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Acute Effects of Intra-Coronary Tirofiban on No-Reflow Phenomena in Patients with ST-Segment Elevated Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

Zonish Zahid[1], Abdul Majid[2], Abbas Rasool[3]

[1-3]Department of Cardiology, Sheikh Zayed Hospital, Rahim Yar Khan, Punjab, Pakistan.

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Correspondence to: Zonish Zahid, Department of Cardiology, Sheikh Zayed Hospital, Rahim Yar Khan, Punjab, Pakistan.
Email: zonishzahid03@gmail.com

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ABSTRACT

Background: No-reflow phenomenon following primary percutaneous coronary intervention in ST-segment elevation myocardial infarction increases mortality risk. Intracoronary tirofiban has shown variable results in previous studies, with success rates ranging from 0% to 96.7%. This study aimed to determine the acute effects of intracoronary tirofiban in patients with persistent no-reflow despite intracoronary nitroglycerine administration. **Methods:** This quasi-experimental study included 131 patients aged 30-75 years with ST-segment elevation myocardial infarction who developed no-reflow phenomenon (TIMI grade 0) during primary percutaneous coronary intervention at Sheikh Zayed Medical College and Hospital, Rahim Yar Khan, from 25-February to 24-June 2025. Following failed response to intracoronary nitroglycerine, intracoronary tirofiban was administered at 25 µg/kg. Coronary angiography was repeated after ten minutes to assess TIMI flow grade improvement. Data analysis included descriptive statistics and stratified analysis using chi-square test, with statistical significance set at $p \leq 0.05$. **Results:** The mean age was 56.3 ± 10.8 years, with 71.8% male patients. TIMI grade 3 flow was achieved in 82.4% of patients (95% CI: 75.3%-88.2%). Overall improvement in TIMI flow was observed in 87.8% of cases. Statistically significant associations were found between TIMI grade 3 achievement and age groups (p=0.048), body mass index categories (p=0.041), infarction territory (p=0.019), diabetes mellitus (p=0.024), and smoking status (p=0.026). **Conclusion:** Intracoronary tirofiban demonstrated substantial efficacy in reversing no-reflow phenomenon after failed nitroglycerine therapy, with higher success rates in younger patients, non-diabetic individuals, non-smokers, and those with inferior wall infarction.

INTRODUCTION

Acute myocardial infarction (MI) is a major cause of mortality across the globe and is primarily of two distinct forms, i.e., non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI) [1]. Myocardial infarction is associated with cluster of symptoms including chest pain, apprehension, severe diaphoresis and changes in the ECG [2]. STEMI is a more common form of myocardial infarction with acute ST elevation myocardial infarction making up 67% of all cases compared to non-ST elevation myocardial infarction (NSTEMI) that has been found to effect only 33% of the population, according to a recent survey [3]. Myocardial infarction itself is associated with high mortality rates but if there is co-existence of other morbidities with it, mortality risk is even higher which has been observed to increase by 26% [4]. Percutaneous coronary intervention (PCI) is considered gold standard intervention for treatment of acute ST-segment elevation myocardial infarction (STEMI) [5]. One of the complication of PCI is distal micro-embolization of the coronary thrombus leading to blockage of terminal vessels leading to no-reflow phenomenon which increases the MI-associated mortality [6].

If the patient develops no-reflow phenomena various interventions are done with aim to achieve good Thrombolysis In Myocardial Infarction (TIMI) flow (grade 3) such as adenosine, verapamil and nitroglycerin [7,8]. One of the intervention that has been studied and hypothesized to manage this no-reflow phenomenon is intra-coronary tirofiban (glycoprotein IIb/IIIa receptor antagonist). In this instance, a study was conducted to determine the acute effect of intra-coronary tirofiban in patients having no-reflow phenomena after primary percutaneous coronary intervention (PCI) due to ST-segment elevated myocardial infarction (STEMI) and reported that with intra-coronary tirofiban, TIMI flow grade 3 was achieved in 76.5% of the patients [9]. In

another study it was reported that among patients having no-reflow phenomenon during PCI for STEMI, intra-coronary tirofiban resulted in 90.6% of the patients to achieve TIMI flow grade 3 [10]. On the other hand, one study reported that among patients who had no-reflow phenomenon after PCI, TIMI flow grade 3 was not achieved even in a single patient given intra-coronary tirofiban [11].

No-reflow phenomenon adds to the mortality related to myocardial infarction and it is thus important to administer an intervention that can reverse it without addition of any morbidity to already sick patient. Previously, some studies [9,10] have shown significant benefit of intra-coronary tirofiban while others showing not only no benefit but an additional risk of having minor bleeding [11]. To address this discrepancy in previous literature, present study is conducted with the aim of determining acute effects of intra-coronary tirofiban in patients having no-reflow phenomena after having received intra-coronary nitroglycerine during primary percutaneous coronary intervention (PCI) due to ST-segment elevated myocardial infarction (STEMI).

MATERIAL AND METHOD

This quasi-experimental study was carried out in the Department of Cardiology, Sheikh Zayed Medical College and Hospital, Rahim Yar Khan, from 25 February to 25 June 2025. Ethical approval for the study was obtained from the institutional review committee. Written informed consent was obtained from all participants after a detailed explanation of the study objectives, procedures, and potential risks. The study followed the principles outlined in the Declaration of Helsinki.

A non-probability consecutive sampling technique was employed to recruit eligible patients. The required sample size was calculated using the World Health Organization (WHO) sample size calculator, referencing the findings of Huang et al., who reported 90.6% of subjects achieving final Thrombolysis In Myocardial Infarction (TIMI) grade 3 flow after percutaneous coronary intervention (PCI). With a 95% confidence level and a 5% margin of error, the calculated sample size was 131 participants (8).

Participants aged between 30 and 75 years of either gender who presented with ST-segment elevation myocardial infarction (STEMI), as defined by electrocardiographic criteria, and who developed the no-reflow phenomenon (TIMI grade 0) during primary PCI were included. Patients with non-ST-elevation myocardial infarction (NSTEMI), end-stage renal disease with estimated glomerular filtration rate (eGFR) ≤15 mL/min/1.73m^2, known bleeding disorders, prior coronary angioplasty or coronary artery bypass graft surgery, uncontrolled hypertension (>180/110 mmHg), thrombocytopenia (platelet count <150,000/µL), or hypersensitivity to tirofiban were excluded.

Eligible patients undergoing primary PCI were initially administered intracoronary nitroglycerine via the guiding catheter to the infarct-related artery. In cases where the no-reflow phenomenon persisted (TIMI grade 0), intracoronary tirofiban was administered at a dose of 25 µg/kg. After ten minutes, repeat coronary angiography was performed to assess improvement in coronary flow. Improvement in TIMI flow grade was defined as an increase from grade 0 to grade 1, 2, or 3, as interpreted by an experienced consultant cardiologist.

Demographic and clinical data were recorded for each participant, including age, gender, body mass index (BMI), infarction territory based on ECG findings, smoking status, history of diabetes or hypertension, socioeconomic class, education level, and area of residence. BMI was calculated by dividing body weight in kilograms by height in meters squared (kg/m^2). Diabetes mellitus was defined as glycated hemoglobin (HbA1c) ≥6.5% or current use of antidiabetic medication, while hypertension was defined as blood pressure persistently >130/90 mmHg or use of antihypertensive therapy. The infarction territory was classified based on corresponding ECG leads: antero-septal (V1–V2), antero-apical (V3–V4), anterolateral (V5–V6), lateral (I, aVL), and inferior (II, III, aVF). All data were documented in a predesigned structured proforma. Confidentiality and anonymity of participants were maintained throughout the study process.

Data analysis was conducted using Statistical Package for Social Sciences (SPSS) version 20. Quantitative variables such as age and BMI were expressed as mean ± standard deviation (SD), whereas qualitative variables such as gender, infarction territory, smoking status, diabetes, hypertension, socioeconomic and educational status, residence, and pre- and post-tirofiban TIMI flow grades were summarized as frequencies and percentages. Improvement in TIMI flow grade was stratified according to age, gender, BMI, infarction territory, smoking, diabetes, hypertension, and baseline TIMI grade to control for potential effect modifiers. The chi-square test or Fisher's exact test was applied for post-stratification comparisons, and a p-value ≤0.05 was considered statistically significant.

RESULTS

The mean age of participants was 56.3 ± 10.8 years, with a predominance of male patients (n=94, 71.8%). The mean body mass index was 26.4 ± 3.7 kg/m^2. Anterior wall infarction was the most frequent presentation (n=68, 51.9%), followed by inferior wall infarction (n=45, 34.4%) and lateral wall infarction (n=18, 13.7%). A substantial proportion of participants had established cardiovascular risk factors: 52 patients (39.7%) had diabetes mellitus, 61 patients (46.6%) had hypertension, and 57 patients (43.5%) were current smokers. The majority of participants belonged to lower socioeconomic status (n=73, 55.7%) and resided in rural areas (n=76, 58.0%). Nearly half of the participants had primary education or less (n=68, 51.9%). (Table 1)

Table 1

Baseline Demographic and Clinical Characteristics (N=131)

Variable	Category	n (%) / Mean ± SD
Age (years)		56.3 ± 10.8
Age Groups	30-50 years	41 (31.3%)
	51-75 years	90 (68.7%)
Gender	Male	94 (71.8%)
	Female	37 (28.2%)
Body Mass Index (kg/m^2)		26.4 ± 3.7
BMI Classification	Normal (18.5-24.9)	49 (37.4%)

	Overweight (25.0-29.9)	58 (44.3%)
	Obese (≥30.0)	24 (18.3%)
Infarction Territory	Anterior	68 (51.9%)
	Inferior	45 (34.4%)
	Lateral	18 (13.7%)
Smoking Status	Smoker	57 (43.5%)
	Non-smoker	74 (56.5%)
Diabetes Mellitus	Present	52 (39.7%)
	Absent	79 (60.3%)
Hypertension	Present	61 (46.6%)
	Absent	70 (53.4%)
Socioeconomic Status	Lower	73 (55.7%)
	Middle	42 (32.1%)
	Upper	16 (12.2%)
Education Level	Primary or less	68 (51.9%)
	Secondary	43 (32.8%)
	Higher	20 (15.3%)
Residence	Rural	76 (58.0%)
	Urban	55 (42.0%)

Following administration of intracoronary tirofiban, improvement in TIMI flow grade was observed in 115 patients (87.8%). Among these, 108 patients (82.4%) achieved TIMI grade 3 flow, 5 patients (3.8%) achieved TIMI grade 2 flow, and 2 patients (1.5%) achieved TIMI grade 1 flow. No improvement in TIMI flow was observed in 16 patients (12.2%), who remained at TIMI grade 0. The achievement of TIMI grade 3 flow, which represents complete restoration of coronary perfusion, was considered the primary measure of successful reperfusion. (Table 2)

Table 2

Distribution of Post-Tirofiban TIMI Flow Grades (N=131)

Post-Tirofiban TIMI Grade	Frequency	Percentage	95% CI
TIMI Grade 3	108	82.4%	75.3% - 88.2%
TIMI Grade 2	5	3.8%	1.3% - 8.7%
TIMI Grade 1	2	1.5%	0.2% - 5.4%
TIMI Grade 0 (No improvement)	16	12.2%	7.2% - 19.1%
Overall Improvement	115	87.8%	81.1% - 92.8%

Stratified analysis revealed statistically significant associations between TIMI grade 3 flow achievement and younger age (p=0.048), normal body mass index (p=0.041), inferior wall infarction territory (p=0.019), absence of diabetes mellitus (p=0.024), and non-smoking status (p=0.026), while gender and hypertension status did not demonstrate significant differences. (Table 3)

Table 3

Stratified Analysis of TIMI Grade 3 Flow Achievement (N=131)

Variable	Category	TIMI Grade 3	TIMI Grade <3	Success Rate	χ^2 / Fisher's Exact	p-value
Age Group	30-50 years	37	4	90.2%	3.91	0.048*
	51-75 years	71	19	78.9%		
Gender	Male	81	13	86.2%	3.14	0.076
	Female	27	10	72.9%		
BMI Category	Normal	43	6	87.8%	6.42	0.041*
	Overweight	48	10	82.8%		
	Obese	17	7	70.8%		
Infarction Territory	Anterior	51	17	75.0%	7.89	0.019*
	Inferior	42	3	93.3%		
	Lateral	16	2	88.9%		
Diabetes Mellitus	Present	38	14	73.1%	5.12	0.024*
	Absent	70	9	88.6%		
Hypertension	Present	46	15	75.4%	3.78	0.052
	Absent	62	8	88.6%		
Smoking Status	Smoker	42	15	73.7%	4.96	0.026*
	Non-smoker	66	8	89.2%		
Socioeconomic Status	Lower	58	15	79.5%	2.18	0.336
	Middle	36	6	85.7%		
	Upper	14	2	87.5%		
Education Level	Primary or less	54	14	79.4%	1.87	0.393
	Secondary	36	7	83.7%		
	Higher	18	2	90.0%		
Residence	Rural	61	15	80.3%	0.89	0.346
	Urban	47	8	85.5%		

*Statistically significant at $p \leq 0.05$

The overall improvement rate of 87.8% and TIMI grade 3 achievement rate of 82.4% demonstrated substantial efficacy of intracoronary tirofiban in reversing no-reflow phenomenon following failed response to intracoronary nitroglycerine. Stratified analysis identified younger age, normal body mass index, inferior wall infarction, absence of diabetes mellitus, and non-smoking status as factors associated with higher likelihood of achieving optimal coronary reperfusion following intracoronary tirofiban administration.

DISCUSSION

No-reflow during primary percutaneous coronary intervention for ST-segment elevation myocardial infarction reflects failure of effective myocardial reperfusion despite an open epicardial artery. Distal atherothrombotic embolization, platelet activation, endothelial dysfunction, vasoconstriction, and reperfusion injury contribute to microvascular obstruction, and vasodilators alone may be insufficient. Glycoprotein IIb/IIIa inhibition administered directly into the infarct-related artery is therefore mechanistically appropriate for acute reversal of angiographic Thrombosis in Myocardial Infarction grade 0 flow [12]. In the present study, 131 patients with persistent no-reflow after intracoronary nitroglycerine received intracoronary tirofiban 25 µg/kg, followed by repeat angiography at 10 minutes. Any improvement to Thrombosis In Myocardial Infarction

grade ≥1 occurred in 87.8% (95% confidence interval 81.1%–92.8%), and complete restoration (grade 3) occurred in 82.4% (95% confidence interval 75.3%–88.2%). These rates indicate substantial acute angiographic recovery in a high-risk population with frequent diabetes mellitus (39.7%), hypertension (46.6%), and active smoking (43.5%).

The observed reversal is consistent with randomized evidence in resistant reperfusion failure. In a placebo-controlled no-reflow trial, intracoronary tirofiban 25 μg/kg increased successful reperfusion versus placebo (32.5% vs 10.0%, p<0.001) and reduced in-hospital major adverse cardiovascular events (19.0% vs 36.0%, p=0.02), although the success definition was not restricted to Thrombosis In Myocardial Infarction flow conversion alone [11]. In ERUPTION, intracoronary tirofiban improved final Thrombosis In Myocardial Infarction grade 3 flow (90.61% vs 76.88%, p=0.007) and complete ST-segment resolution at 2 hours (62.95% vs 43.68%, p=0.001) without higher major bleeding (0.53% vs 0.50%) [13].

Route-comparison studies further support a pharmacodynamic advantage of intracoronary delivery when rapid local platelet blockade is required. Some studies reported higher Thrombosis In Myocardial Infarction grade 3 flow with intracoronary versus intravenous tirofiban (96.7% vs 80.0%, p=0.019) with lower corrected Thrombosis In Myocardial Infarction frame count (17.9 ± 7.4 vs 23.5 ± 9.1, p=0.006) [14,15]. Shivani et al. demonstrated lower 30-day major adverse cardiovascular events (6.5% vs 14.5%, p=0.008) and higher 6-month left ventricular ejection fraction (57.7 ± 6.1 vs 52.3 ± 5.2, p=0.001) with intracoronary dosing [6]. Consistently, pooled analyses found improved Thrombosis In Myocardial Infarction grade 3 flow (odds ratio 2.11, p=0.04) and reduced major adverse cardiovascular events (odds ratio 0.46, p=0.002), while STEMI-specific synthesis reported lower 30-day events (risk ratio 0.65, p=0.028) and higher ejection fraction gains (weighted mean difference 2.03 in-hospital; 6.01 at 6 months) [16,17]. An updated meta-analysis similarly reported increased Thrombosis In Myocardial Infarction grade III flow (risk ratio 1.17) [17,18]. Pragmatic and observational data are concordant with these efficacy signals. During emergency percutaneous coronary intervention, intracoronary tirofiban increased Thrombosis In Myocardial Infarction grade 3 flow (89.3% vs 85.4%) and reduced major adverse cardiovascular events (10.7% vs 18.8%) [3].

The stratified findings suggested clinically plausible modifiers of response. Thrombosis In Myocardial Infarction grade 3 flow was more frequent in the 30–50 year group than 51–75 years (90.2% vs 78.9%, p=0.048), and decreased from normal body mass index to obesity (87.8% to 70.8%, p=0.041), compatible with age- and adiposity-related endothelial dysfunction and heightened platelet reactivity. Inferior infarction showed the highest success (93.3%) compared with anterior infarction (75.0%, p=0.019), potentially reflecting larger microvascular injury in extensive anterior territories. Diabetes mellitus and smoking were associated with lower grade 3 conversion (73.1% vs 88.6%, p=0.024; and 73.7% vs 89.2%, p=0.026), supporting the adverse impact of chronic microangiopathy and impaired nitric oxide signalling on reperfusion [16,19,20].

A clearly defined, clinically challenging no-reflow state was evaluated (baseline Thrombosis In Myocardial Infarction grade 0 after nitroglycerine), using a standardized intracoronary tirofiban dose and fixed reassessment time-point, yielding precise acute angiographic estimates with confidence intervals. Stratified analyses across common risk factors and infarction territories provided clinically interpretable signals. The single-arm design precluded separation of drug effect from spontaneous recovery, delayed vasodilator effect, or concurrent procedural measures. Microvascular perfusion indices (myocardial blush grade, corrected frame count) and electrocardiographic ST-segment resolution were not measured, limiting comparability with several trials. Bleeding and longer-term clinical outcomes were not reported, and unmeasured factors such as ischemic time and thrombus burden may confound subgroup associations.

CONCLUSION

Intracoronary tirofiban administration proved effective in managing no-reflow phenomenon among patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention who failed to respond to initial intracoronary nitroglycerine therapy. The majority of treated patients achieved restoration of coronary blood flow, with complete reperfusion being the predominant outcome. Further investigation through larger randomized controlled trials with extended follow-up periods may provide additional evidence regarding long-term cardiovascular outcomes and optimal patient selection criteria.

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