

# Influences of different dose of tirofiban for acute ST elevation myocardial infarction patients underwent percutaneous coronary intervention

Haixia Wang, BD<sup>a,\*</sup>, Meiqin Feng, MD<sup>b</sup>

## Abstract

Tirofiban is widely used in patients with acute ST elevation myocardial infarction (STEMI) underwent percutaneous coronary intervention (PCI). This drug can efficiently improve myocardial perfusion and cardiac function, but its dose still remains controversial. We here investigated the effects of different dose of tirofiban on myocardial reperfusion and heart function in patients with STEMI. A total of 312 STEMI patients who underwent PCI in our hospital from March 2017 to March 2018 were enrolled and randomly divided into control group (75 cases, 0  $\mu\text{g}/\text{kg}$ ), low-dose group (79 cases, 5  $\mu\text{g}/\text{kg}$ ), medium-dose group (81 cases, 10  $\mu\text{g}/\text{kg}$ ) and high-dose group (77 cases, 20  $\mu\text{g}/\text{kg}$ ). The infarction-targeted artery flow grade evaluated by thrombolysis in myocardial infarction (TIMI), corrected TIMI frame count (CTFC) and sum-ST-segment resolution were recorded. At Day 7 and Day 30 after PCI, the left ventricular ejection fraction (LVEF), left ventricular end diastolic diameter, left ventricular end systolic diameter, major adverse cardiovascular events and the hemorrhage and thrombocytopenia were also evaluated. After PCI, the rate of TIMI grade 3, CTFC and incidence of sum-ST-segment resolution > 50% of high-dose group were significantly higher than those of control group, low-dose group and medium-dose group ( $P < .05$ ), and the CTFC of medium-dose group were significantly higher than that of control group, low-dose group ( $P < .05$ ). Moreover, the LVEF, left ventricular end diastolic diameter and left ventricular end systolic diameter of high-dose group were significantly improved than those of other groups, and the LVEF of medium-dose group was significantly superior to that of low-dose group ( $P < .05$ ). However, the incidence of major adverse cardiac events in high-dose group was significantly decreased, while the hemorrhage and incidence of thrombocytopenia of high-dose group were significantly higher than those of other 3 groups ( $P < .05$ ). The tirofiban can effectively alleviate the myocardial ischemia-reperfusion injury and promote the recovery of cardiac function in STEMI patients underwent PCI. Although the high-dose can enhance the clinical effects, it also increased the hemorrhagic risk. Therefore, the rational dosage application of tirofiban become much indispensable in view of patient's conditions and hemorrhagic risk, and a medium dose of 10  $\mu\text{g}/\text{kg}$  may be appropriate for patients without high hemorrhagic risk.

**Abbreviations:** CTFC = corrected TIMI frame count, LVEDD = left ventricular end diastolic diameter, LVEF = left ventricular ejection fraction, LVESD = left ventricular end systolic diameter, MACE = major adverse cardiac events, PCI = percutaneous coronary intervention, STEMI = ST elevation myocardial infarction, sumSTR = sum-ST-segment resolution, TIMI = thrombolysis in myocardial infarction.

**Keywords:** different dose, myocardial infarction, percutaneous coronary intervention, ST segment elevation, tirofiban

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<sup>a</sup>Department Pharmacy, the Second Clinical Hospital of Shanxi Medical University, Taiyuan, Shanxi, <sup>b</sup>AstraZeneca (Wuxi) trading co. LTD, Wuxi, Jiangsu, China.

\* Correspondence: Haixia Wang, Department Pharmacy, the Second Clinical Hospital of Shanxi Medical University, Taiyuan 030001, Shanxi, China (e-mail: hxwang@email.com).

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## 1. Introduction

Acute ST elevation myocardial infarction (STEMI) is usually caused by the coronary plaque rupture and acute thrombosis, which will result in coronary artery occlusion and myocardial necrosis, thus causing series of clinical symptoms.<sup>[1]</sup> At present, percutaneous coronary intervention (PCI) is widely accepted as a main therapy for STEMI in clinic. However, patency of epicardial vessels can not completely recover myocardial perfusion. Previous reports showed that ischemia-reperfusion injury and microembolization predominately contributed to the reperfusion of ischemic myocardium, which influenced the patients' cardiac function and long-term prognosis severely.<sup>[2-5]</sup> A large body of evidence suggests that serious cardiovascular adverse events such as angina pectoris, heart failure, and even sudden cardiac death may occur after PCI, owing to the lack of effective blood perfusion and oxygen supply in the myocardium.<sup>[6,7]</sup> Tirofiban is a kind of antiplatelet drug belonging to glycoprotein IIb/IIIa inhibitors. This glycoprotein IIb/IIIa inhibitor can inhibit the activation, adherence and aggregation of platelets; alleviate the myocardial perfusion injury; improve cardiac function and reduce the incidence of death. All of them are needed for

anchoring vessel revascularization after PCI.<sup>[8]</sup> However, the dose of tirofiban is still controversial, and its necessity and security also remain in uncertainty.<sup>[9–11]</sup> In this regard, totally 312 STEMI patients underwent PCI with different dose of tirofiban were included for case-control analysis, with aim at investigating the differences of clinical outcome, cardiac function and safety profiles between different dose of tirofiban.

## 2. Methods

### 2.1. Patients

A total of 312 acute STEMI patients who underwent PCI in our hospital from March 2017 to March 2018 were enrolled, referring to the Guidelines for the Diagnosis and Treatment of ST Elevation Acute Myocardial Infarction.<sup>[12]</sup> Inclusion criteria were listed below: patients age ranging from 50 years to 79 years; clinical manifestations with chest pain, nausea, vomiting and so on; the electrocardiography (ECG) showing ST-segment elevation of  $> 0.1$  mV in at least 2 leads, or new left bundle branch block; the level of creatine kinase-MB (CK-MB) and troponin-I (Tn-I) higher than normal level; residual thrombus from infarction-related culprit vessels verified by angiography. Exclusion criteria were set as below: cardiogenic shock or hemodynamic instability; severe hemorrhage inclination, high risk of bleeding (CRUSADE bleeding risk score  $> 40$  points); severe dysfunction of hepatic and kidney; persistent severe hypertension or cerebral hemorrhage within a year; allergic to tirofiban. The study protocols were approved by ethics committee of our hospital (SXR1600013), and written informed consent was obtained from all patients or their authorised relatives.

### 2.2. Treatment protocols

According to random number table, these patients were randomly divided into control group (75 cases, 0  $\mu\text{g}/\text{kg}$ ), low-dose group (79 cases, 5  $\mu\text{g}/\text{kg}$ ), medium-dose group (81 cases, 10  $\mu\text{g}/\text{kg}$ ) and high-dose group (77 cases, 20  $\mu\text{g}/\text{kg}$ ). All patients received 100~300 mg aspirin tablets (Xinhua Pharmaceutical Co., Ltd, Shandong, China) and 300~600 mg clopidogrel (Sanofi Minsheng Pharmaceutical Co., Ltd, Hangzhou, China). On this basis, the control group was treated with no tirofiban. In the low-dose group, a bolus of 5  $\mu\text{g}/\text{kg}$  tirofiban (Huadong pharmaceutical Co., Ltd, Hangzhou, China) was injected intravenously within 5 minutes, followed by continuous intravenous injection at 0.05  $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  for 36 h. In the medium-dose group, a bolus of 10  $\mu\text{g}/\text{kg}$  tirofiban was injected intravenously within 5 minutes, followed by continuous intravenous injection at 0.10  $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  for 36 hour. In the high-dose group, a bolus of 20  $\mu\text{g}/\text{kg}$  tirofiban was injected intravenously within 5 minutes, followed by continuous intravenous injection at 0.225  $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  for 36 hour. The maintenance dosage of tirofiban can be adjusted according to bleeding risk among groups mentioned above. After PCI, all patients were treated with oral aspirin (100 mg/d), and clopidogrel (75 mg/d) for at least 12 months. Simultaneously, other routine treatments, including the treatment of diuretics, statin drugs, angiotensin converting enzyme inhibitor, angiotensin receptor antagonist,  $\beta$ -adrenergic receptor blocker and calcium channel blockers, and so on, were performed according to patients' conditions. With the use of puncture through the right radial artery, perform coronary angiography was performed following catheter being put in to visualize infarction vessels. Based on the target lesions, patients

were treated with balloon dilation, and then stents were implanted routinely, with the ratio of stent diameter and vessel diameter at (1~1.1):1. Only the infarction related artery was intervened during operation. After that, these patients were subject to coronary arteriography examination. The operation was successful when the results showed that the presence of reperfusion of infarction related artery, residual stenosis of culprit lesion less than 30%, and no coronary arterial dissection and perforation. During the operation, for those patients who have bradycardia should be implanted with temporary pacemakers, and for those who appeared hemodynamic instability or cardiogenic shock, the intra-aortic balloon pump can be performed with alternative therapy.

### 2.3. Observational parameters

For the indicators of myocardial reperfusion:<sup>[13]</sup> the myocardial reperfusion was assessed after PCI therapy. The thrombolysis in myocardial infarction (TIMI) grade 3 flow, corrected TIMI frame count and the 90-minutes sum-ST-segment resolution (sumSTR) were recorded. The cardiac function indexes:<sup>[14]</sup> the color Doppler imaging (CDI) was used to measure the left ventricular ejection fraction (LVEF), left ventricular end diastolic diameter (LVEDD) and left ventricular end systolic diameter (LVESD). For the primary clinical end point of the study: major adverse cardiac events (MACE) after 30 days after the PCI were recorded, which included angina pectoris, myocardial infarction, acute heart failure, cardiac death, and target vessel revascularization (TVR), and so on. For the hemorrhage and thrombocytopenia: after PCI, hemorrhage mainly included bleeding at puncture place, hemorrhage of skin and tunica mucosa, gastrointestinal hemorrhage, hematuria and intracranial hemorrhage, and so on. In addition, the thrombocytopenia was recorded.

### 2.4. Statistical analysis

All statistical analysis was conducted by SPSS 25.0. The measurement data were expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ), and analysis of variance were used for comparison among 4 groups. The enumeration data were expressed as percentages (%) and were compared using the Chi-Square ( $\chi^2$ ) test. The rank sum test was adopted to compare the ranked data.  $P < .05$  was considered statistically significant.

## 3. Results

### 3.1. General characteristics of patients

From March 2017 to March 2018, a total of 312 acute STEMI patients who underwent PCI in our hospital were enrolled and randomly assigned to control group (75 cases, 0  $\mu\text{g}/\text{kg}$ ), low-dose group (79 cases, 5  $\mu\text{g}/\text{kg}$ ), medium-dose group (81 cases, 10  $\mu\text{g}/\text{kg}$ ) and high-dose group (77 cases, 20  $\mu\text{g}/\text{kg}$ ). The general data of the 4 groups were analyzed. The 4 groups showed no significant differences in general data ( $P > .05$ ) (Table 1).

### 3.2. Comparisons of postoperative myocardial reperfusion indexes among the 4 groups

TIMI grade 3 flow, CTFC, and sumSTR  $> 50\%$  of high-dose group were significantly higher than those of control group, low-dose group and medium-dose group ( $P = .010, < .001, < .001$ ), and the CTFC of medium-dose group were significantly higher

**Table 1****Comparisons of general data of Patients.**

	Control group (n = 75)	Low-dose group (n = 79)	Medium-dose group (n = 81)	High-dose group (n = 77)	P value
Age, yr	58.64 ± 10.78	57.49 ± 11.52	57.63 ± 12.28	56.85 ± 11.30	.815
Gender					.244
Male (%)	52 (69.33)	47 (59.49)	58 (71.60)	46 (59.74)	
Female (%)	23 (30.67)	32 (40.51)	23 (28.40)	31 (40.26)	
Diabetes (%)	9 (12.00)	15 (18.99)	12 (14.81)	13 (16.88)	.671
Hypertension (%)	40 (53.33)	48 (60.76)	45 (55.56)	46 (59.74)	.763
Hyperlipidemia (%)	28 (37.33)	27 (34.18)	33 (40.74)	32 (41.56)	.767
Smoker (%)	38 (50.67)	45 (56.96)	49 (60.49)	43 (55.84)	.669
Body mass index, kg/m <sup>2</sup>	24.56 ± 3.73	25.46 ± 3.51	25.37 ± 2.46	24.77 ± 3.54	.253
Killip class					.879
I (%)	45 (60.00)	49 (62.03)	51 (62.96)	47 (61.04)	
II (%)	16 (21.33)	19 (24.05)	17 (20.99)	18 (23.38)	
III (%)	9 (12.00)	7 (8.86)	8 (9.88)	8 (10.39)	
IV (%)	5 (6.67)	4 (5.06)	5 (6.17)	4 (5.19)	
CRUSADE bleeding risk score	32.19 ± 7.32	31.52 ± 8.46	29.73 ± 7.94	30.07 ± 8.58	.185
Infarct-related artery					.925
Anterior descending (%)	34 (45.33)	33 (41.77)	34 (41.98)	31 (40.26)	
Circumflex artery (%)	23 (30.67)	24 (30.38)	24 (29.63)	24 (31.17)	
Right coronary artery (%)	18 (24.00)	22 (27.85)	23 (28.39)	22 (28.57)	
Diseased vessels, n					.867
1 vessel (%)	28 (37.33)	31 (39.24)	34 (41.98)	33 (42.86)	
2 vessels (%)	30 (40.00)	26 (32.91)	29 (35.80)	23 (29.87)	
3 vessels (%)	17 (22.67)	22 (27.85)	18 (22.22)	21 (27.27)	
pacemaker	21 (28.00)	20 (25.32)	27 (33.33)	23 (29.87)	.725
intra-aortic balloon pump	9 (12.00)	18 (22.78)	14 (17.28)	12 (15.58)	.345
Onset-to-PCI time (h)	5.79 ± 1.56	6.04 ± 1.61	5.66 ± 1.37	5.73 ± 1.65	.439

PCI=percutaneous coronary intervention.

than that of control group, low-dose group ( $P < .05$ ). However, there was no statistical differences in the comparison of TIMI grade 3 flow and sumSTR >50% among control group, low-dose group and medium-dose group ( $P > .05$ ). (Table 2)

### 3.3. Comparisons of cardiac function index among the 4 groups

Before the PCI, no the differences were observed in the comparisons of LVEF, LVEDD and LVESD among the 4 groups ( $P > .05$ ). At 7 days, 30 days after the PCI, the LVEF, LVEDD and LVESD of high-dose group were all superior to those of control group, low-dose group and medium-dose group ( $P < .001$ ). At 30 days after the PCI, the LVEF, LVEDD and LVESD of medium-dose group were superior to those of control group, and the LVEF of medium-dose group was superior to that of low-dose group, the differences mentioned above showed statistical significant ( $P < .05$ ).

### 3.4. Comparisons of incidence of MACE among the 4 groups

The incidence of MACE in control group, low-dose group, medium-dose group and high-dose group within 30 days were 34.67%, 26.58%, 16.05%, and 7.79%, respectively. The incidence of MACE in high-dose group were significantly lower than that in control group, low-dose group and medium-dose group, and the medium-dose group were significantly lower than that in control group, these differences showed statistical significant ( $P < .05$ ). No significant differences were observed at the incidence of MACE in control group and low-dose group ( $P > .05$ ).

### 3.5. Comparisons of the incidence of the hemorrhage and thrombocytopenia among the 4 groups

The incidence of the hemorrhage in control group, low-dose group, medium-dose group and high-dose group were 10.67%, 6.33%, 11.11%, and 29.87%, respectively, and their individual

**Table 2****Comparisons of postoperative myocardial reperfusion indexes.**

	Control group (n = 75)	Low-dose group (n = 79)	Medium-dose group (n = 81)	High-dose group (n = 77)	P value
TIMI grade 3	54 (72.00)	60 (75.95)	66 (81.48)	71 (92.21) <sup>a,b,c</sup>	.010
CTFC	27.06 ± 6.97	25.29 ± 5.51	22.86 ± 4.64 <sup>a,b</sup>	21.03 ± 5.09 <sup>a,b,c</sup>	<.001
sumSTR >50%	49 (65.33)	54 (68.35)	60 (74.07)	71 (92.21) <sup>a,b,c</sup>	<.001

CTFC=corrected TIMI frame count, sumSTR=sum-ST-segment resolution, TIMI=thrombolysis in myocardial infarction.

<sup>a</sup> compared with control group,  $P < .05$ .

<sup>b</sup> compared with low-dose group,  $P < .05$ .

<sup>c</sup> compared with medium-dose group,  $P < .05$ .

**Table 3**  
Comparisons of indexes for cardiac function.

		Control group (n = 75)	Low-dose group (n = 79)	Medium-dose group (n = 81)	High-dose group (n = 77)	P value
LVEF (%)	Before PCI	45.19 ± 5.48	44.36 ± 5.46	44.86 ± 5.09	43.59 ± 5.17	.267
	7d after PCI	51.76 ± 5.78	52.35 ± 5.04	52.96 ± 4.83	55.75 ± 5.37 <sup>a,b,c</sup>	<.001
	30d after PCI	52.38 ± 5.39	53.03 ± 5.44	55.23 ± 5.67 <sup>a,b</sup>	59.81 ± 6.61 <sup>a,b,c</sup>	<.001
LVEDD (mm)	Before PCI	49.57 ± 5.68	49.63 ± 4.77	50.18 ± 4.82	49.76 ± 4.52	.865
	7d after PCI	45.97 ± 6.85	45.31 ± 5.31	44.84 ± 5.43	42.35 ± 4.69 <sup>a,b,c</sup>	<.001
	30d after PCI	45.33 ± 6.09	44.65 ± 4.01	43.24 ± 4.73 <sup>a</sup>	40.33 ± 4.30 <sup>a,b,c</sup>	<.001
LVESD (mm)	Before PCI	38.81 ± 4.32	38.15 ± 3.48	37.62 ± 3.39	37.66 ± 3.30	.150
	7d after PCI	37.25 ± 3.82	36.13 ± 3.64	35.86 ± 4.37	32.19 ± 4.09 <sup>a,b,c</sup>	<.001
	30d after PCI	34.57 ± 3.81	33.52 ± 4.03	32.44 ± 3.31 <sup>a</sup>	31.59 ± 3.51 <sup>a,b,c</sup>	<.001

LVEDD = left ventricular end diastolic diameter, LVEF = left ventricular ejection fraction, LVESD = left ventricular end systolic diameter.

<sup>a</sup> compared with control group,  $P < .05$ .<sup>b</sup> compared with low-dose group,  $P < .05$ .<sup>c</sup> compared with medium-dose group,  $P < .05$ .**Table 4**  
Comparisons of the incidence of MACE.

	Control group (n = 75)	Low-dose group (n = 79)	Medium-dose group (n = 81)	High-dose group (n = 77)	P value
Myocardial infarction	7 (9.33)	6 (7.59)	3 (3.70)	2 (2.60)	
Angina pectoris	10 (13.33)	6 (7.59)	4 (4.94)	2 (2.60)	
Acute heart failure	5 (6.67)	5 (6.33)	4 (4.94)	2 (2.60)	
Cardiac death	0 (0.00)	1 (1.27)	0 (0.00)	0 (0.00)	
TVR	4 (5.33)	3 (3.80)	2 (2.47)	0 (0.00)	
MACE	26 (34.67)	21 (26.58)	13 (16.05) <sup>a</sup>	6 (7.79) <sup>a,b,c</sup>	<.001

MACE = major adverse cardiac events, TVR = target vessel revascularization.

<sup>a</sup> compared with control group,  $P < .05$ .<sup>b</sup> compared with low-dose group,  $P < .05$ .<sup>c</sup> compared with medium-dose group,  $P < .05$ .

incidence of thrombocytopenia were 4.00%, 6.36%, 12.35%, and 23.38%. The incidence of the hemorrhage and thrombocytopenia in high-dose group were significantly higher than those in control group, low-dose group, medium-dose group ( $P < .001$ ). However, no significant difference was observed for the incidence of the hemorrhage and thrombocytopenia among control group, low-dose group, medium-dose group ( $P > .05$ ).

#### 4. Discussion

Acute STEMI is a common cardiovascular emergency which is induced by severe coronary artery stenosis or occlusion, leading to myocardial ischemia, anoxia, and necrosis in the relevant blood supply area, and is also 1 of the reasons that cause the death of patients with cardiovascular diseases.<sup>[15]</sup> Previous

studies showed that the efficacy of PCI on patients with STEMI was remarkable, which can increase the patency of infarction-related coronary artery, recover the myocardial ischemia-reperfusion injury, and improve the prognosis of patients.<sup>[16,17]</sup> Some studies confirmed that the combined application of IIb/IIIa receptor antagonists for patients with acute myocardial infarction (AMI) undergoing PCI can significantly increase the postoperative coronary TIMI flow grading of infarction-related coronary artery, prompt the myocardial perfusion, reduce the incidence of MACE.<sup>[18–20]</sup> Tirofiban is a non-peptide reversible antagonist of glycoprotein IIb/IIIa receptor, which can block fibrinogen receptor binding to glycoprotein IIb/IIIa complex and effectively inhibit the platelet aggregation after specifically binding to surface receptors of platelet.<sup>[21]</sup> Furthermore, tirofiban can inhibit inflammatory factors and vasoconstrictive substances,

**Table 5**  
Comparisons of the incidence of the hemorrhage and thrombocytopenia.

	Control group (n = 75)	Low-dose group (n = 79)	Medium-dose group (n = 81)	High-dose group (n = 77)	P value
Hemorrhage	Gastrointestinal hemorrhage	2 (2.67)	0	3 (3.70)	6 (7.79)
	Intracranial hemorrhage	0	0	0	3 (3.90)
	Hemorrhage at puncture place	2 (2.67)	3 (3.80)	5 (6.17)	9 (11.69)
	Other hemorrhage	4 (5.33)	2 (2.53)	1 (1.23)	5 (6.49)
	Total incidence	8 (10.67)	5 (6.33)	9 (11.11)	23 (29.87) <sup>a,b,c</sup>
Thrombocytopenia	3 (4.00)	5 (6.33)	10 (12.35)	18 (23.38) <sup>a,b,c</sup>	<.001

<sup>a</sup> compared with control group,  $P < .05$ .<sup>b</sup> compared with low-dose group,  $P < .05$ .<sup>c</sup> compared with medium-dose group,  $P < .05$ .

improve the microcirculation at the early stage, and reduce the incidence of MACE. The efficacy of tirofiban in the treatment of STEMI has drawn global attention. Unfortunately, some studies have suggested that it can also increase the risk of hemorrhage, and the clinical dose has not yet reached a wide consensus. The common recommended clinical dose is 10  $\mu\text{g}/\text{kg}$ , followed by continuous intravenous injection at 0.15  $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ , which is usually accompanied with a high recurrence rate of MACE.<sup>[22]</sup> Hence, the appropriate dosage of tirofiban is still under dispute.

In this study, the LVEF, LVEDD and LVESD of the high-dose group were all superior to those of control group, low-dose group and medium-dose group at 7, 30 days ( $P < .001$ ). Furthermore, the LVEF, LVEDD and LVESD of medium-dose group were all superior to those of control group, and the LVEF of medium-dose group was superior to that of low-dose group at 30 days after PCI, ( $P < .05$ ). These data suggesting that the increase of tirofiban dose may have certain correlations to the improvement of efficacy, which is consistent with other's study.<sup>[23]</sup> The safety concern of tirofiban mainly refers to the risk of hemorrhage. The application of tirofiban can cause thrombocytopenia and increase the risk of hemorrhage-related complications, especially severe hemorrhage such as intracranial hemorrhage, which can lead to death in some patients.<sup>[24,25]</sup> Recently, a study showed that, the incidence and mortality of hemorrhage in AMI patients were positively correlated with the dose of antiplatelet drugs.<sup>[26]</sup>

In order to investigate the clinical effect and safety of tirofiban, the different dose of tirofiban was used for patients with STEMI undergoing PCI. The results demonstrated that the improvements of myocardial ischemia-reperfusion injury and cardiac function in high-dose group was significantly better than that in control group, medium-dose group and low-dose group, and the incidence of MACE in high-dose group was significantly lower than that in control group, medium-dose group and low-dose group ( $P < .001$ ), indicating that high-dose of tirofiban can improve the cardiac function, and reduce the incidence of MACE. The mechanism underpinning this effect might be due to the strong inhibitory effect of high-dose of tirofiban on platelets, which can improve the coronary artery flow, increase blood supply of myocardial cell. More importantly, it can obviously reduce the area of myocardial infarction, and promote the ST segment down-regulation.<sup>[27]</sup> Nevertheless, the incidence of the hemorrhage in the high-dose group was significantly higher than that in control group, low-dose group and medium-dose group ( $P < .001$ ), suggesting the incidence of hemorrhage occurred in a dose-dependent relationship and high-dose of tirofiban increased the incidence of hemorrhage.<sup>[28]</sup>

Several lines of evidence demonstrated that the glycoprotein IIb/IIIa inhibitors had great effect on reducing the incidence of MACE. Fabris E, et al<sup>[29]</sup> argued that tirofiban prehospital treatment can reduce the incidence of MACE and mortality at 30 days, 1-year. Velibey Y, et al<sup>[30]</sup> pointed out that tirofiban was associated with a lower short- and long-term mortality, although the higher incidence of complications in hospital stay. Consistent with this argument, the incidence of MACE in high-dose group was also obviously higher than those in other 3 groups at 30 days (7.79% vs 34.67%, 26.58%, 16.05%), along with higher complications of hemorrhage (29.87% vs 10.67%, 6.33%, 11.11%). Hence, these data suggested that appropriate dosage of tirofiban should be cautiously applied according to patient's hemorrhagic risk.

The results of this study displayed that the application of tirofiban in STEMI patients underwent PCI can alleviate the myocardial ischemia-reperfusion injury and promote early

recovery of cardiac function, along with better clinical efficacy. In other studies, Zhang Y, et al<sup>[32]</sup> drew a conclusion that the 10  $\mu\text{g}/\text{kg}$  tirofiban can effectively prevent stent thrombosis, alleviate the inflammatory reaction in PCI patients, improve the quality of life with safe control of hemorrhagic risk. However, a meta-analysis pointed out that moderate tirofiban was a safe treatment, but the protocol of intra-arterial administration required further research.<sup>[31]</sup> As we know, the assessments and managements of hemorrhagic risk was an important concern for the PCI patients. The CRUSADE bleeding risk score was widely used in assessments of hemorrhagic risk, and CRUSADE bleeding risk score  $>40$  points were considered as high risk of hemorrhage.<sup>[33]</sup> In this study, only patients without hemorrhagic risk were included into study and this study design was not suitable for hemorrhagic risk patients. In addition, the sample size of this study was a little small, which may lead to some statistical bias. The application of tirofiban in treatment for STEMI need to be investigated in randomized study with larger sample from multicenter.

In conclusion, the efficacy of tirofiban for acute STEMI patients underwent PCI was positively correlated with its dose. The high dose can enhance the clinical effects, but also increase the risk of hemorrhage. Therefore, the appropriate dose could be adopted by reference to the specific conditions of patients under assessment of hemorrhagic risk, and a medium dose of 10  $\mu\text{g}/\text{kg}$  may be appropriate for patients without high hemorrhagic risk.

## Author contributions

HW and MF designed and conducted the study, and drafted the manuscript. HW and MF help conducting the study and analyzing the data.

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