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Short-Term Clinical Outcome of Intracoronary Bolus versus Standard Intravenous Administration of Tirofiban during Primary Percutaneous Coronary Intervention in Patients with St-Elevation Myocardial Infarction

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ABSTRACT

Background: Intracoronary (IC) tirofiban might confer therapeutic benefits by delivering higher local drug concentrations at the culprit lesion, potentially enhancing platelet inhibition and thrombus resolution.

Objective: This study aimed to compare the short-term safety and efficacy of IC bolus-only strategy with the standard intravenous (IV) bolus succeeded by infusion in ST-segment elevation myocardial infarction (STEMI) patients undergoing primary percutaneous coronary intervention (PPCI).

Methods: 146 STEMI patients undergoing PCI were enrolled, divided equally into two groups: One receiving standard intravenous tirofiban and the other a single IC bolus. Efficacy and safety outcomes were evaluated during hospitalization and at 30 days.

Results: Left ventricular ejection fraction (LVEF) at discharge was comparable among the IV and IC groups (47.9% vs. 47.4%, p=0.668). TIMI 3 flow was achieved in 64.4% and 71.2% of the IV and IC groups respectively without significant differences in post-PCI flow grades (p=0.667). The composite 30-days major adverse cardiovascular events (MACE) rate was lower in the IC group (20.5% vs. 28.8%), though not statistically significant (p=0.249). A trend toward fewer stent thrombosis events was observed with IC bolus therapy. The most notable benefit of IC administration was its superior safety profile, reflected by markedly lower rates of BARC type 1 bleeding (2.7% vs. 49.3%, p<0.001), BARC type 2 bleeding (4.1% vs. 21.9%, p=0.001), and vascular complications (5.5% vs. 35.6%, p<0.001). Major bleeding was rare in both groups.

Conclusion: In STEMI patients undergoing primary PCI, IC bolus-only tirofiban provided comparable short-term efficacy to standard IV infusion, while markedly reduced bleeding and vascular complications.

Keywords: Primary percutaneous coronary intervention, STEMI, Tirofiban.

INTRODUCTION

Patients with STEMI typically demonstrate marked platelet activation, elevated expression of P2Y12 receptors, and enhanced platelet reactivity. These factors contribute to a higher thrombotic burden and are strongly associated with adverse outcomes following PPCI [1]. As a result, achieving rapid and potent platelet inhibition remains a cornerstone in the contemporary management of STEMI [2].

PPCI is widely regarded as the preferred reperfusion strategy for restoring coronary blood flow when it can be performed promptly in an experienced center. It consistently outperforms fibrinolytic therapy with respect to survival, reinfarction and stroke, provided that it is initiated within guideline-recommended time frames [3, 4]. Current recommendations emphasize performing PPCI within 90 minutes of first medical contact and within 12 hours of symptom onset in eligible patients [5]. Despite adherence to these targets, many patients still experience microvascular obstruction, manifested as slow-flow or no-reflow, which remains a major predictor of poor functional recovery and unfavorable clinical outcomes [6].

To mitigate these complications, adjunctive antiplatelet strategies have been explored, including the use of glycoprotein IIb/IIIa inhibitors (GPIs). These agents offer potent, final-pathway inhibition of platelet aggregation and have been shown to reduce thrombotic sequelae, decrease distal embolization and improve coronary perfusion in selected clinical settings [7]. Nonetheless, the timing, mode of administration and patient populations most likely to benefit from GPI therapy continue to be debated. Some studies advocate early or pre-hospital initiation, whereas others report no additional advantage beyond catheter laboratory administration [8].

Growing interest has focused on whether the route of GPI delivery influences therapeutic impact. Several meta-analyses have suggested that intracoronary (IC) administration may enhance drug bioavailability at the culprit lesion, achieving higher local receptor occupancy and potentially improving angiographic and clinical outcomes compared to standard intravenous (IV) infusion [9]. This is especially relevant for tirofiban, a small, highly selective, non-peptide GPI that prevents the binding of fibrinogen and von Willebrand factor to GP IIb/IIIa receptors on activated platelets, thereby inhibiting the final step of platelet aggregation [10]. Delivering tirofiban directly into the infarct-related artery may offer a pharmacodynamic advantage by increasing local drug concentration and accelerating thrombus modification [11].

However, recommendations regarding GPI use differ across major guidelines. The European Society of

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Cardiology restricts GPI administration primarily to bailout situations—such as heavy thrombus burden, slow flow, or no-reflow—or to specific high-risk patients undergoing interhospital transfer for PPCI [12]. Conversely, the ACC/AHA guidelines assign a class IIa recommendation for combining GPIs with unfractionated heparin in patients undergoing PPCI, irrespective of clopidogrel pretreatment status [13]. These contrasting positions underscore ongoing uncertainty about the optimal use of GPIs in the current era of potent oral P2Y12 inhibitors, radial access and contemporary stent technologies.

Given the pharmacological differences between IC and IV administration as well as the inconsistency among existing recommendations, further evaluation of IC tirofiban use in real-world STEMI populations is warranted. Consequently, the present study aimed to assess the short-term safety and efficacy of an IC bolus-only tirofiban strategy compared with the conventional IV bolus succeeded by continuous infusion in patients undergoing primary PCI for STEMI.

PATIENTS AND METHODS

This prospective interventional study was carried out on 146 patients aged of both sexes, presenting with STEMI and eligible primary PCI (P-PCI) within 12 hours of symptom onset and indicated for GPI administration during the P-PCI procedure, defined as having coronary lesions with a large thrombus burden (TIMI thrombus grade 4 or 5), coronary no-reflow or slow flow. The study was conducted through the period from July 2023 to July 2025.

Exclusion criteria: Administration of fibrinolytics within 24 hours of randomization, recent treatment with warfarin (INR > 2), previous coronary artery bypass graft (CABG) surgery, major surgery or trauma within the previous 15 days, history of cerebrovascular accident (CVA) or transient ischemic attack (TIA) within the previous 30 days, or any history of hemorrhagic CVA, current active bleeding or a history of major bleeding in the previous 30 days, known history of sensitivity to tirofiban, heparin, or DAPT, uncontrolled hypertension (systolic > 180 or diastolic > 110 mm Hg), thrombocytopenia (platelet count < 100,000/mcl) or any known bleeding diathesis and severe hepatic failure and severe renal impairment (glomerular filtration rate < 30%).

Patients were further divided in to two equal groups: **Group 1 (Standard IV tirofiban)** received the standard intravenous dose of tirofiban. This was administered as a 25 mcg/kg bolus over 3 minutes, thereafter, a continuous infusion of 0.15 mcg/kg/min for up to 18 hours [14]. **Group 2 (IC bolus-only)** received a single IC bolus-only dose of tirofiban (25 mcg/kg). This dose was infused over a 3-minute period directly via the guiding catheter after crossing the culprit lesion [15]. All patients were preloaded with DAPT, consisting of 180 mg ticagrelor loading dose and 150-300 mg oral ASA. Anticoagulation during the procedure was achieved with an unfractionated heparin bolus of 100 U/kg.

Standardized preoperative assessments were conducted for all patients: Detailed history and demographics (A full history was taken and baseline data were collected for all patients including demographic data (age & sex), body mass index (BMI) and risk factors such as smoking status, dyslipidemia, hypertension and diabetes mellitus. Clinical presentation, including Killip class and STEMI type, was also recorded.

Laboratory Assessment: Basic laboratory investigations were performed including cardiac troponin I, CBC, coagulation profile, serum creatinine and a metabolic profile (lipid panel & random blood glucose).

Electrocardiogram (ECG) assessment: A standard 12-Lead ECG was performed for all patients at initial admission, 90 minutes after the PCI procedure, and at 12-hour intervals thereafter.

Echocardiographic assessment: Conventional transthoracic echocardiography (TTE) was performed for all participants using a commercially available ultrasound system (GE Vivid E95). Examinations were conducted at baseline (on admission) and again at discharge.

Image Acquisition: Standard 2D, M-mode, and Doppler images were acquired from parasternal (long and short-axis) and apical (4-chamber, 2-chamber and 3-chamber) views.

2D Analysis: Key parameters were analyzed from the 2D images.

LVEF: Calculated using the biplane Simpson's method from the apical 4- and 2-chamber views.

Regional wall motion abnormalities (RWMA): The presence of RWMA was assessed visually in all segments, consistent with the STEMI diagnosis.

Follow-Up: Patients were monitored for clinical outcomes during the index procedure and throughout the duration of the inpatient hospital stay. After discharge, all patients were followed up at 30 days post-procedure. This follow-up was conducted either through a scheduled ambulatory visit to the outpatient clinic or via a structured phone interview to assess for the occurrence of any efficacy or safety endpoints including rehospitalization.

Outcome measurement: Endpoints were assessed during the index procedure, during the hospital stay, and at 30-day follow-up.

Efficacy outcomes: The primary efficacy endpoint was the occurrence of Major Adverse Cardiovascular Events (MACE) at 30 days. Efficacy endpoints also included

cardiovascular death, myocardial infarction (MI), and clinically driven target lesion revascularization (TLR). Rates of re-infarction and stent thrombosis were also assessed.

Safety outcomes: The primary safety endpoints included any vascular or bleeding complications. Bleeding was evaluated according to the Bleeding Academic Research Consortium (BARC) criteria and classified as:

- BARC Minimal (Type 1).
- BARC Minor (Type 2).
- BARC Major (Type 3). The rate of any vascular complication was also recorded as a key safety outcome.

Ethical approval: The study was approved from The Ethical Committee Menoufiya University Hospitals and Mahalla Cardiac Center (MOH hospital) Hospitals. Informed written consents were obtained from the patients. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Analysis was performed using leveraging Jamovi software (The Jamovi Project, version 2.7.12). Continuous variables were summarized as mean ± standard deviation (SD) to provide an estimate of central tendency and variability, while categorical variables were expressed as counts (n) and percentages (%) to illustrate their distribution across study groups. Comparisons of continuous variables among the two study groups (Standard IV Tirofiban versus Intracoronary Bolus-Only) were conducted using the independent samples t-test, which is reported as 'Linear Model ANOVA' in the Jamovi output. For categorical variables, the relationship between each variable and the study groups was evaluated using Pearson's Chi-squared test, allowing for the assessment of differences in proportions. All statistical analyses were two-tailed to account for differences in both directions, and a p-value ≤ 0.05 was considered statistically significant. This approach ensured a robust and standardized assessment of differences and associations among groups across both continuous and categorical data.

RESULTS

The mean age of the total cohort was 63.5 ± 9.6 years, and the majority of patients were males (69.2%). There were no statistically significant differences among the standard IV tirofiban group and the IC bolus-only group in terms of age (p=0.764), sex (p=0.370), smoking status (p=0.741), dyslipidemia (p=0.674), family history (p=0.99) and BMI (p=0.902) (Table 1).

Table (1): Baseline demographics and risk factors

Parameters	Group 1 (IV Tirofiban) (N=73)	Group 2 (IC Bolus-Only) (N=73)	Total (N=146)	p-value
Age (years)	63.2 (9.2)	63.7 (10.1)	63.5 (9.6)	0.764[1]
Sex, n (%)				0.370[2]
Female	20 (27.4%)	25 (34.2%)	45 (30.8%)	
Male	53 (72.6%)	48 (65.8%)	101 (69.2%)	
Smoker, n (%)				0.741[2]
No	35 (47.9%)	37 (50.7%)	72 (49.3%)	
Yes	38 (52.1%)	36 (49.3%)	74 (50.7%)	
Dyslipidemia, n (%)				0.674[2]
Yes	60 (82.2%)	58 (79.5%)	118 (80.8%)	
No	13 (17.8%)	15 (20.5%)	28 (19.2%)	
Family history, n (%)				0.99[2]
Yes	35 (47.9%)	35 (47.9%)	70 (47.9%)	
No	38 (52.1%)	38 (52.1%)	76 (52.1%)	
BMI (kg/m²)	28.7 (2.3)	28.7 (3.0)	28.7 (2.6)	0.902[1]

BMI, body mass index; IC, intracoronary; IV, intravenous; SD, standard deviation. Data are presented as mean (SD) or n (%). p-values derived from: [1]Linear Model ANOVA; [2]Pearson's Chi-squared test.

Hypertension was the most prevalent comorbidity (83.6% of all patients), then diabetes mellitus (58.9%) with no significant difference in their distribution among groups (p=0.655 and p=0.737, respectively). Moreover, the prevalence of chronic kidney disease (CKD), previous myocardial infarction (MI), peripheral vascular disease (PVD) and COPD/asthma was nearly identical across both groups, with all comparisons yielding highly non-significant p-values (Table 2).

Table (2): Baseline clinical history and comorbidities

Parameters	Group 1 (IV Tirofiban) (N=73)	Group 2 (IC Bolus-Only) (N=73)	Total (N=146)	p-value
Hypertension, n (%)				0.655
Yes	60 (82.2%)	62 (84.9%)	122 (83.6%)	
No	13 (17.8%)	11 (15.1%)	24 (16.4%)	
Diabetes mellitus, n (%)				0.737
Yes	42 (57.5%)	44 (60.3%)	86 (58.9%)	
No	31 (42.5%)	29 (39.7%)	60 (41.1%)	
CKD stage, n (%)				0.964
Stage 1	40 (54.8%)	40 (54.8%)	80 (54.8%)	
Stage 2	23 (31.5%)	24 (32.9%)	47 (32.2%)	
Stage 3	10 (13.7%)	9 (12.3%)	19 (13.0%)	
Previous MI, n (%)				0.99
Yes	13 (17.8%)	13 (17.8%)	26 (17.8%)	
No	60 (82.2%)	60 (82.2%)	120 (82.2%)	
PVD, n (%)				0.99
Yes	6 (8.2%)	6 (8.2%)	12 (8.2%)	
No	67 (91.8%)	67 (91.8%)	134 (91.8%)	
COPD/BA, n (%)				0.99
Yes	8 (11.0%)	8 (11.0%)	16 (11.0%)	
No	65 (89.0%)	65 (89.0%)	130 (89.0%)	

BA, bronchial asthma; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; PVD, peripheral vascular disease.

The distribution of STEMI type was similar (p=0.939), with anterior STEMI being the most common presentation in both the IV (64.4%) and IC (60.3%) groups. Furthermore, there was no statistical difference in the severity of presentation, as measured by Killip Class (p=0.509), or in the critical time-to-treatment metrics, including symptom-to-FMC time (181.7 vs. 180.3 min, p=0.896) and Door-to-Balloon time (74.5 vs. 74.7 min, p=0.930) (Table 3).

Table (3): Clinical Presentation and Procedural Timing

Parameters	Group 1 (IV Tirofiban) (N=73)	Group 2 (IC Bolus-Only) (N=73)	Total (N=146)	p-value
Type of STEMI, n (%)				0.939[1]
Anterior	47 (64.4%)	44 (60.3%)	91 (62.3%)	
Inferior	15 (20.5%)	16 (21.9%)	31 (21.2%)	
Lateral	6 (8.2%)	6 (8.2%)	12 (8.2%)	
Inferolateral	2 (2.7%)	4 (5.5%)	6 (4.1%)	
Inferoposterior	3 (4.1%)	3 (4.1%)	6 (4.1%)	
Killip class, n (%)				0.509[1]
I	45 (61.6%)	48 (65.8%)	93 (63.7%)	
II	14 (19.2%)	17 (23.3%)	31 (21.2%)	
III	7 (9.6%)	5 (6.8%)	12 (8.2%)	
IV	7 (9.6%)	3 (4.1%)	10 (6.8%)	
Symptom-to-FMC (min)	181.7 (61.8)	180.3 (64.5)	181.0 (63.0)	0.896[2]
Door-to-balloon (min)	74.5 (13.1)	74.7 (13.4)	74.6 (13.2)	0.930[2]

FMC, first medical contact.

Both groups presented with similarly elevated cardiac enzymes (mean troponin 17.3 vs. 17.6, p=0.737 & mean CK-MB 202.4 vs. 205.0, p=0.636). There were no significant differences in baseline hemoglobin, creatinine and platelet counts. Furthermore, baseline cardiac function was similar, with a mean LVEF of 43.6% in the IV group and 42.9% in the IC group (p=0.485), and 100% of patients in both groups had regional wall motion abnormalities (RWMA) at admission (Table 4).

Table (4): Baseline laboratory and echocardiographic findings

Parameters	Group 1 (IV Tirofiban) (N=73)	Group 2 (IC Bolus-Only) (N=73)	Total (N=146)	p-value
Troponin	17.3 (4.0)	17.6 (4.0)	17.4 (4.0)	0.737[1]
CK-MB	202.4 (35.2)	205.0 (30.7)	203.7 (32.9)	0.636[1]
Hemoglobin (g/dL)	13.7 (1.0)	13.8 (1.2)	13.7 (1.1)	0.741[1]
Creatinine (mg/dL)	1.2 (0.3)	1.2 (0.4)	1.2 (0.3)	0.850[1]
Platelets (x 10^3/µL)	234.8 (59.8)	243.7 (64.1)	239.3 (62.0)	0.389[1]
LVEF (%)	43.6 (6.2)	42.9 (6.6)	43.3 (6.4)	0.485[1]
RWMA present, n (%)	73 (100.0%)	73 (100.0%)	146 (100.0%)	>0.99[2]

CK-MB, creatine kinase-MB, RWMA, regional wall motion abnormality.

Key metabolic markers, including the lipid profile and random blood glucose (p=0.982), were similar at admission. Additionally, the baseline coagulation status was identical, with no differences observed in mean prothrombin time (PT) (p=0.757) or partial thromboplastin time (pTT) (p=0.763) (Table 5).

Table (5): Baseline metabolic and coagulation profile

Parameters	Group 1 (IV Tirofiban) (N=73)	Group 2 (IC Bolus-Only) (N=73)	Total (N=146)	p-value
Urea (mg/dL)	43.4 (10.5)	43.9 (11.6)	43.6 (11.1)	0.771
Total cholesterol (mg/dL)	214.8 (18.5)	215.7 (14.0)	215.2 (16.3)	0.751
LDL (mg/dL)	144.3 (13.3)	145.1 (14.7)	144.7 (14.0)	0.75
HDL (mg/dL)	38.6 (4.6)	38.1 (5.7)	38.3 (5.1)	0.597
Triglycerides (mg/dL)	178.7 (36.4)	178.2 (24.5)	178.4 (30.9)	0.917
PT (sec)	12.7 (0.5)	12.7 (0.5)	12.7 (0.5)	0.757
pTT (sec)	30.8 (2.4)	30.7 (2.5)	30.7 (2.5)	0.763
RBG (mg/dL)	182.2 (52.9)	182.4 (49.4)	182.3 (51.0)	0.982

HDL, high-density lipoprotein, LDL, low-density lipoprotein; PT, prothrombin time; pTT, partial thromboplastin time; RBG, random blood glucose; SD, standard deviation.

The left anterior descending artery (LAD) was the most frequent culprit vessel in both the IV (61.6%) and IC (60.3%) groups, with no significant difference in overall vessel distribution (p=0.880). Similarly, there were no differences in the extent of coronary artery disease, lesion complexity (ACC/AHA type), or the indications for GPI administration, such as high thrombus burden or slow/no-reflow (p=0.879, p=0.826, and p=0.854, respectively). Critically, the baseline TIMI flow before PCI was nearly identical, with the vast majority of patients in both groups presenting with TIMI 0 or 1 flow (p=0.295) (Table 6).

Table (6): Baseline angiographic parameters

Parameters	Group 1 (IV Tirofiban) (N=73)	Group 2 (IC Bolus-Only) (N=73)	Total (N=146)	p-value
Culprit vessel, n (%)				0.88
LAD	45 (61.6%)	44 (60.3%)	89 (61.0%)	
RCA	15 (20.5%)	15 (20.5%)	30 (20.5%)	
LCx	9 (12.3%)	12 (16.4%)	21 (14.4%)	
Diagonal	2 (2.7%)	1 (1.4%)	3 (2.1%)	
LCx-OM	1 (1.4%)	1 (1.4%)	2 (1.4%)	
LM-LAD	1 (1.4%)	0 (0.0%)	1 (0.7%)	
Number of diseased vessels, n (%)				0.879
1	29 (39.7%)	32 (43.8%)	61 (41.8%)	
2	33 (45.2%)	31 (42.5%)	64 (43.8%)	
3	11 (15.1%)	10 (13.7%)	21 (14.4%)	
ACC/AHA lesion type, n (%)				0.826
A	8 (11.0%)	9 (12.3%)	17 (11.6%)	
B1	8 (11.0%)	11 (15.1%)	19 (13.0%)	
B2	24 (32.9%)	20 (27.4%)	44 (30.1%)	
C	33 (45.2%)	33 (45.2%)	66 (45.2%)	
TIMI flow pre-PCI, n (%)				0.295
0	35 (47.9%)	29 (39.7%)	64 (43.8%)	
1	33 (45.2%)	33 (45.2%)	66 (45.2%)	
2	5 (6.8%)	9 (12.3%)	14 (9.6%)	
3	0 (0.0%)	2 (2.7%)	2 (1.4%)	
Indication for GPI, n (%)				0.854
High thrombus burden	43 (58.9%)	40 (54.8%)	83 (56.8%)	
Slow flow	20 (27.4%)	21 (28.8%)	41 (28.1%)	
No-reflow	10 (13.7%)	12 (16.4%)	22 (15.1%)	

ACC/AHA, American College of Cardiology/American Heart Association; GPI, Glycoprotein IIb/IIIa inhibitor; LAD, left anterior descending artery; LCx, left circumflex artery; LM, left main; OM, obtuse marginal; RCA, right coronary artery; TIMI, Thrombolysis in Myocardial Infarction.

Femoral access was the most common approach (59.6% overall) and there was no significant difference in the choice of access site (p=0.458). Similarly, no differences were observed in the rates of aspiration thrombectomy (p=0.383), pre-dilation (p=0.698), post-dilation (p=0.754), or the distribution of drug-eluting stent brands used (p=0.717) (Table 7).

Table (7): Procedural and interventional parameters

Parameters	Group 1 (IV Tirofiban) (N=73)	Group 2 (IC Bolus-Only) (N=73)	Total (N=146)	p-value
Access site, n (%)				0.458
Femoral	46 (63.0%)	41 (56.2%)	87 (59.6%)	
Radial	27 (37.0%)	31 (42.5%)	58 (39.7%)	
Femoral + Radial	0 (0.0%)	1 (1.4%)	1 (0.7%)	
Aspiration thrombectomy, n (%)				0.383
Yes	8 (11.0%)	5 (6.8%)	13 (8.9%)	
No	65 (89.0%)	68 (93.2%)	133 (91.1%)	
Pre-dilation, n (%)				0.698
Yes	69 (94.5%)	70 (95.9%)	139 (95.2%)	
No	4 (5.5%)	3 (4.1%)	7 (4.8%)	
Post-dilation, n (%)				0.754
Yes	68 (93.2%)	67 (91.8%)	135 (92.5%)	
No	5 (6.8%)	6 (8.2%)	11 (7.5%)	
Stent brand (DES), n (%)				0.717
Xience	21 (28.8%)	19 (26.0%)	40 (27.4%)	
Synergy	16 (21.9%)	20 (27.4%)	36 (24.7%)	
Resolute	18 (24.7%)	17 (23.3%)	35 (24.0%)	
Onyx	17 (23.3%)	15 (20.5%)	32 (21.9%)	
Other*	1 (1.4%)	2 (2.7%)	3 (2.1%)	

DES, drug-eluting stent. *Other stent brands include Promus (n=1), Stentys-X-Position (n=1), and Ultimaster (n=1).

Post-procedure, the mean LVEF at discharge was nearly identical in both the IV and IC groups (47.9% vs. 47.4%, p=0.668). Successful angiographic reperfusion, defined as TIMI 3 flow, was achieved in 64.4% of the IV group and 71.2% of the IC group, with no statistical difference in the overall distribution of post-PCI TIMI flow grades (p=0.667). Finally, the overall rate of procedural complications was also similar, occurring in 21.9% of the IV group and 13.7% of the IC group, a difference that was not statistically significant (p=0.313) (Table 8).

Table (8): Procedural outcomes and complications

Parameters	Group 1 (IV Tirofiban) (N=73)	Group 2 (IC Bolus-Only) (N=73)	Total (N=146)	p-value
LVEF at discharge (%), mean (SD)	47.9 (6.9)	47.4 (7.3)	47.7 (7.1)	0.668[1]
TIMI flow post-PCI, n (%)				0.667[2]
TIMI 1	8 (11.0%)	6 (8.2%)	14 (9.6%)	
TIMI 2	18 (24.7%)	15 (20.5%)	33 (22.6%)	
TIMI 3	47 (64.4%)	52 (71.2%)	99 (67.8%)	
Procedural complications, n (%)				0.313[2]
No	57 (78.1%)	63 (86.3%)	120 (8.2%)	
Death	3 (4.1%)	2 (2.7%)	5 (3.4%)	
Cardiogenic shock	3 (4.1%)	0 (0.0%)	3 (2.1%)	
Side branch occlusion	2 (2.7%)	3 (4.1%)	5 (3.4%)	
Other*	8 (11.0%)	4 (5.5%)	12 (8.2%)	

TIMI, Thrombolysis in Myocardial Infarction. *Other complications include: Ventricular Arrhythmia (n=2), Transient Hypotension (n=2), Coronary Dissection (n=2), LM Dissection (n=2), Edge Dissection (n=2), Coronary Perforation (n=1), Wire Fracture (n=1), Abdominal Aorta Dissection (n=1).

The primary composite endpoint of MACE occurred in 28.8% of the standard IV group versus 20.5% in the IC bolus-only group, this difference was not statistically significant (p=0.249). Notably, there was a strong, albeit non-significant, trend toward a lower rate of stent thrombosis in the IC bolus-only group (4.1% vs. 9.6%, p=0.190). There were no statistically significant differences in the individual components of MACE or in the rates of reinfarction (p=0.336) or target lesion revascularization (TLR) (p=0.404) (Table 9).

Table (9): Clinical efficacy endpoints at 30 days

Endpoint	Group 1 (IV Tirofiban) (N=73)	Group 2 (IC Bolus-Only) (N=73)	Total (N=146)	p-value
MACE (Composite endpoint), n (%)	21 (28.8%)	15 (20.5%)	36 (24.7%)	0.249
Components of MACE, n (%)[1]				0.322
Cardiovascular death	0 (0.0%)	1 (1.4%)	1 (0.7%)	
Heart failure	2 (2.7%)	4 (5.5%)	6 (4.1%)	
Myocardial infarction	0 (0.0%)	1 (1.4%)	1 (0.7%)	
Stroke	3 (4.1%)	1 (1.4%)	4 (2.7%)	
Stroke + Heart failure	1 (1.4%)	0 (0.0%)	1 (0.7%)	
Other MACE	15 (20.5%)	8 (11.0%)	23 (15.8%)	
Re-infarction, n (%)	4 (5.5%)	3 (4.1%)	7 (4.8%)	0.336
TLR, n (%)	4 (5.5%)	2 (2.7%)	6 (4.1%)	0.404
Stent thrombosis, n (%)	7 (9.6%)	3 (4.1%)	10 (6.8%)	0.19

TLR, target lesion revascularization. [1]Breakdown of events for patients who experienced MACE.

There was a trend toward a shorter duration of hospitalization in the IC bolus-only group (3.8 days) in contrast to the IV group (4.4 days), but this did not reach statistical significance (p=0.070). There were no significant differences in the rates of in-hospital mortality (p=0.99) or 30-days rehospitalization (p=0.400), with heart failure being the most common cause for readmission in both groups (Table 10).

Table 10: Hospital and 30-days outcomes

Parameters	Group 1 (IV Tirofiban) (N=73)	Group 2 (IC Bolus-Only) (N=73)	Total (N=146)	p-value
Hospital Stay (days)	4.4 (2.0)	3.8 (1.6)	4.1 (1.8)	0.070[1]
Rehospitalization at 30 days, n (%)				0.400[2]
Yes	16 (22.2%)	12 (16.7%)	28 (19.4%)	
No	56 (77.8%)	60 (83.3%)	116 (80.6%)	
Cause of Rehospitalization, n (%)				0.412[1]
Heart failure	9 (56.2%)	6 (46.2%)	15 (51.7%)	
Reinfarction / MI	3 (18.8%)	2 (15.4%)	5 (17.2%)	
Arrhythmia	1 (6.2%)	2 (15.4%)	3 (10.3%)	
Angina	0 (0.0%)	1 (7.7%)	1 (3.4%)	
Other	3 (18.8%)	2 (15.4%)	5 (17.2%)	
In-hospital mortality, n (%)	1 (1.4%)	1 (1.4%)	2 (1.4%)	0.99[2]

The primary safety endpoints revealed the most significant findings of the study, demonstrating a clear safety advantage for the IC bolus-only strategy. The rates of BARC minimal bleeding (49.3% vs. 2.7%, p<0.001) and BARC minor bleeding (21.9% vs. 4.1%, p=0.001) were both dramatically and statistically significantly lower in the IC bolus-only group versus the standard IV group. This safety benefit was also seen in vascular complications, which were significantly reduced in the IC group (5.5%) versus the IV group (35.6%), (p<0.001). There was no statistically significant difference in BARC major bleeding, which was a rare event in both groups (p=0.154) (Table 11).

Table 11: Safety endpoints and bleeding complications

Endpoint	Group 1 (IV Tirofiban) (N=73)	Group 2 (IC Bolus-Only) (N=73)	Total (N=146)	p-value
BARC minimal bleeding (Type 1)	36 (49.3%)	2 (2.7%)	38 (26.0%)	< 0.001
BARC minor bleeding (Type 2)	16 (21.9%)	3 (4.1%)	19 (13.0%)	0.001
BARC major bleeding (Type 3)	2 (2.7%)	0 (0.0%)	2 (1.4%)	0.154
Any vascular complication	26 (35.6%)	4 (5.5%)	30 (20.5%)	< 0.001

In-hospital mortality was identical at 1.4% in both arms (p=0.99), and there were no significant differences in the rates of heart failure (p=0.108), stroke (p=0.245), cardiogenic shock (p=0.549), or unplanned revascularization (p=0.512). However, there was a notable, though not statistically significant, trend toward lower 30-days mortality (1.4% vs. 8.2%, p=0.134) and stent thrombosis (4.1% vs. 9.6%, p=0.190) in the IC bolus-only group against the standard IV group (Table 12).

Table 12: Clinical endpoints: In-hospital and 30-days outcomes

Endpoint	Group 1 (IV Tirofiban) (N=73)	Group 2 (IC Bolus-Only) (N=73)	Total (N=146)	p-value
In-hospital mortality	1 (1.4%)	1 (1.4%)	2 (1.4%)	0.99
30-days mortality	6 (8.2%)	1 (1.4%)	7 (4.8%)	0.134
Heart failure	23 (31.5%)	18 (24.7%)	41 (28.1%)	0.108
Stroke	5 (6.8%)	2 (2.7%)	7 (4.8%)	0.245
Cardiogenic shock	6 (8.2%)	6 (8.2%)	12 (8.2%)	0.549
Unplanned Revascularization	6 (8.2%)	4 (5.5%)	10 (6.8%)	0.512
Stent thrombosis	7 (9.6%)	3 (4.1%)	10 (6.8%)	0.19

There was a strong, statistically significant negative correlation between door-to-balloon time and LVEF at discharge (r=−0.674, p<.001). This finding showed that shorter door-to-balloon times were associated with significantly higher left ventricular ejection fractions at hospital discharge (Figure 1 A). A moderate, statistically significant negative correlation was found among the symptom-to-FMC time and the baseline troponin level (r=−0.470, p<.001). This indicated that patients who presented later had, on average, lower troponin levels at admission, a finding that may be related to the natural peak-and-decay kinetics of troponin (Figure 1 B). A weak but statistically significant positive correlation was found between baseline troponin levels and LVEF at discharge (r=0.174, p=0.036). This suggests that patients with higher troponin levels at admission had slightly higher ejection fractions at discharge, though the association was very weak (Figure 1 c).

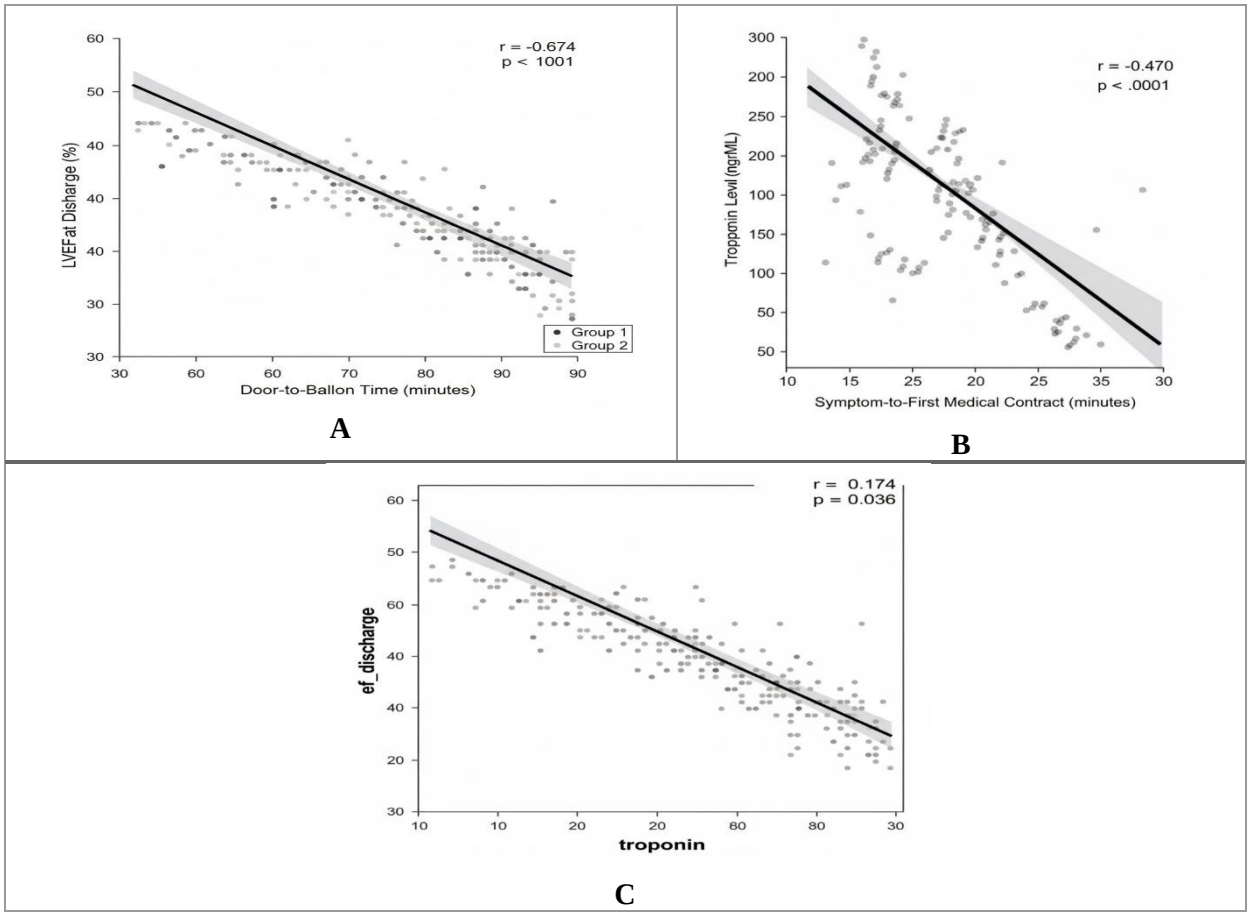

Figure (1): (A) Correlation between door-to-balloon time and left ventricular ejection fraction at discharge, (B) Correlation between symptom-to-FMC time and baseline troponin level, (C) Correlation between baseline troponin and LVEF at discharge.

DISCUSSION

Tirofiban is another GP IIb/IIIa antagonist, typically administered as an IV bolus injection succeeded by a maintenance infusion of 18–36 hours in STEMI patients. Despite its routine use in this standard regimen, evidence regarding the efficacy of IC administration remains very limited. To date, only a single clinical trial has investigated the use of IC tirofiban in ACS patients, underscoring the scarcity of data on this approach. The lack of additional studies highlights a gap in understanding whether IC administration could offer advantages in terms of clinical outcomes, safety, or procedural efficiency compared to the conventional IV route. This limited evidence base emphasizes the need for further trials to evaluate optimal dosing strategies, timing and patient selection for IC tirofiban in ACS management [16].

In the current study the mean age of the cohort was 63.5 ± 9.6 years, with males comprising 69.2% of patients, consistent with typical STEMI demographics. No significant differences were found among the IV and IC tirofiban groups regarding age, sex, smoking, dyslipidemia, family history and BMI ensuring that subsequent outcome comparisons were not influenced by baseline variability. This is consistent with the study of **Tian *et al.*** [17] who found that the mean age was 56 ± 10 years in the IV tirofiban group and 55 ± 12 years in the IC tirofiban group (p = 0.96). No significant differences were observed among the two groups regarding cardiovascular risk factors, cardiac history, or TIMI flow grade before and after PCI. Additionally, **Ghonim *et al.*** [18] evaluated 95 consecutive STEMI patients undergoing primary PCI, who received a 25 μg/kg tirofiban bolus, then a 0.15 μg/kg/min infusion for 24 hours, either intravenously or IC. The two groups were comparable in terms of cardiovascular risk factors, baseline parameters, and concomitant medications. The mean age was 58.5 ± 10.2 years in the IV group and 55.9 ± 11.7 years in the IC group.

In the present study, hypertension (83.6%) and diabetes mellitus (58.9%) were the most common comorbidities among participants. No significant differences were observed among the IV and IC tirofiban groups regarding hypertension, diabetes, CKD stage, previous MI, PVD and COPD/asthma indicating the comparability of both cohorts for subsequent outcome analysis. Consistent with our findings, **Aboushahba *et al.*** [19] studied 374 STEMI patients screened for primary PCI and reported that no significant differences among groups in age, sex, BMI, smoking status, medical history, heart rate, blood pressure, infarct location, hemoglobin, platelet count, or serum creatinine.

In the current study anterior STEMI was the most frequent presentation (62.3% overall), with similar distribution across groups. There were no significant differences in Killip class distribution, indicating comparable hemodynamic status at presentation. Additionally, both symptom-to-first medical contact and door-to-balloon times were nearly identical among the IV and IC tirofiban groups. Similarly, a meta-analysis evaluating the effects of IC low-dose tirofiban versus IV administration on clinical outcomes in patients with STEMI reported no significant differences in Killip class distribution among the two approaches [20]. Also, **Tang *et al.*** [21] conducted a randomized study involving 180 STEMI patients undergoing primary PCI, assigning 90 participants to the IV group and 90 to the IC group. The study found no significant differences in onset-to-balloon or door-to-balloon times (p = 0.08 and 0.3 respectively). The proportion of patients with Killip class > I was 18% in the IV group and 24% in the IC group, a difference that was not statistically significant (p = 0.33). These findings suggest that IC administration does not adversely affect hemodynamic status or procedural timing compared to standard IV therapy, supporting its safety and feasibility in STEMI patients.

In the present study cardiac biomarkers, including troponin and CK-MB, were similarly elevated in both groups. No significant differences were observed in hemoglobin and creatinine or platelet levels. Echocardiographic assessment showed comparable left ventricular systolic function, with mean LVEF values of 43.6% and 42.9% in the IV and IC groups respectively and all patients exhibited regional wall motion abnormalities at baseline.

Previous studies have examined the effects of IC versus IV tirofiban on myocardial injury markers. Zeng ***et al.*** [22] reported no significant differences in peak CPK or CPK-MB levels among the IC and IV groups. In a subgroup analysis, anterior MI patients in the IV group had higher peak CPK and CPK-MB levels compared to the IC group, though the differences were not statistically significant. In contrast, **Asfour *et al.*** [23] found that peak CK-MB and hs-TnT values were significantly lower in the IC group (CK-MB: 155.7 ± 121 U/L; hs-TnT: 4291 ± 334 ng/dL) than in the IV group, indicating a potential myocardial-protective effect of IC administration. These results suggest that IC tirofiban may reduce enzymatic evidence of myocardial injury, although further studies are needed to confirm these findings and their clinical relevance. **Saddique *et al.*** [24] reported that echocardiographic evaluation in a subset of patients (15 in the IC group and 36 in the IV group) demonstrated a trend toward higher left ventricular ejection fraction in the IC group (50 ± 7%) compared to the IV group (45 ± 6%). Although this difference did not reach statistical significance (p = 0.06), it suggests a potential benefit of IC administration on cardiac function.

In the current study, baseline biochemical parameters, including Lipid profile, as well as random blood glucose levels, were comparable among the IV and IC tirofiban groups, indicating similar metabolic profiles. Coagulation indices, specifically PT and PTT

were also nearly identical across the 2 groups, reflecting equivalent baseline haemostatic function. These observations align with findings by **Tian *et al.*** [17] who reported differences in baseline lipid profiles among groups but not statistically significant. Collectively, these results support the notion that the study groups were well-matched in terms of both cardiovascular and metabolic risk factors, strengthening the validity of subsequent comparisons of clinical and procedural outcomes.

In the present study, the LAD was the most frequently identified culprit vessel in both groups, succeeded by the RCA and LCx. No evidence of a significant difference was observed among groups in the number of diseased vessels and lesion complexity according to the ACC/AHA classification or indications for GPI use including high thrombus burden and slow or no-reflow phenomena. Pre-PCI TIMI flow grades were also comparable with most patients presenting with TIMI 0 or 1 flow. Consistent with these findings, a retrospective study reported similar distributions of culprit vessels, with LM involvement in 4.5% versus 3.4% (P = 0.77), LAD in 51.5% versus 55.2% (P = 0.27), RCA in 14.1% versus 17.0% (P = 0.17), and CX in 31.1% versus 27.3% (P = 0.18) of patients [25]. These data indicate that baseline angiographic parameters and procedural risk factors were well balanced among groups supporting the validity of subsequent outcome comparisons. Moreover, a meta-analysis by **Verdoia *et al.*** [26] of IC vs IV tirofiban in STEMI reported that more than 87% of the patients presented with TIMI grade 0–1 flow before PC across the pooled trials.

In this study, procedural outcomes and complications were similar among the IV and IC tirofiban groups. Mean LVEF at discharge was comparable (47.9% vs. 47.4%, p=0.668) and successful reperfusion (TIMI 3 flow) was achieved in 64.4% of the IV group and 71.2% of the IC group, while not statistically significant in post-PCI TIMI flow distribution (p=0.667). The overall rate of procedural complications, including death, cardiogenic shock, side branch occlusion and other events was also comparable among groups (21.9% vs. 13.7%, p=0.313). In contrast to our findings, **Shi *et al.*** [20] reported that procedural outcomes were significantly improved with IC tirofiban in contrast to the IV group, with higher TIMI flow grades and TMP grade 3 observed in the IC group (P = 0.022 and P = 0.014, respectively). These results suggest that IC administration may enhance myocardial perfusion during PCI, although differences in study design and patient populations could account for the discrepancy with our findings. Consistent with these findings, **Madurska** [27] reported rates of death, reinfarction or target vessel revascularization between IC and intravenous tirofiban administration during PCI as non-significant for acute coronary syndrome.

At 30 days, clinical efficacy outcomes were comparable between the IV and IC tirofiban groups. Composite MACE occurred in 28.8% of patients in the IV group versus 20.5% in the IC group with no statistically significant difference (p = 0.249). Individual components of MACE including cardiovascular death, heart failure, myocardial infarction and stroke were similarly distributed between the groups. Rates of reinfarction (5.5% vs. 4.1%, p = 0.336) and target lesion revascularization (5.5% vs. 2.7%, p = 0.404) were also comparable. Although not statistically significant, there was a trend toward lower stent thrombosis in the IC group (4.1% vs. 9.6%, p = 0.190) suggesting a potential benefit of IC administration that may warrant further investigation in larger studies. In contrast to our findings, a meta-analysis of randomized controlled trials reported that IC tirofiban significantly reduced 30-days major adverse cardiovascular events (MACE) compared to IV administration [28]. Conversely, another meta-analysis was consistent with our results showing no statistically significant difference in MACE among the IC and IV groups (relative risk [RR] 0.74, 95% confidence interval [CI] 0.51–1.10) [29]. These conflicting results underscore the ongoing uncertainty regarding the relative benefits of IC versus IV administration. Variations in study populations, procedural parameters and dosing strategies may contribute to these differences. Moreover, procedural endpoints such as TIMI and TMP flow, as well as markers of myocardial injury, may be differentially affected by the route of tirofiban administration, suggesting that IC administration could confer advantages in myocardial perfusion even when overall MACE rates were similar. Further well-designed trials are needed to clarify the impact of administration route on both short-term outcomes and myocardial protection. These contrasting findings highlight the ongoing debate regarding the clinical superiority of IC over IV tirofiban and underscore the need for further well-designed studies to clarify its impact on short-term cardiovascular outcomes.

In the current study safety endpoints clearly favoured the IC bolus-only strategy. Rates of BARC minimal bleeding (2.7% vs. 49.3%, p<0.001) and minor bleeding (4.1% vs. 21.9%, p=0.001) were significantly lower in the IC group versus the IV group. Vascular complications were also markedly reduced (5.5% vs. 35.6%, p<0.001). Major bleeding events were rare and comparable among groups (p=0.154). These results indicated a superior safety profile for IC bolus-only tirofiban administration.

Similarly, **Liu *et al.*** [30] and **Tian *et al.*** [17] reported significantly fewer bleeding and vascular complications in the IC group contrary to the IV group, while the incidence of major bleeding did not differ significantly among the two. Consistent with our findings, **Zhu *et al.*** [31] demonstrated that IC administration of tirofiban improved angiographic perfusion, as measured by TIMI and TMP flow without

a significant increase in bleeding complications compared to intravenous administration. These results support the potential of IC administration to enhance procedural myocardial perfusion while maintaining a favorable safety profile.

LIMITATIONS

The relatively small sample size of the study may have limited its statistical power to detect rare but clinically important outcomes, such as major bleeding events or stent thrombosis. Additionally, the study was conducted at only two hospitals within the same geographic region, which could restrict the generalizability of the results to other populations, healthcare systems or clinical settings with different practices. Patient follow-up was conducted over a relatively short period, potentially limiting the ability to observe long-term outcomes or delayed adverse events. Furthermore, echocardiographic evaluation was confined to measuring LVEF and assessing regional wall motion abnormalities, without more detailed or advanced imaging parameters. Finally, only a single dosing regimen of tirofiban was investigated, which may not capture the range of responses seen with different dosing strategies in routine clinical practice. Collectively, these factors should be considered when interpreting the study findings and their applicability to broader patient populations.

CONCLUSION

In patients with STEMI undergoing PPCI, intracoronary bolus-only administration of tirofiban achieved short-term clinical outcomes comparable to those of standard intravenous infusion, while offering a more favorable safety profile, notably through a significant reduction in bleeding and vascular complications.

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