Original Article

The Relationship Between High-Dose Atorvastatin Loading and the No-Reflow Phenomenon in STEMI Patients Undergoing Primary PCI

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ABSTRACT

Background: Percutaneous coronary intervention (PCI) is the preferred reperfusion strategy for acute coronary syndrome. However, no-reflow can still occur and is associated with worse in-hospital and long-term prognoses. This study aims to assess the impact of high-dose atorvastatin loading before primary PCI on ST-elevation myocardial infarction (STEMI) patients with no-reflow and major adverse cardiovascular events (MACE) after 1 month.

Methods: Two hundred STEMI patients undergoing primary PCI were allocated and randomized into 2 groups: the study group received high-intensity statin (80 mg of atorvastatin) in addition to guideline-recommended therapy before primary PCI, while the control group received guideline-recommended therapy before primary PCI. Angiographic and echocardiographic assessments were thoroughly conducted for both groups.

Results: No significant differences in demographic data were observed between the 2 groups. A significant decrease in the no-reflow phenomenon was seen in the study group compared with the control group (28% vs 47%; $P = 0.006$). Moreover, a better myocardial blush grade was noted in the study group (0–1: 28% vs 43% and 2–3: 72% vs 57%; $P = 0.027$), along with a higher ejection fraction 24 hours after PCI (mean ± SD = 48.35 ± 8.78 vs 45.20 ± 7.89; $P = 0.008$) and improved ejection fraction after 1 month (43% vs 20%; $P = 0.039$). Nonetheless, no significant impact on MACE was found after 1 month.

Conclusions: High-dose atorvastatin loading before primary PCI led to improvements in postprocedural myocardial blush grade, the no-reflow phenomenon, and ejection fraction (both after 24 hours and 1 month). Still, no significant reduction in MACE was observed after 1 month. Despite this, our findings support the routine use of high-dose atorvastatin before primary PCI in patients presenting with STEMI. ***(Iranian Heart Journal 2025; 26(1): 54-66)***

KEYWORDS: High-dose atorvastatin, No-reflow, STEMI, PCI

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Although many patients undergo successful coronary revascularization with primary percutaneous coronary intervention (PCI), a considerable portion of these patients do not achieve coronary reperfusion, as indicated by the absence of improvement in the indirect signs of ischemia. These signs include ECG changes and

improvements in perfusion abnormalities, which would typically be expected following successful revascularization. Patients experiencing this condition often exhibit an angiographic phenomenon marked by evidence of the slow-flow phenomenon in the affected vessel (thrombolysis in myocardial infarction [TIMI] flow score ≤ 2) and a lack of contrast uptake, or "blush," by the subtended myocardium. This phenomenon is known as no-reflow. [1]

A range of strategies have been suggested for the prevention and treatment of the no-reflow phenomenon, aimed at addressing the underlying pathophysiology. These measures include shortening the door-to-balloon time, maintaining optimal blood pressure and preprocedural blood sugar levels, administering statins, performing thrombus aspiration, and using various vasodilators that can be given intra-coronary during the procedure, such as adenosine, nitroprusside, nicardipine, and verapamil. [2, 3]

A substantial body of research has demonstrated that, in addition to their lipid-lowering properties, statins exhibit various pleiotropic effects. These effects include enhancing endothelial function, increasing the expression of endothelial nitric oxide synthase (eNOS), exhibiting potent antioxidant potential, and demonstrating anti-inflammatory properties. Collectively, these effects serve to protect the myocardium from lethal ischemia/reperfusion (I/R) injury. [4] The cardioprotective potential of statins can be attributed to several mechanisms, including the phosphatidyl inositol (PI3)-kinase/Akt/eNOS pathway, which plays a crucial role in promoting NO production. The activation of ATP-sensitive potassium channels by NO leads to improved myocardial metabolism, while the release of endogenous adenosine, facilitated by increased activity of adenosine-forming enzymes, contributes to further cardioprotection. Further, statins have been shown to inhibit reactive oxygen species production, decrease oxidative stress, and attenuate apoptosis. [4]

Evidence supporting the benefits of high-intensity statin loading in acute STEMI patients undergoing primary PCI remains a topic of ongoing debate. While previous studies have shown the advantages of statin pre-treatment before PCI for patients with stable angina pectoris and acute coronary syndrome (ACS) (unstable angina and non-STEMI), further investigation is needed to establish the efficacy of statin loading in the context of acute STEMI. [4]

This study aimed to investigate the effect of high-dose atorvastatin (80 mg) loading before primary PCI on the incidence of the no-reflow phenomenon and major adverse cardiovascular events (MACE) at 30 days in patients presenting with STEMI.

METHODS

The present study is a randomized controlled clinical trial conducted in the coronary care units and coronary catheterization lab of the Cardiology Department at Ain Shams University Hospitals.

Participants in this clinical trial included patients presenting with STEMI and scheduled for primary PCI between April 2021 and October 2021. To be eligible for allocation, patients were required to be statin naïve.

Patients were randomly divided into 2 groups:

- The study group received high-intensity statin (80 mg of atorvastatin) in addition to guideline-recommended therapy just before primary PCI.
- The control group received guideline-recommended therapy before primary PCI and 40 mg of atorvastatin within 24 hours after the procedure.

To minimize potential bias, all cardiac catheterization laboratory operators and

echocardiographers were blinded to the patient's randomization. This blinding ensured that the assessments and interpretations of outcomes were objective and not influenced by knowledge of the assigned treatment.

STEMI was defined as persistent chest discomfort or other symptoms indicative of ischemia with STEMI in at least 2 contiguous leads, following the 2017 European Society of Cardiology guidelines. In adherence to these guidelines, patients in both the study and control groups received guideline-recommended therapy, which included a combination of dual antiplatelet agents and anticoagulation. This study adhered to the guidelines of the Helsinki Declaration. The study protocol was approved by the Ain Shams University Cardiology Department Council and the hospital's ethics committee. All participants were informed about the research objectives, research protocol, and treatment alternatives involved in the study. Additionally, all participants provided written informed consent to participate in the study.

The study was revised according to the CONSORT statement (Fig. 1) and registered at www.clinicaltrials.gov, Unique Protocol (ID: A123NRF.)

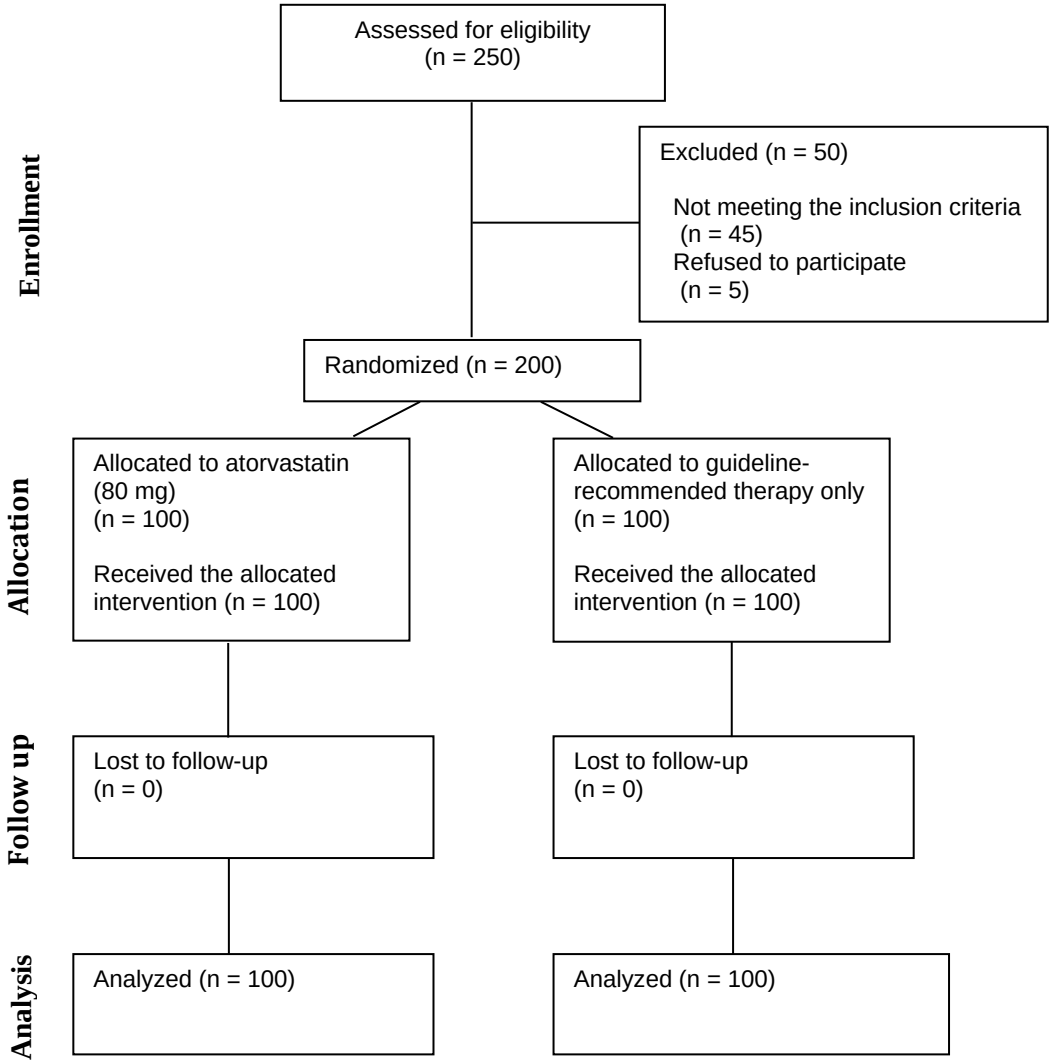

Figure 1: The CONSORT diagram shows the flow of participants through each stage of the study.

Inclusion Criteria: Participants were required to be aged between 18 and 75 years and have experienced STEMI within 24 hours of symptom onset.
Exclusion Criteria: Patients were excluded if they had pre-PCI hyperglycemia (serum glucose > 200 mg/dL), cardiogenic shock (blood pressure < 90/60 mm Hg plus hypoperfusion), were on chronic statin therapy, had left main disease or severe triple-vessel disease, or had received thrombolytic reperfusion therapy.

During the study period, 200 patients (100 in each group) with STEMI presented to Ain Shams University hospitals, met the inclusion criteria, and subsequently underwent primary PCI.

Relevant patient data were collected for each participant, including age and sex, prior diagnosis or hospitalization due to ischemic heart disease or heart failure, chief complaint (eg, chest pain, dyspnea, or fatigue), history of associated comorbidities (eg, hypertension, diabetes mellitus, valvular heart disease, and chronic renal insufficiency), prior drug therapy, prior coronary angiography or PCI, and prior device therapy.

A thorough physical examination was performed for each participant, including the measurement of blood pressure and heart rate. A complete general and local cardiac examination was conducted, which involved auscultation of the back of the chest for rales detection, assessment of lower limb edema, and evaluation of signs of peripheral ischemia.

ECGs were obtained before and 60 minutes after primary PCI to assess the extent of ST-segment resolution (STR). STR was calculated as single-lead STR, determined by comparing 1 ECG lead with the most prominent ST-segment deviation at baseline and at a given time point after primary PCI. STR was expressed as a percentage, with complete early STR defined as STR ≥ 70%.

Experienced operators performed coronary angiography to identify the coronary anatomy, locate the culprit vessel, and execute primary PCI. The culprit lesion was treated using drug-eluting stents, and the TIMI flow score and myocardial blush grade (MBG) were documented for each patient.
The angiographic no-reflow phenomenon was identified based on the presence of TIMI flow scores < 3 or TIMI flow scores of 3 with MBG 0 or 1 without any angiographic signs of mechanical vessel obstruction. [5]
The TIMI flow score was assessed as a TIMI of 0, 1, 2, or 3. [6]
MBG was evaluated using the following criteria:

- MBG 0: No contrast opacification observed in the myocardial zone
- MBG 1: Minimal contrast opacification or persistent stain without washout
- MBG 2: Reduced but noticeable blush in the infarct zone compared with the contralateral non-involved territory
- MBG 3: Normal opacification of the myocardium with appropriate clearance at the end of the washout phase, similar to the non-involved territory.

Transthoracic echocardiography (TTE) was performed 24 hours after primary PCI for all patients to assess left ventricular ejection fraction (LVEF) using the bi-plane Simpson method, to identify any mechanical complications, and to evaluate valvular function and pericardial effusions.

All patients were followed up for 1 month after discharge from the CCU to monitor MACE and assess changes in LVEF. TTE was performed after 1 month, and LVEF was calculated using the bi-plane Simpson method. This result was compared with the

LVEF obtained from the TTE conducted 24 hours after primary PCI.
A clinically significant improvement in LVEF was defined as a ≥ 5% increase in EF after 1 month.

Statistical Analysis
Data management and statistical analysis were performed using the Statistical Package for Social Science (IBM SPSS) version 21. Collected data were coded, reviewed for accuracy, and entered into the software for analysis.
Quantitative data with parametric distribution were summarized as mean, standard deviation (SD), and range, providing a comprehensive description of the numerical variables. Comparisons between groups involving qualitative data were conducted using the χ^2 or Fisher exact test when the expected count in any cell was < 5%.

For comparisons between 2 independent groups involving quantitative data with parametric distribution, an independent *t*-test was employed. This statistical test allowed for the evaluation of mean differences between the groups.
A 95% confidence interval (CI) and a 5% margin of error were set to ensure a high degree of certainty in the results. The *P* value was used to determine the significance of the findings, with the following thresholds applied:

- $P > 0.05$: Nonsignificant (NS)
- $P < 0.05$: Significant (S)
- $P < 0.01$: Highly significant (HS).

RESULTS

In this study, comparisons between the 2 groups were performed for several key variables. These included traditional coronary artery disease risk factors, TIMI flow score, MBG, STR, echocardiographic parameters, 1-month MACE, and LVEF. Following the initial comparisons, an additional analysis was conducted between the reflow and no-reflow groups to pinpoint factors that most significantly impacted the outcomes.

The mean age of participants was 53.60 ± 11.73 years, with a range of ages likely falling between the early 40s and mid-60s. The study population consisted of 61% males and 39% females. Various cardiovascular risk factors were observed among the patients: 31.5% had a history of hypertension, 31% had diabetes mellitus, and 64% were smokers.

No statistical differences were observed between the control and study groups regarding demographic characteristics and risk factors (Table 1).

Both the control and study groups received standard antiplatelet loading doses as part of the guideline-recommended therapy for STEMI management. Participants in both groups were statin naïve, ensuring a homogeneous study population concerning prior statin exposure. Furthermore, all patients had Killip class I heart failure. The femoral artery was used as the vascular access site for primary PCI in all patients.
Analysis of periprocedural parameters revealed no statistically significant differences between the control and study groups (Table 2).

No complications occurred in both groups. Statistically significant differences were noted between the control and study groups in terms of MBG (0–1: 43% vs 28% and 2–3: 57% vs 72%; $P = 0.027$), the no-reflow phenomenon (47% vs 28%; $P = 0.006$), and LVEF 24 hours after PCI (mean ± SD = 45 ± 7 vs 48 ± 8; $P = 0.008$) (Table 3).

Table 1: Demographic Characteristics and Risk Factors of the Studied Patients and their Comparisons Between the Control and Study Groups

		All Patients (No = 200)	Control Group (No = 100)	Study Group (No = 100)	*P* value
Age	mean±SD	53.60 ± 11.73	53.00 ± 11.20	54.47 ± 12.64	0.385
	range	25 – 77	25 – 85	29 – 75	
Sex		122 (61.0%)			0.772
	Male		62 (62.0%)	60 (60.0%)	
Hypertension		63 (31.5%)			0.287
	Yes		28 (28.0%)	35 (35.0%)	
Diabetes mellitus		62 (31.0%)			0.359
	Yes		28 (28.0%)	34 (34.0%)	
Smoking		128 (64.0%)			0.768
	Yes		65 (65.0%)	63 (63.0%)	

Table 2: Comparisons Between the Control and Study Groups Concerning Periprocedural Parameters

		Control Group (No = 100)	Study Group (No = 100)	*P* value
Type of STEMI	Anterior	53 (53.0%)	53 (53.0%)	0.059
	Inferior	38 (38.0%)	43 (43.0%)	
	Anterolateral	5 (5.0%)	0 (0.0%)	
	Posterior	2 (2.0%)	0 (0.0%)	
	Lateral	0 (0.0%)	3 (3.0%)	
	Inferoposterior	2 (2.0%)	1 (1.0%)	
Pain-to-balloon time, h	mean±SD	8.73 ± 4.32	8.63 ± 3.88	0.864
	range	2 – 21	3 – 20	
Random blood sugar before PCI (15–30 min before PCI)	mean±SD	147.68 ±24.49	146.25 ±31.08	0.718
	range	90 –196	90 –198	
Culprit lesion	RCA	30 (30.0%)	38 (38.0%)	0.404
	LAD	57 (57.0%)	53 (53.0%)	
	LCX	13 (13.0%)	9 (9.0%)	
TIMI flow score on angiography	Grade 0	86 (86.0%)	94 (94.0%)	0.139
	Grade 1	7 (7.0%)	4 (4.0%)	
	Grade 2	7 (7.0%)	2 (2.0%)	
	Grade 3	0 (0.0%)	0 (0.0%)	
PCI on the culprit vessel	1 drug-eluting stent	94 (94.0%)	94 (94.0%)	1.000
	2 drug-eluting stents	6 (6.0%)	6 (6.0%)	

STEMI: ST-segment elevation myocardial infarction, PCI: percutaneous coronary intervention, TIMI: thrombolysis in myocardial infarction, RCA: right coronary artery, LAD: left anterior descending artery, LCX: left circumflex artery

Table 3: Comparisons Between the Control and Study Groups Concerning Revascularization Parameters and Echocardiographic Findings 24 Hours after PCI

		Control Group (No = 100)	Study Group (No = 100)	*P* value
TIMI flow score just after PCI	1	10 (10.0%)	4 (4.0%)	0.096
	3	90 (90.0%)	96 (96.0%)	
MBG	(0–1)	43 (43.0%)	28 (28.0%)	0.027
	(2–3)	57 (57.0%)	72 (72.0%)	
STR > 50% 60 min after PCI				0.069
	Yes	62 (62.0%)	74 (74.0%)	
No-reflow events				0.006
	Yes	47 (47.0%)	28 (28.0%)	

Echocardiography 24 hours post-PCI, EF (%)	mean±SD	45 ± 7	48 ± 8	0.008
	range	25 – 65	30 – 70	
Echocardiography 24 hours post-PCI, MR	No	50 (50.0%)	55 (55.0%)	0.463
	Mild	41 (41.0%)	41 (41.0%)	
	Moderate	8 (8.0%)	4 (4.0%)	
	Severe	1 (1.0%)	0 (0.0%)	
Echocardiography 24 hours post-PCI, apical thrombus				0.155
	Yes	2 (2.0%)	0 (0.0%)	
Echocardiography 24 hours post-PCI, pericardial effusions	No	98 (98.0%)	97 (97.0%)	0.367
	Mild	1 (1.0%)	3 (3.0%)	
	Moderate	1 (1.0%)	0 (0.0%)	

PCI: percutaneous coronary intervention, MBG: myocardial blush grade, EF: ejection fraction, MR: mitral regurgitation, STR: ST-segment resolution

Table 4: Comparisons Between the Control and Study Groups Concerning the 1-Month Follow-Up

		Control Group (No = 100)	Study Group (No = 100)	*P* value
MR after 1 month	No	55 (55.0%)	61 (61.0%)	0.470
	Mild	42 (42.0%)	38 (38.0%)	
	Moderate	3 (3.0%)	1 (1.0%)	
Apical thrombus after 1 month				0.316
	Yes	1 (1.0%)	0 (0.0%)	
Pericardial effusions after 1 month				–
	Yes	0 (0.0%)	0 (0.0%)	
MACE after 1 month	None	91 (91.0%)	93 (93.0%)	0.602
	Heart failure	9 (9.0%)	7 (7.0%)	
EF after 1 month, %)	mean±SD	48 ± 8	50 ± 8	0.186
	range	25 – 70	30 – 70	
Improvement in EF after 1 month				0.039
	Yes	29 (29.0%)	43 (43.0%)	
Improvement of MR at 1 month (improvement by at least 1 grade)				0.547
	Yes	13 (13.0%)	16 (16.0%)	
Improvement of pericardial effusions at 1 month (improvement by at least 1 grade)				0.651
	Yes	2 (2.0%)	3 (3.0%)	

MR: mitral regurgitation, MACE: major adverse cardiovascular events, EF: ejection fraction

There was a statistically significant difference between the control and study groups in terms of improvements in LVEF at the 1-month follow-up (29% vs 43%; *P* = 0.039) (Table 4).

No statistical differences were observed between the reflow and no-reflow groups regarding demographic characteristics (Table 5).

Statistically significant differences were noted between the reflow and no-reflow groups in terms of the pain-to-balloon time (mean ± SD = 7.70 ± 3.61, range = 2–21 vs mean ± SD = 10.32 ± 4.35, range = 4–21; *P* < 0.01), atorvastatin loading (57.6% vs 37.3%; *P* = 0.006), and random blood sugar before (15–30 min) primary PCI (mean ± SD = 142.90 ± 27.93, range = 90–195 vs mean ± SD = 153.73 ± 26.73, range = 90–198; *P* = 0.008) (Table 5).

At 24 hours after primary PCI, no significant differences were noted between the reflow and no-reflow groups regarding echocardiography criteria (Table 5).

At the 1-month follow-up, statistically significant differences were observed between the reflow and no-reflow groups regarding MACE (0.8% vs 20%; $P < 0.01$), LVEF (mean ± SD = 52.25 ± 6.96, range = 38–70 vs mean ± SD = 45.39 ± 8.56, range = 25–62; $P < 0.01$), and improvements in LVEF (68% vs 4%; $P < 0.01$) (Table 5).

Table 5: Comparisons Between the Reflow and No-Reflow Groups

		The Reflow Group (No = 125)	The No-Reflow Group (No = 75)	*P* value
Age	mean±SD	52.46 ± 11.75	55.87 ± 12.03	0.050
	range	29 – 75	25 – 85	
Sex				0.822
	Male	77 (61.6%)	45 (60.0%)	
Hypertension				0.665
	Yes	38 (30.4%)	25 (33.3%)	
Diabetes mellitus				0.580
	Yes	37 (29.6%)	25 (33.3%)	
Smoking				0.761
	Yes	79 (63.2%)	49 (65.3%)	
Type of STEMI	Anterior	71 (56.8%)	35 (46.7%)	0.574
	Inferior	45 (36.0%)	36 (48.0%)	
	Anterolateral	3 (2.4%)	2 (2.7%)	
	Posterior	2 (1.6%)	0 (0.0%)	
	Lateral	2 (1.6%)	1 (1.3%)	
	Inferoposterior	2 (1.6%)	1 (1.3%)	
Pain-to-balloon time, h	mean±SD	7.70 ± 3.61	10.32 ± 4.35	< 0.01
	range	2 – 21	4 – 21	
Atorvastatin loading	Yes	72 (57.6%)	28 (37.3%)	0.006
Random blood sugar before PCI	mean±SD	142.90 ± 27.93	153.73 ± 26.73	0.008
	range	90 – 195	90 – 198	
Culprit lesion	RCA	40 (32.0%)	28 (37.33%)	0.430
	LAD	73 (58.4%)	37 (49.33%)	
	LCX	12 (9.6%)	10 (13.33%)	
TIMI flow score on angiography	Grade 0	113 (90.4%)	67 (89.3%)	0.417
	Grade 1	8 (6.4%)	3 (4.0%)	
	Grade 2	4 (3.2%)	5 (6.7%)	
	Grade 3	0 (0.0%)	0 (0.0%)	
PCI on the culprit vessel	1 drug-eluting stent	117 (93.6%)	71 (94.7%)	0.758
	2 drug-eluting stents	8 (6.4%)	4 (5.3%)	

TIMI: thrombolysis in myocardial infarction, PCI: percutaneous coronary intervention, STEMI: ST-segment-elevation myocardial infarction, RCA: right coronary artery; LAD: left anterior descending artery, LCX: left circumflex artery

Table 5 (Continued)**:** Comparisons Between the Reflow and No-Reflow Groups

		The Reflow Group (No = 125)	The No-Reflow Group (No = 75)	*P* value
Echocardiography 24 hours post-PCI, EF (%)	mean±SD	47 ± 8	45 ± 8	0.058
	range	30 – 70	25 – 65	
Echocardiography 24 hours post-PCI, MR	No	65 (52.0%)	40 (53.3%)	0.127
	Mild	55 (44.0%)	27 (36.0%)	
	Moderate	4 (3.2%)	8 (10.7%)	
	Severe	1 (0.8%)	0 (0.0%)	
Echocardiography 24 hours post-PCI, apical thrombus				0.714
	Yes	1 (0.8%)	1 (1.3%)	
Echocardiography 24 hours post-PCI,	No	122 (97.6%)	73 (97.3%)	0.648

pericardial effusions	Mild	2 (1.6%)	2 (2.7%)	
	Moderate	1 (0.8%)	0 (0.0%)	
MR after 1 month	No	74 (59.2%)	42 (56.0%)	0.289
	Mild	50 (40.0%)	30 (40.0%)	
	Moderate	1 (0.8%)	3 (4.0%)	
Apical thrombus after 1 month				0.437
	Yes	1 (0.8%)	0 (0.0%)	
Pericardial effusion after 1 month				–
	Yes	0 (0.0%)	0 (0.0%)	
MACE after 1 month	None	124 (99.2%)	60 (80.0%)	< 0.01
	HF	1 (0.8%)	15 (20.0%)	
EF after 1 month, %	mean±SD	52 ± 6	45 ± 8	< 0.01
	range	38 – 70	25 – 62	
Improvements in EF at 1 month				< 0.01
	Yes	68 (54.4%)	4 (5.3%)	
Improvements in MR at 1 month				0.437
	Yes	20 (16.0%)	9 (12.0%)	
Improvements in pericardial effusions at 1 month				0.907
	Yes	3 (2.4%)	2 (2.7%)	

MR: mitral regurgitation, EF: ejection fraction, MACE: major adverse cardiovascular events, PCI: percutaneous coronary intervention

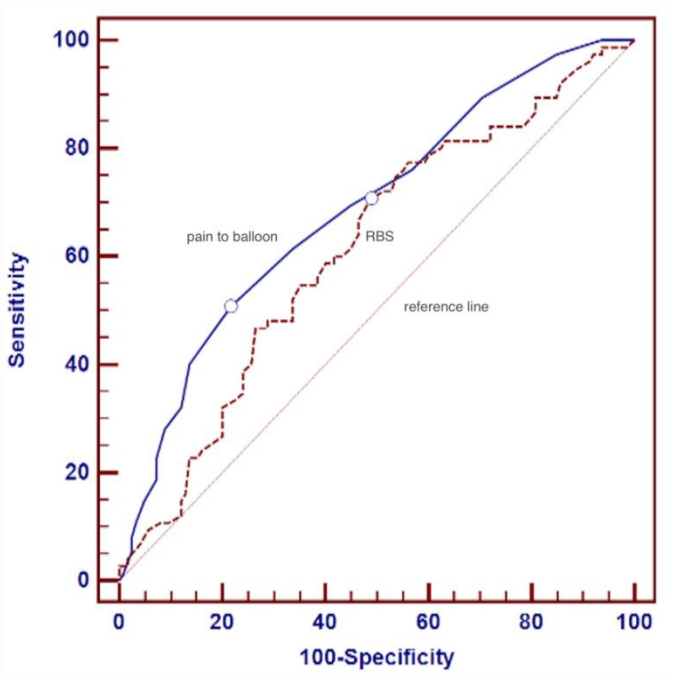

Figure 1: The receiver operating characteristic (ROC) curve presents cutoff values for the pain-to-balloon time and random blood sugar (RBS) before primary percutaneous coronary intervention, differentiating reflow from no-reflow.

DISCUSSION

The present study examined the effects of high-dose atorvastatin loading before primary PCI on myocardial perfusion and the occurrence of no-reflow events in STEMI patients. Following the procedure, patients were monitored and assessed after 1 month for MACE and changes in LVEF using the bi-plane Simpson method. Our results revealed a statistically significant improvement in the study group compared

with the control group concerning no-reflow events (28% vs 47%; *P* = 0.006) and MBG (0–1: 28% vs 43%, 2–3: 72% vs 57%; *P* = 0.027). Additionally, the study group demonstrated a higher LVEF 24 hours after PCI (mean ± SD = 48.35 ± 8.78 vs 45.20 ± 7.89; *P* = 0.008) and greater EF improvements at the 1-month follow-up (43% vs 20%; *P* = 0.039). However, there was no significant difference in MACE at the 1-month follow-up (7% vs 9%; *P* = 0.602). These findings align with a trial conducted by Garcia-Mendez et al [8] (2018), in which 103 STEMI patients were randomized into 2 groups: the AST group (atorvastatin plus standard treatment, n = 49) and the ST group (standard treatment, n = 54). Patients underwent primary PCI and were followed up for 30 days. The results showed a significant difference in the frequency of no-reflow events between the groups, with 27% in the AST group and 63% in the ST group (*P* < 0.0001). The results reported by Garcia-Mendez and colleagues also showed a similar nonsignificant difference in MACE at 30 days between the AST and ST groups (47% vs 57%; *P* = 0.28). Nonetheless, utilizing the Kaplan-Meier curve to analyze the event-free survival rate for MACE up to 30 days revealed a notable difference. The event-free survival rate was 73.5% for patients receiving the loading dose of 80 mg of atorvastatin plus standard treatment, compared with 37% for those receiving standard treatment alone (*P* < 0.0001). Our findings are consistent with those from the STATIN-STEMI trial, in which a total of 171 STEMI patients were randomized to receive either 80 mg of atorvastatin (n=86) or 10 mg of atorvastatin (n=85) as pre-treatment before PCI. In that trial, MBG after primary PCI was significantly higher in the 80-mg atorvastatin arm than in the 10-mg atorvastatin arm (MBG = 2.2 ± 0.8 vs 1.9 ± 0.8; *P* = 0.02). Moreover, a postprocedural TIMI flow score of 3 was higher in the 80-mg atorvastatin arm (83) than in the 10-mg atorvastatin arm (76), although this difference did not reach statistical significance (*P* = 0.07). [9] Nevertheless, our results regarding LVEF 24 hours after PCI differed from those reported in the STATIN-STEMI trial. In that trial, the mean EF was 47% for all patients, with no significant difference observed between the 2 treatment groups.[9] This discrepancy can be explained by the fact that in our study the control group did not receive a statin dose before primary PCI, while in the STATIN-STEMI trial, the control group received 10 mg of atorvastatin.

Our results were not concordant with the NAPLES-II trial, where 668 statin-naïve patients were randomly assigned to a single dose of 80 mg of atorvastatin (the atorvastatin group; n = 338) or no statin treatment (control group; n = 330) the day before elective PCI, and the results showed no significant difference in postprocedural TIMI flow scores (*P* = 0.68). [10] The difference between our studies can be explained by the fact that in the NAPLES-II trial, patients underwent elective PCI, denoting that they had no acute thrombotic occlusion and, thus, had a lower risk of no-reflow events.

In our study, we observe no statistically significant differences between the 2 groups regarding MACE at 1 month. This finding chimes with the results of the SECURE-PCI trial, where 4191 patients with ACS and planned invasive management were randomized to receive 2 loading doses of 80 mg of atorvastatin (n = 2087) or matching placebo (n = 2104) before and 24 hours after a planned PCI. All patients received 40 mg of atorvastatin for 30 days starting 24 hours after the second dose of study medication. At 30 days, MACE was not reduced as 130 patients (6.2%) in the atorvastatin group and 149 (7.1%) in the placebo group had a

MACE (absolute difference = 0.85%; 95% CI, −0.70% to 2.41%; hazard ratio, 0.88; 95% CI, 0.69 to 1.11; $P = 0.27$). [11]
Our findings differ from those of the ARMYDA-ACS trial, which randomized 171 patients with non–STE ACS to pretreatment with atorvastatin (80 mg 12 hours before PCI and an additional 40 mg pre-procedure dose, n = 86) or placebo (n = 85). All patients received long-term atorvastatin treatment (40 mg/d) thereafter. The primary endpoint was the 30-day incidence of MACE, including death, myocardial infarction, or unplanned revascularization. The ARMYDA-ACS trial demonstrated a statistically significant difference in MACE at 30 days, with 5% of patients in the atorvastatin arm experiencing events compared with 17% in the placebo arm (P = 0.01). The discrepancies between our findings and those of the ARMYDA-ACS trial might be attributed to the longer duration between atorvastatin loading and PCI in their study (12 h), as well as the administration of an additional pre-procedure atorvastatin dose.

CONCLUSIONS

Our study demonstrated that high-dose atorvastatin loading prior to primary PCI led to improved postprocedural MBG and a subsequent reduction in no-reflow events. This positive effect was accompanied by a significant increase in the number of patients exhibiting complete STR following the procedure. Additionally, we observed an improvement in LVEF as assessed by the bi-plane Simpson method at both 24-hour and 1-month follow-ups. Given the findings of our study, we strongly advocate for the routine administration of high-intensity statin before primary PCI in patients presenting with STEMI. However, due to the limitations of our study, including a relatively small sample size and short follow-up duration, we acknowledge the need for further investigations. These studies should involve a larger patient population and extend the follow-up period to more comprehensively evaluate the long-term effects of high-intensity statin pretreatment on MACE and other clinically relevant outcomes.

Study Limitations

The current study was conducted at a single center, which may limit the generalizability of the findings to other healthcare settings and patient populations. Furthermore, the small sample size and short follow-up period may affect the statistical power of the study and the ability to detect clinically significant differences between the control and study groups. In addition, while TIMI flow, MBG, and STR are established methods for assessing myocardial perfusion, incorporating additional techniques, such as cardiac magnetic resonance imaging or myocardial contrast echocardiography, could provide a more comprehensive evaluation of coronary microvascular function. Further validation of the results is required through larger, randomized controlled trials to confirm or refute the findings of this study and to determine the broader applicability of high-dose atorvastatin loading in patients with STEMI.

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- **Authors' Contributions: Amr M Mohammed**: Contributed to the conception and design of the study, performed material preparation, and collected and analyzed data.
- **Bassam S Hennawy**: Contributed to the conception and design of the study, drafted the initial manuscript, and incorporated feedback from co-authors.
- **Khaled A Fouad**: Provided supervision for the overall project, contributed to the conception and design of the study, and reviewed the manuscript.
- **All authors**: Participated in critical discussions and revisions of the manuscript, and approved the final version for submission.

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Consent to Participate: Informed consent was acquired from all individual participants involved in the study.

Consent for Publication: The authors confirm that consent for publication has been obtained from all human research participants involved in the study.

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