Comparison of Intracoronary Versus Intravenous Tirofiban in Acute STEMI Patients Undergoing Primary PCI

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Research Article

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Abstract

Objective: This study aimed to investigate the effect of intracoronary tiroban compared to intravenously administered tiroban in acute ST-elevation myocardial infarction (STEMI) patients treated with primary percutaneous coronary intervention (PPCI).

Methods: This study included 180 patients who were admitted with the diagnosis of acute STEMI and undergoing primary PCI. Patients were randomized into an observation group (n = 90) and control group (n = 90). Both groups received typical treatments, such as aspirin and clopidogrel/ticagrelor. During the procedure, the observation and control groups were administered intracoronary (IC) or intravenous (IV) injections of tiroban, respectively, followed by an intravenous infusion of tiroban for 24 hours. Changes in thrombolysis in myocardial infarction (TIMI) flow grading, TIMI myocardial perfusion grade 3 (TMP grade 3), thrombus aspiration, brain natriuretic peptide (BNP) levels, creatine kinase peak and inflammatory factor levels, infarct size, resolution of the sum of ST-segment elevation (Sum-STR) two hours after the operation, and cardiac functional parameters were investigated before and/or after treatment and 6 months after discharge. The incidence of major adverse cardiovascular events (MACE) and adverse reactions (AEs) such as bleeding were compared between the two groups.

Results: There were no statistically significant differences observed in the indices of BNP, creatine kinase peak, cardiac functional parameters, thrombus aspiration, or incidence of bleeding between the two groups before treatment. Following treatment, TIMI flow grading and TMP grade 3 were improved in the observation group that received intracoronary tiroban compared to the control group (p = 0.022 and p = 0.014, respectively). Additionally, the Sum-umi two hours after operation in the observation group was better than that in the control group (p = 0.029). The incidence of MACEs in patients given IC tiroban administration was lower than that in those given IV tiroban (p = 0.012). Furthermore, levels of glutamic oxaloacetictransaminase (AST), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and myocardial troponin I (TNI) in the observation group was significantly decreased compared to the control group after five days of treatment (p = 0.039, p = 0.040, p = 0.001, and p = 0.041, respectively). Functional heart parameters including CO and LVEF were significantly improved in the observation group 6 months after discharge.

Conclusion: This study found that IC administration of tiroban in patients with STEMI who underwent PPCI improved TIMI, TMP flow and cardiac function including CO and LVEF 6 months after discharge, and reduced CRP, ESR, and TNI. However, the incidence of bleeding between the two groups was comparable. These findings suggest that IC administration should be applied in certain acute STEMI patients.

Introduction
Acute ST-elevation myocardial infarction (STEMI) is the most severe form of coronary artery disease, contributing to increased morbidity, mortality, and rehospitalization. Primary percutaneous coronary intervention (PPCI) is accepted as the most effective therapy for STEMI [1–4]. However, the restoration of large-vessel flow does not necessarily equate to recovery of myocardial tissue perfusion and lessening of ischemia-reperfusion injury. Studies demonstrated that serious cardiovascular adverse events, such as cardiac failure, cardiogenic shock, malignant arrhythmia, and sudden cardiac death, appear after PPCI, due to a lack of effective myocardial perfusion and insufficient oxygen supply in the myocardium [3–5]. Thromboembolic complications range from 5–25% in STEMI patients undergoing PPCI with slow flow or no-reflow complications, also promoting morbidity and mortality [6, 7]. Glycoprotein IIb/IIIa inhibitors (GPI) reduce fibrous protein in plasma and block the GP IIb/IIIa receptor to inhibit platelet aggregation. GPI is recommended for use in STEMI patients undergoing PPCI with hyperthrombotic burden or as a prophylactic treatment when the risk of thrombi formation is significant [8–10]. Yet, optimal application of GPIs to prevent thromboembolic complications remains to be determined. The current study investigated whether intracoronary (IC) administration of the GPI tirofiban has an advantage over intravenous IV administration in STEMI patients undergoing PCI with a hyperthrombotic burden.

**Methods**

**Study design**

The study protocol was approved by the local ethics committee (Approval #: 201601B003). The study enrolled patients between January 1, 2019, and February 28, 2021 who were diagnosed with STEMI and undergoing PPCI with hyperthrombotic burden. The included patients consented to participate in the study who were informed consent. STEMI was defined in accordance with acute myocardial infarction (AMI) guidelines [1]. This study was a prospective, randomized, open-label trial. All included patients received the same drug regimen, except for the administration route of GPI, including ACEIs/ARBs, β-blockers, and statins in accordance with the guidelines for the management of AMI [1, 2, 4]. The included patients were randomized into either IC or IV bolus of GPI (tirofiban, 10 µg/kg, 1–3 min) with subsequent intravenous infusion over 24 hours, at 0.15 µg/kg per minute. All researchers involved in this study were physicians.

Inclusion criteria were: 1) age > 18 years; 2) diagnosed with STEMI within 12 hours, in accordance with guidelines for the management of AMI; 3) underwent PPCI with hyperthrombotic burden; 4) Killip class ≤ 3; and 5) informed consent obtained.

Exclusion criteria were: 1) cardiogenic shock; 2) life-threatening diseases or malignant tumor; 3) malignant systema sanguineum disease; 4) severe hepatic and/or renal dysfunction; 5) anemia defined as a haemoglobin less than 60 g/L; 6) no provision of informed consent; and 7) suspected mechanical complications of AMI (e.g., septal rupture, wall rupture, or ischemic mitral valve regurgitation).

**Study endpoints**
The primary endpoints were the indices of coronary artery and myocardial perfusion, including thrombolysis in myocardial infarction (TIMI) flow grading, TIMI myocardial perfusion grade 3 (TMP grade 3), the number of thrombus aspirations in the operation, resolution of the sum of ST-segment elevation (Sum-STR) two hours after the operation, and certain blood indices. These included brain natriuretic peptide (BNP), creatine kinase (CK) and isoenzyme (CK-MB), serum glutamic pyruvic transaminase (ALT), glutamic oxaloacetictransaminase (AST), N-terminal pro-brain natriuretic peptide (NT-pro-BNP), blood uric acid (UA), blood glucose, glycosylated haemoglobin A1c (HbA1c), serum urea, serum creatinine (Cr), and myocardial troponin I (TNI). Other study endpoints were left-ventricular end-diastolic dimension (LVEDD), left-ventricular ejection fraction (LVEF), and cardiac output (CO). Additionally, the study examined inflammatory factors in serum including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), serum tumour necrosis factor (TNF-α), transforming growth factor-β1 (TGF-β1), interleukin-6 (IL-6), and interleukin-10 (IL-10). The second endpoints were bleeding events and major adverse cardiovascular events (MACEs) following PPCI. Bleeding events were classified by the Global Utilization of Streptokinase and GPI for Occluded Coronary Arteries (GUSTO) criteria. MACEs were defined as sudden cardiac death, angina pectoris, nonfatal reinfarction, target vessel rethrombosis, and heart failure. Of note, the study examined HbA1c as a primary endpoint among patients with diabetes.

**Follow-up**

All data were collected in the hospital. CK, CKMB, cTnI, UA, NT-pro-BNP, blood glucose, serum urea, and Cr were assessed immediately on presentation and again at 6 AM on day 2 post-procedure. ALT, AST, HbA1c, CRP, TNF-α, TGF-β1, IL-6, and IL-10 were assessed on day 2 post-procedure. Some indices, including ALT, AST, cTnI, CRP, UA, ESR, serum urea, and Cr, were tested again at 6 AM on day 5 post-procedure. Cardiac functional parameters, including LVEDD, LVEF, and CO, were determined on days 5 or 6 post-procedure and 6 months after discharge. ECGs were collected before PPCI and at two hours after PPCI. The Sum-STR was obtained to determine if there was difference between the two groups. According to the guidelines issued by the European Society of Cardiology and the American College of Cardiology/American Heart Association [1, 5, 11], a Sum-STR ≥ 50% was considered effective myocardial perfusion and a Sum-STR < 50% was taken as incomplete or ineffectual myocardial perfusion. TIMI and TMP grades were used to evaluate coronary blood flow and myocardial perfusion and were determined during the procedure. The determination of TIMI and TMP grade was made by two experienced physicians. TIMI flow grade was classified as 0, 1, 2, or 3. A TIMI flow grade of 0 is defined as no-reflow in the culprit artery; TIMI flow grade 1 is defined as partial contrast penetration without distal vessel filling; TIMI flow grade 2 indicates full perfusion with slow filling and clearance rates; and TIMI flow grade 3 indicates full perfusion with normal filling and clearance rates. TMP flow was also graded into 0, 1, 2, or 3. TMP flow was classified as follows: grade 0 indicated no myocardial perfusion in the distribution of the infarct vessel; grade 1, slight penetration of contrast medium, without clearance from the coronary microcirculation; grade 2, moderate penetration of contrast medium, with slow clearance from the coronary microcirculation; and grade 3, normal myocardial perfusion with normal blush. In this study, TIMI flow grade 3 and TMP flow grades 2–3 were considered good coronary perfusion and efficient...
myocardial perfusion. In addition, bleeding events and MACEs that occurred within the hospital were recorded.

**Statistical analyses**

PASS 15.0 software was used to calculate the sample size. Indicators of myocardial perfusion were noted significantly improved in a high-dose treatment group (20 µg/kg) over the medium-dose group (10 µg/kg), while resolution of the Sum-STR two hours after operation was 92.21% in the high-dose treatment group and 74.07% in the medium-dose group [5]. In our study, results in the IC group were expected to be consistent with those of the high-dose group. We sought to achieve 90% power at a 5% significance level (2-sided). Therefore, 85 patients per group were estimated to be needed to demonstrate a treatment effect. The current study included 90 patients in both the control and experimental groups.

Statistical analyses were performed using SPSS 20.0 (SPSS Inc., Chicago, IL). Continuous variables were analyzed using the Student’s t test and are expressed as mean ± SD. Dichotomous variables were analyzed using the chi-square test. All comparisons were two-tailed, and p < 0.05 was considered statistically significant.

**Results**

A total of 184 STEMI patients were randomized into either IC or IV bolus tirofiban (10 µg/kg, 1–3 min), with both groups receiving an intravenous infusion over 24 hours at 0.15 µg/kg per minute (Fig. 1). Four patients were excluded because of no follow-up, resulting in 90 patients in the IC and IV cohorts. Baseline characteristics of the included patients are presented in Table 1. No age or sex differences were observed between groups [age: (59.92 ± 10.96) vs (59.21 ± 9.95), p = 0.649, sex: male 71% vs 69%, p = 0.745]. There were no significant differences between groups regarding the distribution of infarction location [acute anterior myocardial infarction: 41(46%) vs 30 (33%), p = 0.093]. The onset-to-wire times were also similar between groups [(3.46 ± 1.95) vs (4.05 ± 3.19) hours, p = 0.133]. The numbers of stents placed were comparable between the groups [(1.08 ± 0.55) vs (1.14 ± 0.57), p = 0.425]. Comorbid diseases between the IC and IV groups were also similar (see Table 1). Routine treatments and the baseline biochemical criterion were not found to be significantly different between the two groups (Tables 2 and 3).
### Table 1  
**Baseline clinical characteristics**

| Characteristic                                                  | Intravenous tirofban (n = 90) | Intracoronary tirofban (n = 90) | p value |
|----------------------------------------------------------------|-------------------------------|---------------------------------|---------|
| Age (years)                                                    | 59.92 ± 10.96                  | 59.21 ± 9.95                    | 0.649   |
| Male, n (%)                                                    | 64 (71%)                       | 62 (69%)                        | 0.745   |
| Diabetes mellitus, n (%)                                       | 30 (33%)                       | 33 (37%)                        | 0.639   |
| Hypertension n (%)                                             | 57 (63%)                       | 51 (57%)                        | 0.361   |
| Hyperlipidaemia n (%)                                          | 7 (8%)                         | 11 (12%)                        | 0.320   |
| Previous myocardial infarction, n (%)                          | 7 (8%)                         | 14 (16%)                        | 0.104   |
| • Previous cerebrovascular and peripheral vascular diseases, n (%) | 23 (25%)                       | 18 (20%)                        | 0.374   |
| • Previous digestive disorders, n (%)                          | 5 (6%)                         | 6 (7%)                          | 0.550   |
| Current or previous smoker, n (%)                              | 50 (55%)                       | 44 (49%)                        | 0.371   |
| Current or previous alcoholism, n (%)                          | 22 (24%)                       | 16 (18%)                        | 0.273   |
| Distribution of infarction location (anterior myocardial infarction), n (%) | 41 (46%)                       | 30 (33%)                        | 0.093   |
| Onset-to-wire time, hours                                      | 3.46 ± 1.95                    | 4.05 ± 3.19                     | 0.133   |
| Distribution of infarction location                            | 30 (33%)                       | 44 (49%)                        | 0.097   |
| Number of stents                                                | 1.08 ± 0.55                    | 1.14 ± 0.57                     | 0.425   |

### Table 2  
**Pharmacologic treatments**

| Drug               | Intravenous tirofban (n = 90) | Intracoronary tirofban (n = 90) | p value |
|--------------------|-------------------------------|---------------------------------|---------|
| Aspirin            | 90                            | 90                              | –       |
| Ticagrelor         | 85                            | 80                              | 0.178   |
| β-blockers         | 46                            | 57                              | 0.097   |
| ACEIs/ARBs         | 35                            | 42                              | 0.292   |
| Statins            | 88                            | 84                              | 0.278   |
| Nitrates           | 81                            | 84                              | 0.418   |

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.
Table 3
Baseline laboratory data at admission.

| Index       | Intravenous tirofiban (n = 90) | Intracoronary tirofiban (n = 90) | p value |
|-------------|--------------------------------|---------------------------------|---------|
| CK          | 190.6 ± 154.6                  | 153.6 ± 85.6                    | 0.052   |
| CKMB        | 19.63 ± 14.9                   | 16.8 ± 5.2                      | 0.088   |
| cTNI        | 0.8 ± 2.9                      | 1.5 ± 4.3                       | 0.217   |
| UA          | 373.8 ± 120.0                  | 392.9 ± 131.7                   | 0.321   |
| NT-pro-BNP  | 1596.3 ± 4936.7                | 1752.8 ± 4863.3                 | 0.857   |
| Cr          | 78.5 ± 46.7                    | 85.5 ± 52.2                     | 0.344   |
| Urea        | 6.9 ± 2.5                      | 7.8 ± 6.0                       | 0.206   |
| Glucose     | 10.1 ± 4.5                     | 10.5 ± 4.6                      | 0.605   |

CK and CK-MB, serum creatine kinase and its isoenzyme; cTNI, cardiac troponin I; UA, blood uric acid; NT-pro-BNP, N-terminal pro-Brain Natriuretic Peptide; Cr, serum creatinine

Study endpoints

CK, CKMB, cTNI, ALT, AST, NT-pro-BNP, blood glucose, HbA1C, CRP, TNF-α, TGF-β1, IL-6, and IL-10 were not significantly lower among cohorts at day 2 post-procedure (p = 0.112, p = 0.056, p = 0.074, p = 0.830, p = 0.972, p = 0.787, p = 0.316, p = 0.774, p = 0.334, p = 0.809, p = 0.183, p = 0.593, and p = 0.677 respectively). However, by day 6 post-procedure, cTNI, AST, CRP, and ESR were lower in the IC versus the IV group (p = 0.041, p = 0.039, p = 0.040, and p = 0.001, respectively; Table 4). Markers of kidney function, including serum urea, Cr, and UA, were not significantly different between groups (p = 0.749, p = 0.412, and p = 0.163, respectively; Table 4). In addition, the study showed no difference in LA, LVEDD, CO, or LVEF between groups (p = 0.163, p = 0.160, p = 0.555, and p = 0.360, respectively; Table 5). However, various indicators of cardiac function, including CO and LVEF 6 months after discharge, were increased, albeit modestly, in the observation group (p = 0.019 and p = 0.026, respectively; Table 5). Still, TIMI flow grade 3 after PPCI, TMP flow grades 2–3 after PPCI, Sum-STR ≥ 50%, and in-hospital MACEs were improved in the IC versus the IV group (p = 0.022, p = 0.014, p = 0.029, and p = 0.012, respectively). Bleeding events were not significantly different between the two groups (p = 0.703).
### Table 4
In-hospital post-admission laboratory data.

| Index            | Intravenous tirofiban (n = 90) | Intracoronary tirofiban (n = 90) | p value |
|------------------|---------------------------------|-----------------------------------|---------|
| CK on day 2      | 2029.2 ± 1293.1                 | 2505.3 ± 2417.4                  | 0.112   |
| CKMB on day 2    | 179.4 ± 115.7                   | 224.4 ± 181.1                    | 0.056   |
| cTNI on day 2    | 74.0 ± 40.3                     | 86.5 ± 51.9                      | 0.074   |
| cTNI on day 6    | 8.9 ± 6.4                       | 6.9 ± 6.6                        | 0.041   |
| ALT on day 2     | 41.5 ± 32.6                     | 40.5 ± 27.8                      | 0.830   |
| AST on day 2     | 96.8 ± 124.3                    | 96.3 ± 95.9                      | 0.972   |
| ALT on day 6     | 39.3 ± 36.7                     | 45.6 ± 39.1                      | 0.272   |
| AST on day 6     | 60.8 ± 58.7                     | 45.0 ± 39.4                      | 0.039   |
| Cr on day 6      | 80.5 ± 49.3                     | 78.3 ± 41.2                      | 0.749   |
| Urea on day 6    | 6.5 ± 3.2                       | 6.1 ± 2.5                        | 0.412   |
| UA on day 6      | 360.4 ± 128.7                   | 390.9 ± 144.8                    | 0.163   |
| Glucose on day 2 | 6.9 ± 2.7                       | 6.6 ± 1.9                        | 0.316   |
| HbA1C on day 2   | 6.6 ± 1.5                       | 6.7 ± 1.6                        | 0.774   |
| NT-pro-BNP on day 2 | 2079.0 ± 3654.6               | 1891.0 ± 3634.2                  | 0.787   |
| CRP on day 2     | 110.2 ± 203.1                   | 84.3 ± 151.4                     | 0.334   |
| TNF-α on day 2   | 53.4 ± 92.7                     | 50.2 ± 83.0                      | 0.809   |
| TGF-β1 on day 2  | 69.3 ± 130.3                    | 47.2 ± 86.8                      | 0.183   |
| IL-6 on day 2    | 8.4 ± 13.6                      | 7.4 ± 10.2                       | 0.593   |
| IL-10 on day 2   | 17.3 ± 26.8                     | 15.8 ± 21.8                      | 0.677   |
| CRP on day 6     | 38.6 ± 42.1                     | 26.5 ± 24.5                      | 0.040   |
| ESR on day 6     | 33.2 ± 18.6                     | 24.0 ± 14.9                      | 0.001   |
Table 5
In-hospital (days 5–6 post-procedure) and 6 months after discharge echocardiogram indices (±s)

| Index            | Intravenous tirofiban (n=90) | Intracoronary tirofiban (n= 90) | P value |
|------------------|-----------------------------|---------------------------------|---------|
| LA (mm)          | 37.2±3.9                    | 36.3±3.7                        | 0.146   |
|                  | 37.2±3.9                    | 36.3±3.7                        | 0.146   |
| LVEDD (mm)       | 53.3±6.3                    | 52.0±5.3                        | 0.160   |
|                  | 53.9±6.2                    | 52.4±5.2                        | 0.135   |
| CO (L/min)       | 5.4±1.1                     | 5.3±1.0                         | 0.555   |
|                  | 5.1±0.9                     | 5.4±0.9                         | 0.019   |
| LVEF (%)         | 54.4±8.6                    | 56.0±11.8                       | 0.360   |
|                  | 55.0±8.5                    | 58.1±8.5                        | 0.026   |

LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension; CO, cardiac minute output.
| Index                                      | Intravenous tirofiban (n = 90) | Intracoronary tirofiban (n = 90) | P value |
|-------------------------------------------|--------------------------------|----------------------------------|---------|
| Thrombus aspiration, n (%)                | 28 (31%)                       | 19 (21%)                         | 0.127   |
| TIMI flow after PPCI (Grade 3), n (%)      | 77 (86%)                       | 86 (96%)                         | 0.022   |
| TMP flow after PPCI (Grades 2–3), n (%)   | 66 (73%)                       | 79 (88%)                         | 0.014   |
| Sum-STR ≥ 50%                             | 76 (84%)                       | 85 (94%)                         | 0.029   |
| MACEs                                     | 39 (43%)                       | 23 (26%)                         | 0.012   |
| Sudden cardiac death                      | 0                              | 1 (1%)                           | 1.000   |
| Angina pectoris                           | 17 (19%)                       | 12 (13%)                         | 0.311   |
| Acute heart failure                       | 20 (22%)                       | 10 (11%)                         | 0.046   |
| Recurrent MI                              | 1 (1%)                         | 0                                | 1.000   |
| Repeat revascularization                   | 1 (1%)                         | 0                                | 1.000   |
| Bleeding (total incidence)                | 18 (20%)                       | 16 (18%)                         | 0.703   |
| Intracranial hemorrhage, n (%)            | 0                              | 0                                | --      |
| Gastrointestinal hemorrhage, n (%)        | 4 (4%)                         | 2 (2%)                           | 0.678   |
| Hemorrhage at puncture place, n (%)       | 5 (6%)                         | 7 (8%)                           | 0.550   |
| Other hemorrhage, n (%)                   | 9 (10%)                        | 7 (8%)                           | 0.600   |
| Thrombocytopenia                          | 0                              | 0                                | --      |

MACEs, major adverse cardiovascular events; TIMI, thrombolysis in myocardial infarction; PPCI, primary percutaneous coronary intervention; TMP, TIMI myocardial perfusion; Sum-STR, resolution of the sum of ST-segment elevation; MI, myocardial infarction
Table 7
Comparison of cardiac ultrasound indices between treatment groups

|                      | LA  | LVEDD | LVEF  | CO     |
|----------------------|-----|-------|-------|--------|
| Intravenous tirofban (n = 90) | 37 ± 4 | 53 ± 5 | 54 ± 9 | 5.1 ± 1.1 |
| Intracoronary tirofban (n = 90) | 36 ± 4 | 51 ± 6 | 56 ± 8 | 5.3 ± 0.9 |
| t value              | 1.290 | 1.100 | 0.777 | 0.789  |
| p value              | 0.200 | 0.274 | 0.439 | 0.432  |

LA, left heart atrium; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension; CO, cardiac minute output.

Discussion

AMI is caused by unstable plaque rupture, intima injury, platelet aggregation, and thrombosis during its progression [1–4]. PPCI is an important treatment for acute ST-segment elevation myocardial infarction (STEMI), and is the preferred strategy in STEMI patients if it can be performed within 12 hours of symptom onset [1–4]. Antiplatelet therapy is also a cornerstone of AMI treatment. Yet, regardless of intervention, no-reflow is common and can occur after PPCI [3–7, 12–5]. Indeed, in severe instances this is termed thromboembolic syndrome [12–17]. Studies found that GPI administration improved TIMI flow, ameliorated myocardial reperfusion injury, prevented myocardial ischemia, reduced MACEs, and improved prognosis [5, 18–21].

Tirofiban is a highly specific, reversible antagonist of platelet GP IIb/IIIa receptor. It inhibits platelet aggregation by binding to the glycoprotein IIb/IIIa complex, thereby reducing thrombi levels. In the current randomized study, IC administration of tirofiban to STEMI patients with angiographic intracoronary thrombus significantly improved TIMI and TMP flow and improved Sum-STR, consistent with other reports [5, 18–21]. However, there were no significant benefits observed in terms of in-hospital cardiac function, or hepatic and kidney function. Sum-STR can reflect early microcirculation and myocardial recovery from ischemia and reperfusion injury after PPCI in STEMI patients. The present study found that the number of patients with sum-STR ≥ 50% was significantly higher in patients given IC tirofiban versus patients treated with IV tirofiban. We postulate that IC tirofiban provided for increased targeted delivery of the drug compared to standard IV administration and that this accounted for, in part, the study findings. While not definitive, the findings of reduced myocardial infarction and increased Sum-STR support this idea [5, 18–21].

The changes in inflammatory markers observed may be secondary to injury-related hypoxia. CRP, TNF-α, TGF-β1, IL-6, IL-10, and ESR are deemed early markers of inflammation and tissue damage. Markers of inflammation and cTNI are correlated to myocardial ischemia and injury and are useful for diagnosis and evaluation when treating AMI [3, 22–29]. Inflammatory marker and cTnl levels positively correlated with culprit artery thrombosis, no-reflow of the culprit artery, and MACEs [22, 25, 26], as previous studies have...
also shown [5, 18]. We found that cTNI, AST, CRP, and ESR levels were significantly lower in STEMI patients given IC tirofiban compared to IV by day 6 post-procedure. However, IC therapy was not associated with obvious differences in CK, CKMB, cTnI, NT-pro-BNP, blood glucose, HbA1C, ALT, AST, CRP, TNF-α, TGF-β1, IL-6, or IL-10 on day 2, or UA on day 6 post-procedure. The incidence rate of MACEs was lower in IC treated versus IV treated patients, with acute heart failure being the largest contributor to this difference. However, we did not observe a significant difference in sudden cardiac death, angina pectoris, nonfatal reinfarction, or target vessel revascularization among treatment groups. In addition, we observed a statistically significant difference in cardiac ultrasound findings including CO and LVEF 6 months after discharge.

The present study has several limitations. First, this study sample size was small and likely genetically non-diverse. Second, this study did not conduct an economic benefit analysis. Third, the follow-up duration was short and limited to in-hospital time and 6 months after discharge. Future studies should include longer follow-up. Finally, this study was not a double-blind trial, which may have introduced observer and patient bias.

**Conclusions**

Compared to IV administration, IC tirofiban administration in STEMI patients with intracoronary thrombus reduced myocardium infarct size; improved TIMI, TMP flow and cardiac function, including CO and LVEF 6 months after discharge; lowered levels of certain inflammation-associated proteins; and reduced MACEs. These benefits were obtained through a simple change in the route of administration and without increasing the expense of care. IC tirofiban should be considered more often in AMI patients with increased thrombosis.

**Declarations**

**Author Contributions**

Xiuying Tang conceived and designed the experiment. Xiuying Tang and Runjun Li performed the experiment and analysed the data. Xiuying Tang and Runjun Li wrote first draft of the paper.

**Conflict of interest**

The authors declare that they have no conflicts of interest in relation to the manuscript.

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**Data availability statements**

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.
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Figures

Figure 1
Flowchart of patient enrollment. STEMI, acute ST-segment elevation myocardial infarction; IC, intracoronary; PPCI, primary percutaneous coronary intervention.