Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v31i6.7399

COMPARATIVE STUDY OF THE IMPACT OF LOADING DOSES OF ATORVASTATIN AND ROSUVASTATIN ON THE IMMEDIATE POST-PCI TIMI FLOW IN PATIENTS RECEIVING PRIMARY PERCUTANEOUS CORONARY INTERVENTION

Dr Muhammad Bilal[1], Zaghum Abbas[2*], Dr Rabail Irfan[3], Dr Moazama Shakeel Ahmed[4], Dr Hajra Mateen[5], Syed Zain Raza Naqvi[6]

[1]Consultant Cardiologist, Emergency Department, Type D Hospital Oghi Mansehra, KPK, Pakistan
[2*] Post Graduate Resident Nephrology, MBBS, Quaid-e-Azam Medical College Bhawalpur, Pakistan
[3]Medical Doctor, Hayatabad Medical Complex Peshawar, Pakistan
[4]House Officer, Department of Internal Medicine, King Edward Medical University/ Mayo Hospital Lahore, Pakistan
[5]Assistant Professor, Pharmacology Department, Islam Medical College Sialkot, Pakistan
[6]House Officer, Central Park Medical College Lahore, Pakistan

***Corresponding author:** Zaghum Abbas,
*****Email: drzaghumabbas@gmail.com

ABSTRACT

Objective

This study aims to assess and contrast the immediate effects of administering loading doses of atorvastatin and rosuvastatin on Thrombolysis in Myocardial Infarction (TIMI) flow following primary percutaneous coronary intervention (PCI) in patients with acute myocardial infarction.

Methodology

From April 2023 to April 2024, a prospective randomized controlled trial was conducted at XYZ Hospital involving 110 eligible patients to compare the effects of administering a loading dose of rosuvastatin (40 mg) versus atorvastatin (80 mg) on Thrombolysis In Myocardial Infarction (TIMI) flow immediately following percutaneous coronary intervention (PCI), left ventricular ejection fraction (LVEF) at discharge, and Major Adverse Cardiovascular Events (MACE) over a one-month period in patients with ST-elevation myocardial infarction (STEMI). Eligible participants were adults aged 18 and older with confirmed STEMI requiring primary PCI, excluding those with contraindications to statin therapy, severe hepatic or renal impairments, pregnancy, lactation, recent clinical trial participation, or ineligibility for PCI. Baseline demographic and clinical data were collected, including age, gender, BMI, smoking status, and medical history. TIMI flow grades post-PCI were assessed, with TIMI-3 indicating complete perfusion. Secondary endpoints included peak troponin-I levels 24 hours post-PCI and LVEF at discharge. MACE were monitored during a one-month follow-up. Statistical analyses were performed using multivariable regression to adjust for confounders, and results were analyzed with IBM SPSS Statistics version 25. The study adhered to ethical standards, with informed consent obtained and approval from the institute's ethical review board.

Results

Both groups, each comprising 55 patients, were comparable in terms of mean age, gender distribution, BMI, and cardiovascular risk factors. No significant differences were found in the extent of coronary

artery disease, with similar rates of single, two, and three-vessel disease. Post-PCI TIMI-3 flow, indicating complete perfusion, was achieved in 81.8% of the rosuvastatin group and 83.6% of the atorvastatin group. Secondary endpoints, including peak highly-sensitive troponin-I levels and left ventricular ejection fraction (LVEF) at discharge, showed no significant differences between the groups. Major adverse cardiovascular events (MACE) within one month were also comparable, occurring in 5.5% of the rosuvastatin group and 9.1% of the atorvastatin group. The study concluded that both statins provided similar outcomes in terms of coronary blood flow restoration and cardiac function post-PCI.

Conclusion

Our study shows that pre-loading patients with both rosuvastatin and atorvastatin are effective in restoring coronary blood flow after primary PCI in STEMI patients. The similar TIMI-3 flow grades and peak troponin levels indicate both statins are equally capable of reducing acute myocardial damage. Rosuvastatin also showed a trend towards fewer major adverse cardiovascular events and improved LV ejection fraction. The management of acute coronary syndrome with high-intensity statins is supported by these findings.

Keywords High-intensity statin, loading dose, atorvastatin, rosuvastatin, TIMI flow, PCI, Acute coronary syndrome, STEMI.

Introduction

Ischemic heart disease (IHD) has emerged as a key global health concern that is largely responsible for the alarming levels of morbidity and mortality observed globally.1 Several individuals with coronary artery disease (CAD) nevertheless need percutaneous coronary intervention (PCI), an important invasive technique that lowers cardiovascular risks and relieves symptoms, even in the face of preventive efforts.2

PCI, commonly known as coronary angioplasty, offers substantial benefits but is associated with potential complications such as elevated cardiac enzymes, coronary dissection, thrombosis, and no-reflow phenomenon. These complications can compromise the effectiveness of revascularization, highlighting the need for strategies to minimize their occurrence and improve patient outcomes.[3-4]

Recent advancements in PCI techniques have introduced new-generation stents and procedural devices designed to lower both short and long-term consequences.[5] Additionally, statins like atorvastatin and rosuvastatin have shown promise in enhancing PCI outcomes by lowering LDL cholesterol levels and providing anti-inflammatory and plaque-stabilizing effects.[6] Studies have suggested that pre-treatment with loading doses of statins may be particularly beneficial for patients enduring PCI for ST-elevation myocardial infarction(STEMI), potentially reducing complications such as no-reflow and improving TIMI flow.[7-8]

This study seeks to provide insights into optimizing treatment approaches and enhancing outcomes in individuals undergoing invasive cardiac procedures.

Objective

This study aims to assess and contrast the immediate effects of administering loading doses of atorvastatin and rosuvastatin on Thrombolysis In Myocardial Infarction (TIMI) flow following primary percutaneous coronary intervention (PCI) in patients with acute myocardial infarction.

Materials and Methods

Study Design, Participants Eligibility & Data Collection Process:

From April 2023 to April 2024, a prospective randomized controlled trial was conducted at XYZ Hospital involving 110 eligible patients. The study aimed to compare the effects of administering a loading dose of rosuvastatin (40 mg) versus atorvastatin (80 mg) on Thrombolysis In Myocardial Infarction (TIMI) flow immediately following percutaneous coronary intervention (PCI), as well as on left ventricular ejection fraction (LVEF) at discharge. Additionally, the trial evaluated Major Adverse

Cardiovascular Events (MACE) over a one-month period in patients diagnosed with ST-elevation myocardial infarction (STEMI). Participants included adults aged 18 and older with confirmed STEMI necessitating primary PCI, who were capable of providing informed consent. Exclusion criteria were set to eliminate those with contraindications to statin therapy, allergies to the study medications, severe hepatic or renal impairments, pregnancy, lactation, recent participation in another clinical trial, ineligibility for PCI, or inability to comply with study procedures. Upon enrollment, comprehensive baseline demographic and clinical information was gathered, including details on age, gender, BMI, smoking habits, presence of hypertension, diabetes, dyslipidemia, family history of coronary artery disease (CAD), current smoking status, history of prior PCI or coronary artery bypass grafting (CABG), and other relevant medical backgrounds. Additionally, clinical assessments encompassed measurements of blood pressure, heart rate, and initial laboratory results.

Primary Endpoint (TIMI-3 Flow Grade Assessment):
All patients enrolled in the study underwent coronary angiography to assess the severity and extent of coronary artery disease. Post primary PCI, we evaluated the efficacy of coronary blood flow restoration using the TIMI flow grading system. This system categorized TIMI flow grades into four levels: TIMI-0 indicated no perfusion, TIMI-1 indicated penetration without significant perfusion, TIMI-2 indicated partial perfusion, and TIMI-3 indicated complete perfusion.

Secondary Endpoints (Peak Troponin-I levels and LVEF assessment):
Biochemical analyses included assessing serum levels of highly-sensitive troponin-I (hsTnI) 24 hours post-PCI, while left ventricular ejection fraction (LVEF) was evaluated via echocardiography at hospital discharge following primary angioplasty for STEMI. Major Adverse Cardiovascular Events (MACE), comprising acute coronary syndrome, stroke, or mortality, were observed during a one-month follow-up period subsequent to PCI.

Statistical Analysis:
The study employed multivariable regression analysis to account for potential confounding variables, including gender, age, smoking habits, diabetes, hypertension, hyperlipidemia, and time from door to balloon. Using IBM SPSS Statistics version 25, statistical analyses were performed. For continuous variables, mean± standard-deviation was specified, while for categorical variables, frequencies and percentages were used.

Ethical Considerations:
Informed consent was obtained from each participant before enlisting, and the study got approval from the institute's ethical review board, ensuring adherence to ethical standards and maintaining patient safety throughout the study period.

Results
This study enrolled 110 consecutive patients presenting with acute STEMI for primary angioplasty, evenly divided into two groups of 55 patients each, one receiving rosuvastatin and the other atorvastatin. Table 1A shows the mean age in the rosuvastatin group was 58.3±9.7 years compared to 57.9 ±9.5 years in the atorvastatin group ($p = 0.732$). Both groups exhibited a male predominance, with 67.3% males in the rosuvastatin group and 65.5% in the atorvastatin group, signifying a balanced gender distribution ($p = 0.821$). The mean BMI was 27.6±3.9 kg/m² for the rosuvastatin group and 28.1±4.2 kg/m² for the atorvastatin group ($p = 0.589$).
Table 1B summarizes the cardiovascular risk factors for both groups. In the rosuvastatin group, 29.1% had diabetes mellitus vs. 27.3% in the atorvastatin group ($p = 0.812$). Hypertension was present in 58.2% of those on rosuvastatin and 56.4% on atorvastatin ($p = 0.879$). Hyperlipidemia affected 36.4% of rosuvastatin users and 40.0% of atorvastatin users ($p = 0.654$). A positive family history of CAD was reported by 18.2% in the rosuvastatin group and 21.8% in the atorvastatin group ($p = 0.589$). Active

smoking was noted in 25.5% on rosuvastatin and 23.6% on atorvastatin (p = 0.812). Previous PCI was reported by 14.5% on rosuvastatin and 16.4% on atorvastatin (p = 0.879), while prior CABG rates were 1.8% and 3.6%, respectively (p = 0.789).

Table-1A: Demographic data of study groups

Variable	Rosuvastatin(n=55)	Atorvastatin(n=55)	P-value
Age(years)	58.3 ± 9.7	57.9 ± 9.5	0.732
Males, n (%)	37 (67.3)	36 (65.5)	0.821
Females, n (%)	18 (32.7)	19 (34.5)	0.821
BMI (kg/m²)	27.6 ± 3.9	28.1 ± 4.2	0.589

Table-1B: Risk factors distribution across study groups

Risk Factors	Rosuvastatin (n=55)	Atorvastatin (n=55)	P-value
Diabetes mellitus, n (%)	16 (29.1)	15 (27.3)	0.812
Hypertension, n (%)	32 (58.2)	31 (56.4)	0.879
Dyslipidemia, n (%)	20 (36.4)	22 (40.0)	0.654
Positive family History of CAD, n (%)	10 (18.2)	12 (21.8)	0.589
Active Smokers, n (%)	14 (25.5)	13 (23.6)	0.812
Previous PCI, n (%)	8 (14.5)	9 (16.4)	0.879
Prior CABG, n (%)	1 (1.8)	2 (3.6)	0.789

Table 2 illustrates the severity of coronary artery disease (CAD) in both treatment groups, based on the extent of vessel involvement as determined by angiography. In the rosuvastatin group, 50.9% of patients were found to have single vessel disease, 32.7% had two vessel disease, and 16.4% had three vessel disease. In comparison, the atorvastatin group showed 45.5% of patients with single vessel disease, 36.4% with two vessel disease, and 18.2% with three vessel disease. Statistical analysis revealed no significant differences between the two groups regarding the extent of vessel involvement, with all comparisons yielding p-values greater than 0.05.

Table-2: Severity of CAD according to vessel involvement on angiography

No. of vessels involved	Rosuvastatin(n=55)	Atorvastatin(n=55)	P-value
One vessel disease	28 (50.9%)	25 (45.5%)	0.578
Two vessel disease	18 (32.7%)	20 (36.4%)	0.689
Three vessel disease	9 (16.4%)	10 (18.2%)	0.821

In the rosuvastatin group, 81.8% of patients achieved TIMI-3 flow, indicating complete perfusion, while 14.5% and 3.6% achieved TIMI-2 and TIMI-1 flows, respectively. Conversely, in the atorvastatin group, 83.6% achieved TIMI-3 flow, with 12.7% and 1.8% achieving TIMI-2 and TIMI-1 flows, respectively. The two groups were observed to be similar in achieving TIMI-3 flow (p = 0.879), suggesting comparable outcomes in terms of immediate coronary blood flow restoration following PPCI with either rosuvastatin or atorvastatin.

Table-3: Primary Endpoint (TIMI-3 flow grade immediately after PPCI)

TIMI Flow Grade	Rosuvastatin (n=55)	Atorvastatin (n=55)	P-value
TIMI-0	0 (0.0%)	1 (1.8%)	0.312
TIMI-1	2 (3.6%)	1 (1.8%)	0.654
TIMI-2	8 (14.5%)	7 (12.7%)	0.789
TIMI-3	**45 (81.8%)**	**46 (83.6%)**	**0.879**

Table 4 presents the secondary endpoints assessed at both 24 hours post-PPCI and at a one-month follow-up in patients treated with either rosuvastatin (n=55) or atorvastatin (n=55) pre-treatment. Peak levels of highly-sensitive troponin-I (hsTnI) at 24 hours were comparable between the two groups, with rosuvastatin measuring 3020.5 ± 55.6 ng/mL and atorvastatin measuring 3015.2 ± 54.7 ng/mL (p = 0.657). Similarly, left ventricular ejection fraction (LVEF) after 24-hours post-PPCI showed no significant difference, with rosuvastatin at 52.3% ± 3.8 and atorvastatin at 51.7% ± 3.6 (p = 0.687). At one-month, major adverse cardiovascular events(MACE) happened in 5.5% of participants in the rosuvastatin group and 9.1% in the atorvastatin group, with no significant difference observed (p = 0.463).

Table-4: Secondary Endpoints at 1st post-PCI day and at one-month interval

Variable	Rosuvastatin (n=55)	Atorvastatin (n=55)	P-value
Peak hsTnI (ng/mL) – at 24h	3020.5 ± 55.6	3015.2 ± 54.7	0.657
LVEF (%) – at 24h	52.3 ± 3.8	51.7 ± 3.6	0.687
MACE, n (%) – at one month	3 (5.5%)	5 (9.1%)	0.463

Discussion

Statins have revolutionized the management of cardiovascular diseases by markedly reducing the incidence of significant adverse cardiovascular events through their multifaceted benefits, including lipid-lowering properties and other therapeutic effects. Extensive research has robustly validated their efficacy in acute coronary syndrome, particularly in improving outcomes following primary PCI.[9-10]

The present study illustrated the efficacy of both rosuvastatin and atorvastatin in achieving coronary blood flow restoration, assessing their impact on immediate post-perfusion TIMI flow in patients undergoing primary PCI. This is consistent with other studies, such as those by Ozkalayci et al., Alidoosti et al., and Adel et al., showing similar effectiveness of these drugs in reestablishing coronary blood flow after acute myocardial infarction (AMI).[11,12,13]

Our findings indicated comparable rates between the atorvastatin and rosuvastatin groups concerning the achievement of TIMI-3 flow grade post-PCI, with no significant statistical variance observed. Specifically, 81.8% of participants in the rosuvastatin group and 83.6% in the atorvastatin group achieved TIMI-3 flow, consistent with the results reported by Alidoosti et al. and Adel et al.[12-13]

Moreover, the study revealed that peak troponin levels measured 24 hours post-PCI were almost identical between the two groups. These elevated concentrations are expected in STEMI patients, as troponin levels peak within 24 hours of myocardial injury, reflecting the extent of myocardial damage. Interestingly, our study found that LVEF at hospital discharge was slightly lower than average in both groups, with rosuvastatin showing 52.3 ± 3.8% and atorvastatin showing 51.7 ± 3.6%. This finding is in line with research by Zhou et al.[6] and Reindl et al., which highlighted the beneficial impact of rosuvastatin on LVEF improvement in acute myocardial infarction patients undergoing PCI.[14]

Major adverse cardiovascular events (MACE) at one month were observed in 5.5% of the rosuvastatin group and 9.1% of the atorvastatin group, though the p-value did not yield significance. This trend suggests a potential advantage of rosuvastatin in reducing early post-PCI complications, as supported by studies such as those by Garcia-Mendez et al. and Yun et al., who reported lower rates of adverse events with high-dose statin therapy before PCI.[15-16]

The angiographic findings indicated a comparable distribution of coronary artery disease (CAD) severity between the two groups, with similar rates of single, double, and triple vessel involvement. In the rosuvastatin group, 50.9% of patients had single vessel disease, while 45.5% in the atorvastatin group had the same condition. Additionally, triple vessel disease was present in 16.4% of the rosuvastatin group and 18.2% of the atorvastatin group. These results align with the findings reported by Alidoosti et al., further demonstrating the comparability of the study cohorts.[10]

Hence, this study corroborates the existing literature on the efficacy statins in managing patients with STEMI via primary PCI. While both statins demonstrated similar efficacy in achieving TIMI-3 flow and comparable biochemical & echocardiographic outcomes, rosuvastatin showed a non-significant trend towards lower MACE rates, suggesting its potential benefit in early post-PCI recovery. A greater number of participants and longer follow-up times are required for future research in order to validate these results and completely comprehend the long-term effects of high-dose statin administration in this group of patients.

Conclusion

Our study shows that pre-loading patients with both rosuvastatin and atorvastatin are effective in restoring coronary blood flow after primary PCI in STEMI patients. The similar TIMI-3 flow grades and peak troponin levels indicate both statins are equally capable of reducing acute myocardial damage. Rosuvastatin also showed a trend towards fewer major adverse cardiovascular events and improved LV ejection fraction. The management of acute coronary syndrome with high-intensity statins is supported by these findings. In order to validate these results and investigate long-term consequences, more research is required.

References

1. Dai H, Much AA, Maor E, Asher E, Younis A, Xu Y, Lu Y, Liu X, Shu J, Bragazzi NL. Global, regional, and national burden of ischaemic heart disease and its attributable risk factors, 1990-2017: results from the Global Burden of Disease Study 2017. Eur Heart J Qual Care Clin Outcomes. 2022 Jan 5;8(1):50-60. doi: 10.1093/ehjqcco/qcaa076. PMID: 33017008; PMCID: PMC8728029.
2. Abubakar M, Javed I, Rasool HF, Raza S, Basavaraju D, Abdullah RM, Ahmed F, Salim SS, Faraz MA, Hassan KM, Hajjaj M. Advancements in Percutaneous Coronary Intervention Techniques: A Comprehensive Literature Review of Mixed Studies and Practice Guidelines. Cureus. 2023 Jul 3;15(7):e41311. doi: 10.7759/cureus.41311. PMID: 37539426; PMCID: PMC10395399.
3. Sabin P, Koshy AG, Gupta PN, Sanjai PV, Sivaprasad K, Velappan P, Vellikat Velayudhan R. Predictors of no- reflow during primary angioplasty for acute myocardial infarction, from Medical College Hospital, Trivandrum. Indian Heart J. 2017 Apr;69 Suppl 1(Suppl 1):S34-S45. doi: 10.1016/j.ihj.2016.12.012. Epub 2017 Jan 6. PMID: 28400037; PMCID: PMC5388018.
4. Kodeboina M, Piayda K, Jenniskens I, Vyas P, Chen S, Pesigan RJ, Ferko N, Patel BP, Dobrin A, Habib J, Franke J. Challenges and Burdens in the Coronary Artery Disease Care Pathway for Patients Undergoing Percutaneous Coronary Intervention: A Contemporary Narrative Review. Int J Environ Res Public Health. 2023 Apr 25;20(9):5633. doi: 10.3390/ijerph20095633. PMID: 37174152; PMCID: PMC10177939.
5. Bianchini E, Bianchini F, Lunardi M, Zito A, Romagnoli E, Aurigemma C, Paraggio L, Dato I, Burzotta F, Trani C. Outcomes, risk factors, and procedural management of acute myocardial infarction caused by stent thrombosis. Vessel Plus. 2024; 8: 20. http://dx.doi.org/10.20517/2574-1209.2024.13
6. Zhou L, Hu X, Zhang H, Lu H, Lin Y, Wang W, Yu B, Liang W, Zhou Y, Li G, Dong H. Effects of atorvastatin and rosuvastatin on dysfunctional coronary circulation in patients with ST-segment elevation myocardial infarction. J Int Med Res. 2023 Jun;51(6):3000605231182547. doi: 10.1177/03000605231182547. PMID: 37377087; PMCID: PMC10328025.
7. de Liyis, B.G., Jagannatha, G.N.P., Kosasih, A.M. et al. Efficacy of single high-dose statin prior to percutaneous coronary intervention in acute coronary syndrome: a systematic review and meta-analysis. Egypt Heart J 76, 49 (2024). https://doi.org/10.1186/s43044-024-00481-7
8. Lanza O, Cosentino N, Lucci C, Resta M, Rubino M, Milazzo V, De Metrio M, Trombara F, Campodonico J, Werba JP, Bonomi A, Marenzi G. Impact of Prior Statin Therapy on In-Hospital Outcome of STEMI Patients Treated with Primary Percutaneous Coronary Intervention. J Clin Med. 2022 Sep 8;11(18):5298. doi: 10.3390/jcm11185298. PMID: 36142948; PMCID: PMC9502753.

9. Morofuji Y, Nakagawa S, Ujifuku K, Fujimoto T, Otsuka K, Niwa M, Tsutsumi K. Beyond Lipid-Lowering: Effects of Statins on Cardiovascular and Cerebrovascular Diseases and Cancer. Pharmaceuticals (Basel). 2022 Jan 26;15(2):151. doi: 10.3390/ph15020151. PMID: 35215263; PMCID: PMC8877351.
10. Khatiwada N, Hong Z. Potential Benefits and Risks Associated with the Use of Statins. Pharmaceutics. 2024; 16(2):214. https://doi.org/10.3390/pharmaceutics16020214
11. Ozkalayci, F., Türkyılmaz, E., Karagoz, A., Karabay, C. Y., Tanboga, İ. H., and Oduncu, V. (2022). A Clinical Score to Predict "Corrected Thrombolysis in Myocardial Infarction Frame Count" in Patients With ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention. Angiology 73, 365-373.
12. Alidoosti M, Salarifar M, Hajizeinali A, Kassaian SE, Kasemisaleh D, Goodarzynejad H. Outcomes of primary percutaneous coronary intervention in acute myocardial infarction at Tehran Heart Center. Med Princ Pract. 2007;16(5):333–8.
13. Adel EM, Elberry AA, Abdel Aziz A, Naguib IA, Alghamdi BS, Hussein RRS. Comparison of the Treatment Efficacy of Rosuvastatin versus Atorvastatin Loading Prior to Percutaneous Coronary Intervention in ST-Segment Elevation Myocardial Infarction. J Clin Med. 2022 Aug 31;11(17):5142. doi: 10.3390/jcm11175142. PMID: 36079090; PMCID: PMC9457390.
14. Reindl, M., Eitel, I., and Reinstadler, S. J. (2020). Role of cardiac magnetic resonance to improve risk prediction following acute STelevation myocardial infarction. Journal of Clinical Medicine 9, 1041.
15. Garcia-Mendez RC, Almeida-Gutierrez E, Serrano-Cuevas L, SanchezDiaz JS, Rosas-Peralta M, Ortega-Ramirez JA, et al. Reduction of No Reflow with a Loading Dose of Atorvastatin before Primary Angioplasty in Patients with Acute ST Myocardial Infarction. Arch Med Res. 2018;49(8):620–9. doi: 10.1016/j.arcmed.2018.10.006. [PubMed: 30446246].
16. Yun KH, Jeong MH, Oh SK, Rhee SJ, Park EM, Lee EM, et al. The beneficial effect of high loading dose of rosuvastatin before percutaneous coronary intervention in patients with acute coronary syndrome. Int J Cardiol. 2009;137(3):246–51. doi: 10.1016/j.ijcard.2008.06.055. [PubMed: 18706705].