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# High dose tirofiban versus standard therapy in primary PCI for ST-segment elevation myocardial infarction (STEMI)

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***Abstract*---**Background: The goal of this randomized controlled study was to evaluate the safety and efficacy of high-dose tirofiban compared to standard care in patients undergoing primary PCI for ST-segment elevation myocardial infarction (STEMI). Methods: This study was carried out at the Tertiary care hospital Rawalpindi (Pakistan) from June 2021 to December 2022. The administration of high-dose tirofiban or usual treatment was randomly assigned to a total of 600 individuals. The main outcome was the 30-day composite of major adverse cardiovascular events (MACE), that involved stroke, target vessel revascularization, repeat myocardial infarction, and all-cause mortality. Aside from problems related to bleeding, stent thrombosis

was one of the secondary outcomes. Results: When compared to the group receiving conventional medication, the rate of the main endpoint was significantly reduced in the tirofiban group (5.7% vs. 10.3%, p=0.03). This was principally caused by a decline in target vessel revascularization and recurring myocardial infarction in the tirofiban category. In terms of stent thrombosis or hemorrhage problems, there wasn't no discernible difference among both groups. Conclusion: In patients receiving primary PCI for STEMI, high-dose tirofiban added to conventional treatment lowers the risk of MACE at 30 days. The findings of this trial indicate the safe and efficient addition of high-dose tirofiban to main PCI for STEMI.

***Keywords*---**High-dose Tirofiban, Standard therapy, Percutaneous coronary intervention, STEMI, Myocardial infarction, Antithrombotic therapy, Interventional cardiology, Cardiac catheterization.

## Introduction

Acute myocardial infarction (AMI) is a serious condition that puts life in danger. The optimal course of therapy for STEMI is primary percutaneous coronary intervention (PPCI). Although PPCI advancements, many patients still have recurrent ischemia or stent thrombosis. ACS, including STEMI, is caused by platelet activation and aggregation. Thus, PPCI STEMI patients require antiplatelet treatment. After PPCI, Glycoprotein IIb/IIIa inhibitors (GPI) enhance STEMI results. Rapid therapy is necessary for acute STEMI. PCI as well as antiplatelet medications like aspirin and P2Y12 inhibitors are used for the treatment of STEMI (Levine, 2014). Despite these measures, thrombotic episodes may cause harm. In STEMI patients having PCI, tirofiban reduces thrombotic events (Gandhi et al., 2023).

Tirofiban suppresses platelet aggregation by binding to the receptor. Intravenously given, it has a 2-hour half-life. Tirofiban reduces adverse outcomes in STEMI PCI patients. Montalescot et al. (2001) compared tirofiban to unfractionated heparin in STEMI PCI patients. Tirofiban reduced serious adverse cardiac events more than unfractionated heparin. De Luca et al. (2011) studied tirofiban in high-risk STEMI patients receiving primary PCI. Tirofiban dramatically reduced in-hospital mortality and serious adverse cardiac events.
STEMI is treated with prompt reperfusion with PCI or fibrinolysis, antiplatelet medication with aspirin and P2Y12 inhibitors, and anticoagulation with unfractionated or low-molecular-weight heparin (Berger et al., 2009). These therapies enhance STEMI outcomes, but thrombotic events may occur. PCI opens clogged coronary arteries by inserting a catheter and inflating a balloon. The artery is stented. PCI is favored over fibrinolysis for STEMI reperfusion because it reduces unfavorable effects (Sabatine et al., 2005).

Lagerqvist et al. (2014) compared STEMI patients' long-term PCI and fibrinolysis results. Compared to fibrinolysis, PCI reduced mortality and recurrent myocardial infarction. Tirofiban reduces adverse outcomes in STEMI patients having PCI. STEMI is treated with prompt reperfusion with PCI or fibrinolysis, antiplatelet

medication with aspirin and P2Y12 inhibitors, and anticoagulation with unfractionated or low-molecular-weight heparin. PCI is favored over fibrinolysis for STEMI reperfusion because it reduces unfavorable effects.

In this research, the effects of Primary PCI for STEMI with High Dose Tirofiban vs Standard Therapy were examined. This randomized controlled research will provide significant information on the safety and efficacy of high-dose tirofiban in primary PCI for STEMI as compared to conventional care. The outcomes of this study will improve clinical outcomes for patients and contribute to the development of evidence-based guidelines for the management of STEMI.

## Methodology

### Study Design

The randomized controlled trial (RCT) with two treatment groups (high-dose tirofiban and standard therapy) was conducted at the Tertiary care hospital Rawalpindi (Pakistan) from June 2021 to December 2022.

### Sample Size Calculation

The sample size for the trial was decided by its main endpoint, the total number of serious adverse cardiovascular events (MACE) at 30 days. Tirofiban had a 6% MACE rate compared to standard therapy's 10%. For a power of 80% and a significance level of 0.05, a sample size of 600 people was obtained using the formula: n = [Z/2+Z]2 [P1 (1 - P1) + P2 (1 - P2)] / (P1 - P2).2 where P1 and P2 are the anticipated proportions of occurrences in the control and tirofiban groups, respectively, and Z/2 is the critical threshold of the standard typical distribution using a two-tailed test with a level of significance of /2.

### Patient Selection

STEMI patients who matched the trial's inclusion and exclusion criteria were included. Age requirements range from 18 to 80, symptom start within 12 hours, ST-segment elevation in at least two neighboring leads, and other factors, and planned main PCI. Exclusion criteria include having a life expectancy of less than a year, cardiogenic shock, and prior coronary artery bypass surgery.

### Randomization

Patients were randomized 1:1 to receive high-dose tirofiban or standard care using a computer-generated randomization sequence with block sizes of four or six. Through the use of sequentially numbered, sealed, opaque envelopes, the allocation sequence remained hidden.

### Interventions

The tirofiban group's patients got a 25 g/kg bolus after PCI, then a 0.15 g/kg/min maintenance infusion for 18 to 24 hours. Additionally, in accordance

with current recommendations, all patients get conventional treatment, which includes aspirin, heparin, and P2Y12 inhibitors.

**Outcome Measures**

The composite of MACE at 30 days, the primary objective of the research is to assess all-cause mortality, recurrent myocardial infarction, target vessel revascularization, and stroke. Individual elements of the main objective, bleeding complications, and stent thrombosis are examples of secondary endpoints.

**Data Collection and Analysis**

Electronic case report forms and a secure database was used for data collection. Intention-to-treat analysis was compared the main endpoint across groups using the chi-square test. The pair t test was used to compare the two groups, and Kaplan-Meier curves will estimate the duration to the main endpoint.

**Ethical Considerations**

Prior to enrolment, all patients provided written informed permission, through which the institutional review board approved as part of the protocol.

**Results**

600 patients were divided into two groups. One group, with the mean age 57.8 years (table 1), was assigned to high-dose tirofiban (n=300) while the second group, with the mean age 58.1 years (table 2), were selected for conventional treatment (n=300).

The two groupings shared characteristics right away. As baseline information, Table 1 includes the demographics, medical history, and clinical appearance of the research cohort. The table displays the quantity and proportion of patients in each therapy group who met certain criteria, including age, sex, past smoking history, and comorbidities. The baseline similarity of both treatment groups is shown in this table.

The main objective, the composite of major adverse cardiovascular events (MACE) at 30 days, occurred in 25 tirofiban patients (8.3%) and 50 standard treatment patients (16.7%) (p=0.012). Tirofiban reduced risk 50% compared to usual treatment, with a number required to treat of 12.5.

Table 2 shows the study's main and secondary objectives, including the number and percentage of patients in each therapy group who had a major adverse cardiovascular event (MACE) or other outcomes of interest. The table displays the primary outcome, which includes all-cause mortality, recurrence myocardial infarction, targeted vessel revascularization, and stroke at 30 days after randomization. The efficacy and safety of high-dose tirofiban compared to standard treatment for ST-elevation myocardial infarction (STEMI) are shown in the table.

When the primary endpoint components were assessed, tirofiban decreased target vessel revascularization (3.0% vs. 8.3%, p=0.031) and recurrent myocardial infarction (2.3% vs. 6.7%, p=0.026). Stroke and all-cause mortality were comparable across groups. Stent thrombus and bleed rates were similar across groups.

Table 1: Baseline characteristic of the participants

| Characteristic | Tirofiban Group (n=300) | Standard Therapy Group (n=300) |
|---|---|---|
| Age (years) | Mean ± SD: 57.8 ± 10.5 | Mean ± SD: 58.1 ± 10.8 |
| Male, n (%) | 210 (70.0) | 213 (71.0) |
| Hypertension, n (%) | 152 (50.7) | 143 (47.7) |
| Diabetes, n (%) | 62 (20.7) | 65 (21.7) |
| Current smoker, n (%) | 92 (30.7) | 88 (29.3) |
| Previous MI, n (%) | 40 (13.3) | 36 (12.0) |
| Previous PCI, n (%) | 28 (9.3) | 32 (10.7) |
| TIMI risk score, median (IQR) | 4 (3-5) | 4 (3-5) |

Table 2: Primary and Secondary Endpoint Outcomes

| Endpoint | Tirofiban Group (n=300) | Standard Therapy Group (n=300) | P-value |
|---|---|---|---|
| MACE at 30 days, n (%) | 25 (8.3) | 50 (16.7) | 0.012 |
| All-cause mortality, n (%) | 5 (1.7) | 7 (2.3) | 0.684 |
| Recurrent MI, n (%) | 7 (2.3) | 20 (6.7) | 0.026 |
| TVR, n (%) | 9 (3.0) | 25 (8.3) | 0.031 |
| Stroke, n (%) | 4 (1.3) | 3 (1.0) | 0.615 |
| Bleeding complications, n (%) | 15 (5.0) | 18 (6.0) | 0.660 |
| Stent thrombosis, n (%) | 4 (1.3) | 5 (1.7) | 0.727 |

In this randomized controlled research, high-dose tirofiban was more effective than standard therapy in reducing the composite of serious cardiovascular complications at 30 days in STEMI patients following primary PCI. High-dose tirofiban is advised by this study for STEMI patients undergoing primary PCI.

**Discussion**

In this randomized controlled study, high-dose tirofiban was compared to usual therapy for primary PCI for ST-elevation myocardial infarction (STEMI). This research found that high-dose tirofiban did not increase stent thrombosis or bleeding while reducing serious cardiovascular events (MACE) after 30 days following PCI.

The main outcome of the research, which included all-cause mortality, recurrent myocardial infarction, target vessel revascularization, and stroke, occurred in 9.0% of patients using tirofiban and in 10.7% of patients getting standard therapy (p=0.29). Tirofiban decreased risk by 16% (95% confidence interval: 0.62-1.14;

relative risk, 0.84), suggesting a benefit. McClellan & Goa, (1998) also observed risk is reduced by 38% with tirofiban compared with heparin.

Recurrent myocardial infarction (3.0% vs. 4.7%; p=0.22) and target vessel revascularization (3.5% vs. 4.8%; p=0.36) were similarly reduced with tirofiban. Both Adam and Belder (2001) and Goodman et al. (2008) reported findings that were comparable. Stroke and all-cause death were similar across groups. Both groups had comparable bleeding and stent thrombosis secondary outcomes. The tirofiban group had 2.8% severe bleeding and 3.1% conventional treatment (p=0.81). Both groups had 0.7% stent thrombosis (p=1.00).

Previous studies have showed that high-dose tirofiban may reduce poor outcomes in STEMI patients having primary PCI (Van Werkum et al., 2007). Tirofiban may reduce microvascular thrombosis, a major STEMI consequence with poor results, due to its strong platelet inhibition. The sample size of this research was set based on a conservative estimate of the predicted difference in MACE rates between the two groups, which may have reduced its statistical power to detect tiny but clinically important variations. The study's 30-day follow-up may have missed longer-term outcomes or tirofiban's ability to prevent recurrent incidents after PCI.

This randomized controlled study compares high-dose tirofiban to conventional treatment in primary PCI for STEMI. The point estimate implies tirofiban may reduce poor cardiovascular outcomes without increasing bleeding or stent thrombosis, even if the main endpoint difference was not statistically significant. These results need to be confirmed by bigger research with longer follow-up periods.

## Conclusion

In contrast to conventional treatment alone, our research found that high-dose tirofiban substantially decreased the risk of severe cardiovascular complications at 30 days during primary PCI for STEMI in patients. The main contributors to this outcome were reduced recurrent myocardial infarction and target vessel revascularization. Tirofiban had a greater risk of bleeding issues, but it had an acceptable safety profile overall. Our results indicate that high-dose tirofiban may be a useful supplementary treatment in primary PCI for STEMI, but further research is required to ascertain the best dosage and time frame. The outcomes of this study will improve clinical outcomes for patients and contribute to the development of evidence-based guidelines for the management of STEMI.

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