	1 (19.23)[a]	1 (18.87)[a]
3	40 (75.47)[c]	50 (96.15)[a,c]	52 (98.11)[a,c]
Preoperative TMPG grade			
0	51 (96.23)	51 (98.08)	52 (98.11)
1~2	2 (3.77)	1 (1.92)	1 (1.89)
3	0	0	0
Postoperative TMPG grade			
0	9 (16.98)[d]	1 (1.92)[a,d]	1 (1.89)[a,d]
1~2	12 (22.64)[d]	2 (3.85)[a]	2 (3.77)[a]
3	32 (60.38)[d]	49 (94.23)[a,d]	50 (94.34)[a,d]

Note: Compared with group A: [a]P<0.05; compared with group B: [b]P < 0.05; compared with TIMI in the same level before surgery in the group: [c]P before < 0.05; compared with TMPG in the same level before surgery in the group: [d]P < 0.05.

Characteristics of coronary artery disease

The single, double, three branches and combination of left main disease, target vessels treated in the emergency PCI, the diameter and length of the implanted stents of the three groups were no significant difference ($P > 0.05$). Compared with group A (dual anti-platelet agents), TIMI3 flow grade and myocardial perfusion TMPG 3 of patients in the group B and C (standard dose and half-dose tirofiban group) after PCI was significantly higher ($P < 0.05$); and the difference between the groups B and C was not statistically significant ($P > 0.05$, **Table 2**).

Length of hospital stay, PCI characteristics and complication rates

The average time during admission and balloon, the number of implanted stents in emergency PCI, the secondary PCI on selective day during hospitalization of the three groups had no significant difference ($P > 0.05$). Compared with dual anti-platelet control group (A), the average hospital stay of Group B and C were significantly shorter ($P < 0.05$), reinfarction during hospitalization, post-infarction angina, severe arrhythmia and the occurrence of heart function above KillipIII level were significantly lower ($P < 0.05$). The difference between group B and C was not statistically significant ($P > 0.05$).

One patients in group A had acute stent thrombosis within six hours, one case had subacute thrombosis within 35 hours. Both were performed secondary emergency PTCA through catheter to treat thrombotic lesions, while no thrombotic events in group B and group C. One case in group A was in a state of shock on

Table 3. Hospital stay, PCI features and the incidence of complications of the patients in the three groups

Items	Dual antiplatelet group (Group A, 53 cases)	Standard-dose tirofiban group (Group B, 52 cases)	Half dose tirofiban group (Group C, 53 cases)
Average length of stay (d)	11.2 ± 3.7	8.6 ± 2.1[a]	8.3 ± 2.9[a]
Time during admission and balloon (min)	85.2 ± 29.7	83.9 ± 30.8	88.7 ± 39.6
Two or more stents [cases (%)]	10 (18.87)	15 (28.85)	18 (33.96)
Inpatient secondary PCI on elective day [cases (%)]	15 (28.30)	19 (36.54)	21 (39.62)
Post-infarction angina [cases (%)]	14 (26.42)	4 (7.69)[a]	5 (9.43)[a]
Reinfarction [cases (%)]	8 (15.09)	1 (1.92)[a]	1 (1.89)[a]
Thrombosis within stent [cases (%)]	2 (1.79)	0	0
Severe arrhythmia [cases (%)]	16 (30.19)	5 (9.62)[a]	6 (11.32)[a]
Heart function of KillipIII level above [cases (%)]	13 (24.52)	4 (7.69)[a]	4 (7.55)[a]
Cardiogenic shock after PCI [cases (%)]	3 (5.66)	1 (1.92)	0
Mortality within 30d [cases (%)]	2 (3.77)	2 (3.85)	1 (1.89)
Bleeding [cases (%)]			
Severe bleeding	0	4 (76.92)[a]	0[b]
Moderate bleeding	0	8 (15.38)[a]	1 (1.89)[b]
Slight bleeding	1 (5.67)	8 (15.09)[a]	9 (13.21)[a]

Note: Compared with group A: [a]$P < 0.05$; compared with group B: [b]$P < 0.05$.

admission, two cases died of cardiogenic shock after PCI: the left circumflex artery of one case was severe stenosis on the basis of chronic occlusion of the right coronary artery, anterior descending artery were acute occlusion for 3 hours on admission, died in three hours after the emergency PCI, another case had left main artery + three branch lesions, the beginning part of left anterior descending artery was occlusion, admitted within two hours after onset, and performed emergency PCI under IABP support, died of shock after 30 hours. One case in group B had cardiogenic shock at admission, and performed emergency PCI under IABP support. No cases in group C had cardiogenic shock. One patient in group C died of severe arrhythmia, 2 patients in group B died of intracranial hemorrhage, but the cardiogenic shock and mortality within 30 days among the three groups showed no significant difference ($P > 0.05$). Group B had severe bleeding, the incidence of moderate bleeding was significantly higher than that in group A and group C ($P < 0.05$), 4 cases in group B had severe bleeding including two cases of intracranial hemorrhage, after careful questioning for history, a history of preoperative blood pressure was understood, and long-term blood pressure control did not meet the standard, but admission and monitoring blood pressure after PCI were not high. One case had gastrointestinal bleeding with a previous history of peptic ulcer disease. One case occurred hemoptysis in four hours after emergency PCI, and the laboratory platelets decreased to 19.3×10^9/L. The minor bleeding incidence of group B and group C was significantly higher than that of group A ($P < 0.05$), there was not statistically significant difference between group B and C ($P > 0.05$, **Table 3**).

Discussion

Two-thirds of patients with AMI was due to the instability of coronary plaque rupture, platelet activation induced platelet adhesion, aggregation and thrombosis [1]. Early, sustained, full opening of the infarct-related artery in order to save endangered cardiac death, to prevent the expansion of infarction, myocardial ischemia narrow range, maximum protection and maintain heart function were the most important principles of treatment for AMI [2-5]. Compared with the thrombolytic therapy, emergency PCI to open infarct-related artery for both diabetic and non-diabetic patients with AMI had better outcomes [16], the slow flow or no-reflow after the opening of infarct-related artery was one of the major complications of primary PCI, acute or subacute thrombosis was the main reason for the most serious complication and major adverse cardiac events (MACE) after PCI [6, 7].

Diabetes was a dangerous disease ranked equally to coronary heart disease. Glucose

metabolism disorder was one of the most important risk factor causing atherosclerosis [17-19]. The diabetic patients had specific pathophysiology different from non-diabetic patients, risk factors of diabetic patients with atherosclerosis was 2-4 times of non-diabetic patients [17]. The anti-platelet therapy in diabetic patients had poorer effect compared with non-diabetic patients [18]. Coronary artery disease was often multi-vessel involvement, diffuse lesions were more common, and often complicated by microvascular diabetic neuropathy and cardiomyopathy [19]. The incidence of slow or no-reflow after emergency PCI and thrombotic events were significantly higher than that in the general population [15].

Thrombosis within stents was one of the serious complications of PCI. Studies showed that adequate antiplatelet, anticoagulant can effectively prevent the occurrence of stent thrombosis. Double anti-platelet therapy of thromboxane (TXA2) inhibitor, aspirin and P2Y12 receptor inhibitors were the main treatment measure to prevent thrombosis [2-7, 11]. Due to serious adverse hematologic reaction caused by the first generation of P2Y12 receptor inhibitor ticlopidine was not widely applied (caused life-threatening adverse blood reactions, including neutropenia/agranulocytosis, thrombotic thrombocytopenic purpura, and aplastic anemia). While the second-generation P2Y12 receptor inhibition of clopidogrel has been applied in clinical for more than ten years, which played an important role in the prevention of thromboembolic events, but with the application of time and the accumulation of experience, it was found to have a certain limitations, such as slow onset, moderate efficient role, more individual genetic variation because of the population polymorphism, irreversible effects [11]. Another second-generation P2Y12 receptor inhibitor prasugrel enhanced the efficacy of antiplatelet bleeding but associated with an increased risk at the same time [20, 21]. The third generation of P2Y12 receptor inhibitor ticagrelor had its unique advantages because of its dual inhibition, reversible binding, the role of fast, powerful, consistent, as well as increasing coronary blood flow besides a beneficial effect of antiplatelet outside, especially antiplatelet therapy for non-responders to clopidogrel [21]. The study of PLATO including 43 states, 862 centers, 18,624 patients demonstrated [22] that the primary endpoint (composite endpoint of cardiovascular (CV) death/myocardial infarction/stroke) of efficacy for ticagrelor decreased by 16% compared with clopidogrel, and significantly reduced thrombosis within the stents and cardiovascular mortality within 1 year of the acute coronary syndromes (ACS) patients, and did not increase the incidence of bleeding. Based on the results of the PLATO study, a number of type I domestic and international guidelines recommended ticagrelor as a kind of treatment for ACS [2-5].

However, even in the application of dual antiplatelet therapy, some patients still had serious complications because of thrombosis [10, 11]. IIb/IIIa receptor inhibitors plus dual anti-platelet therapy can effectively reduce the occurrence of slow flow and no-reflow, reduce acute and subacute thrombosis, reduce the incidence of complications of AMI and MACE [11]. The incidence of no-reflow or slow flow for diabetic patients with AMI in emergency PCI was significantly higher than that for non-diabetic patients with AMI [8, 9, 15, 17-19, 23]. Tirofiban hydrochloride was a non-peptide potent reversible antagonists for platelet glycoprotein IIba/IIIa receptor, which can significantly reduce the incidence of slow flow or no-reflow during PCI [10, 15, 21, 24]. Restoring blood flow to the infarct-related artery reaching TIMI3 level was considered to be the gold standard of successful reperfusion therapy, but when blood flow of epicardial coronary reached TIMI3 level, perfusion levels of peripheral coronary varied widely. Studies showed that PCI made epicardial coronary blood flow return to normal forward blood flow, myocardial tissues of 25-30% patients were still not received effective reperfusion, that is, slow flow and no-reflow phenomenon [25]. In fact, the success of myocardial tissue perfusion was the final standard of successful reperfusion. As the standards of myocardial perfusion level, TMPG, including the contrast agent in myocardial perfusion and emptying, can more accurately evaluate the myocardial tissue perfusion [26]. Diabetic patients with large epicardial coronary diffuse lesions were often accompanied with microvascular disease and microvascular abnormalities. High blood sugar can increase the capacity of the inflammatory response, increase platelet-dependent micro-thrombosis, reduce endothelium-dependent dilation of blood vessels, thus aggravated

coronary microcirculation disorders [25, 26]. Studies showed that the mortality of TMPG0~1 (microvascular occlusion) for patients with epicardial coronary blood flow in TIMI3 level was significantly higher than that for TMPG2~3 patients [23, 25]. This study showed that intracoronary tirofiban can effectively reduce the occurrence of no-reflow and slow flow, increase blood flow in TIMI3 level and the perfusion rate of myocardial tissue, effectively reduce the occurrence of serious complications such as reinfarction, post-infarction angina, severe heart rhythm disorders and heart failure, half-dose tirofiban and standard-dose tirofiban had the same effect.

Adequate antiplatelet and anticoagulant can effectively prevent the occurrence of stent thrombosis [10, 20-22, 27]. In this study, one case in dual anti-platelet group occurred acute thrombosis within stents after 6 hours, 1 patient had subacute thrombosis after 35 hours, while no case had thromboembolic events in standard conventional-dose and half-dose tirofiban groups during observation period, indicating that compared with aspirin, the application of dual anti-platelet therapy with tirofiban and ticagrelor for diabetic patients with AMI can reduce the incidence of thrombotic events after thrombus PCI. Due to strong anti-platelet effect for tirofiban, plus dual anti-platelet drugs aspirin and ticagrelor, bleeding complication was a problem catching close attention of cardiovascular physicians [10, 21], the life-threat complications such as cerebral hemorrhage and gastrointestinal bleeding may occur, especially for diabetic patients with AMI. This study showed that the incidence of bleeding using standard conventional doses of tirofiban significantly increased, including four cases of severe bleeding and two cases of intracranial hemorrhage, after careful questioning history, both had a history of hypertension before surgery and long-term blood pressure control did not meet the standard, but the admission blood pressure and monitor blood pressure after PCI were not high, suggesting that we should not only pay attention to the treatment plus and blood pressure in CCU monitoring on admission and after PCI in the application of dual antiplatelet combined with tirofiban, but also pay attention to whether the past blood pressure control reached the standard, one case had gastrointestinal bleeding with a previous history of peptic ulcer disease, one case occurred hemoptysis in four hours after emergency PCI, the tests of platelet declined to 19.3×10^9/L, immediately stopped the use of tirofiban, and gave 40 mg/day of prednisolone in the first class by intravenous injection in close focusing on blood sugar fluctuations, reviewed platelets per day, the platelet recovered to 52.6×10^9/L after 5 days, the bleeding stopped, so the prednisolone in the first class was stopped. Elcioglu reported two cases had bleeding due to thrombocytopenia in the application of tirofiban, in the timely monitoring of platelet changes, decreased platelet was found, and the tirofiban was promptly stopped using to reduce the incidence of bleeding [28]. Whitmore et al reported pulmonary hemorrhage in the combination of aspirin and ticagrelor, bleeding was stopped after discontinuation of anti-platelet therapy, drug-induced lung injury in was found lung biopsy [29]. In this study, the platelet patients with massive hemoptysis decreased significantly, and the bleeding was stopped after discontinuation of tirofiban, which may be related with platelet decrease caused by tirofiban, suggesting that we must pay close attention to platelets change in the application of tirofiban. Mild skin bleeding including mucous membrane bleeding of half dose or standard dose tirofiban group was significantly higher than the control group, there was no adverse consequences. The incidence of bleeding in 3807 patients with ACS was 1.5% in the statistical analysis of Liu et al, including 9.6% bleeding was fatal, intracranial hemorrhage rate was 0.24%, mortality was 4.1%. The risk factors of bleeding were 70 years or older elderly patients, a history of previous bleeding, renal and heart failure history and clopidogrel GP IIb/III receptor antagonists [30]. The incidence of bleeding in this study may increase because all patients were treated by tirofiban on the basis of dual anti-platelet combination of the aspirin and ticagrelor. PLATO's studies showed that ticagrelor had faster efficacy, stronger anti-platelet effect and more durable compared with clopidogrel [23]. In this study, a standard dose for the occurrence of bleeding complications in the tirofiban group was significantly higher than the half-dose tirofiban group, indicating that the combined use of half the standard dose of tirofiban in the dual anti-platelet of aspirin and ticagrelor treatment can effectively prevent the occur-

rence of serious bleeding complications. In the combined application of the second generation of P2Y12 receptor inhibitor clopidogrel, the third-generation P2Y12 receptor inhibitor ticagrelor and tirofiban. As to whether the efficacy and side effects had differences, DiNicolantonio et al believed that compared with clopidogrel, although ticagrelor had a faster and more sustained antiplatelet effect, but it significant increased intracranial bleeding, hematuria, subcutaneous bleeding, mucosal bleeding and other adverse events [31].

In summary, the combination of dual anti-platelet treatment by aspirin plus ticagrelor and tirofiban in emergency PCI for diabetic patients with AMI can effectively improve TIMI flow and TMPG myocardial tissue perfusion, reduce post-infarction angina, reinfarction, serious arrhythmias, heart failure and other serious complications. But compared with half dose of tirofiban, tirofiban with standard dose significantly increased the incidence of bleeding complications. The combined used of tirofiban with half-dose and dual anti-platelet agents by aspirin and ticagrelor was safe and effective.

Acknowledgements

This study was supported by Leading talent project, technological innovation, Zhengzhou City (096SYJH33114).

Disclosure of conflict of interest

None.

Address correspondence to: Hengliang Liu, Department of Cardiology, People's Hospital of Zhengzhou, Southern Medical University, No. 33 Huanghe Road, Zhengzhou 450002, Henan, China. Tel: +86 371 67077035; Fax: +86 371 67077635; E-mail: cnyhdoc@126.com

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