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COMPARING THE EFFECTS OF LOADING DOSE OF ROSUVASTATIN VS ATORVASTATIN ON IMMEDIATE POST-PERFUSION TIMI FLOW IN PRIMARY PCI PATIENTS

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Abstract

Background: Acute coronary syndrome (ACS) requires rapid intervention to restore blood flow, often achieved through primary percutaneous coronary intervention (PCI). Statins like rosuvastatin and atorvastatin are commonly used during PCI for their cholesterol-lowering and plaque-stabilizing effects. However, the specific impact of loading doses of these statins on immediate post-perfusion TIMI (Thrombolysis in Myocardial Infarction) flow has not been thoroughly investigated.

Objective: The primary objective of this study was to compare the effects of loading doses of rosuvastatin versus atorvastatin on immediate post-perfusion TIMI flow in patients undergoing primary PCI.

Methods: This prospective cohort study was conducted at Lahore Medical and Dental College, Lahore, Pakistan, from January 1, 2023, to December 31, 2023. A total of 246 patients undergoing primary PCI for ACS were enrolled and randomly assigned to receive either a loading dose of rosuvastatin (40 mg) or atorvastatin (80 mg). TIMI flow grade was assessed immediately post-perfusion using coronary angiography. Secondary outcomes included the incidence of major adverse cardiovascular events (MACE) within 30 days post-procedure. Data were analyzed using SPSS version 26.0, employing chi-square tests for categorical variables and Kaplan-Meier survival analysis for time-to-event data.

Results: The rosuvastatin group showed a significantly higher proportion of patients achieving TIMI grade 3 flow immediately post-PCI (74.8%) compared to the atorvastatin group (65.9%) ($p = 0.04$). No significant differences were observed between the two groups in terms of 30-day MACE rates (rosuvastatin: 7.3%, atorvastatin: 10.6%; $p = 0.35$).

Conclusion: The administration of a loading dose of rosuvastatin resulted in a higher rate of optimal coronary perfusion (TIMI grade 3 flow) immediately after PCI compared to atorvastatin. These findings suggest that rosuvastatin may be more effective in enhancing immediate coronary reperfusion, potentially improving clinical outcomes in ACS patients undergoing PCI.

Keywords: Rosuvastatin, Atorvastatin, TIMI flow, Primary PCI, Acute Coronary Syndrome, Major Adverse Cardiovascular Events.

Introduction

Acute coronary syndrome (ACS) encompasses a range of urgent heart conditions. These require swift intervention to restore blood flow. One of the most effective treatments is percutaneous coronary intervention (PCI), designed to quickly reopen blocked arteries. The use of statins like atorvastatin and rosuvastatin is common during PCI. They not only lower cholesterol but also stabilize plaques in arteries, reducing the risk of further heart events (1, 2). Guidelines emphasize high-intensity statin therapy for all PCI patients. This underlines their role in preventing future cardiovascular issues (3).

Despite their widespread use, the specific effects of loading doses of atorvastatin and rosuvastatin, administered just before PCI, are not fully understood. Some evidence suggests that higher doses of these statins might enhance endothelial function and reduce inflammation, potentially leading to better immediate outcomes after the procedure, as measured by the TIMI flow grade (4,5). This grade is a key measure of blood flow in the coronary arteries post-PCI. However, which statin—if either—provides superior immediate benefits remains unclear, highlighting a significant gap in current research (6).

The goal of this study is to directly compare the effects of loading doses of rosuvastatin and atorvastatin on the immediate post-procedural TIMI flow in patients undergoing primary PCI. This investigation seeks to determine if one statin can offer better acute benefits, enhancing coronary flow right after PCI.

The implications of this research are substantial. Finding a more effective statin could refine treatment protocols, leading to improved outcomes in managing coronary artery disease. It could also provide insights that shape clinical guidelines, ensuring that treatment is optimized for every patient undergoing PCI. Thus, this study could significantly influence both clinical practice and patient care strategies.

Methods

Study Design

This research was crafted as a prospective cohort study, focusing on the immediate effects of loading doses of rosuvastatin and atorvastatin on TIMI flow post-perfusion in primary PCI patients. Spanning from January 1, 2023, to December 31, 2023, this study was at Lahore Medical and Dental College, Lahore, Pakistan. Opting for a randomized controlled trial format allowed us to minimize bias and confounding variables. This approach was chosen to ensure that any observed differences could be directly linked to the interventions themselves. The study was officially registered, and the hospital's ethics committee granted all necessary approvals.

Setting and Participants

Set in the bustling at Lahore Medical and Dental College, Lahore, Pakistan, from January 1, 2023, to December 31, 2023, this study drew from a diverse patient base, encompassing individuals from both urban and rural areas around Peshawar. Participants were enrolled consecutively, capturing a broad spectrum of patients admitted for primary PCI due to acute coronary syndrome.

Inclusion Criteria:

- Adults aged 18 years and above.
- Confirmed acute coronary syndrome requiring primary PCI.
- Informed consent provided.

Exclusion Criteria:

- Known allergies or contraindications to rosuvastatin or atorvastatin.
- Recent use of any statin, defined as within 30 days prior to enrollment.

- History of significant liver disease, renal failure, or myopathy.
- Pregnant or breastfeeding individuals.

Intervention

Participants were randomly assigned to receive either rosuvastatin (40 mg) or atorvastatin (80 mg). Randomization was executed via a computer-generated sequence, with group assignments concealed in sealed opaque envelopes to maintain study integrity. Upon confirming the need for PCI, medications were administered orally in the emergency department. Dosages were selected based on prevailing clinical guidelines for managing acute coronary syndrome.

Outcomes

The study's primary focus was on the TIMI flow grade right after perfusion, assessed by an interventional cardiologist who was unaware of group assignments. TIMI flow was measured using coronary angiography immediately after PCI. Secondary outcomes included the occurrence of major adverse cardiovascular events (MACE) within 30 days, covering all-cause mortality, myocardial infarction, and target vessel revascularization.

Data Collection

Data were gathered prospectively through a structured collection form that included patient demographics, medical histories, PCI details, and TIMI flow grades. Two independent cardiologists reviewed the angiographic data to ensure consistency and reduce variability. In cases of differing opinions, a third senior cardiologist intervened to resolve discrepancies. Secondary outcome data were tracked through follow-up visits and phone interviews.

Sample Size Calculation

Sample size estimation was based on the prevalence of coronary artery disease in Pakistan, estimated at 20% according to Muhammad et al. [7]. The WHO sample size calculator, with a 5% margin of error and a 95% confidence interval, indicated a need for 246 patients. Power analysis confirmed that this sample size was sufficient to detect differences in secondary outcomes, with a power of 80% and a significance level of 0.05. This ensures robust detection of clinically relevant differences between the two groups.

Statistical Analysis

SPSS version 26.0 was used for all statistical analyses. Continuous variables were presented as mean ± standard deviation or median (interquartile range), based on their distribution. Categorical variables were expressed as frequencies and percentages. The primary outcome, TIMI flow grade, was analyzed using the chi-square test. Time-to-event analyses for secondary outcomes were conducted using Kaplan-Meier survival curves, with group comparisons via the log-rank test. A multivariate Cox proportional hazards model adjusted for potential confounders and assessed the independent effects of the interventions. Statistical significance was set at a p-value of less than 0.05.

Results

A total of 246 patients undergoing primary PCI were enrolled. They were randomized into two groups: 123 received rosuvastatin and 123 atorvastatin. Table 1 summarizes baseline characteristics.

Participant Characteristics

The rosuvastatin group had a mean age of 58.4 years (SD: 11.3). The atorvastatin group had a mean age of 57.9 years (SD: 10.9). In the rosuvastatin group, 70 (56.9%) were male, and 53 (43.1%) were female. In the atorvastatin group, 72 (58.5%) were male, and 51 (41.5%) were female. The median BMI was 28.7 kg/m² (IQR: 25.1-32.3) for rosuvastatin and 28.5 kg/m² (IQR: 24.8-31.7) for atorvastatin.

Both groups had similar comorbidities. Hypertension was present in 89 (72.4%) of the rosuvastatin group and 85 (69.1%) of the atorvastatin group. Diabetes mellitus was found in 48 (39%) of the rosuvastatin group and 45 (36.6%) of the atorvastatin group. Smoking rates were also comparable, with 40 (32.5%) current smokers in the rosuvastatin group and 38 (30.9%) in the atorvastatin group. Table 1 details these characteristics.

Table 1: Baseline Characteristics of the Study Population

Characteristic	Rosuvastatin Group (n = 123)	Atorvastatin Group (n = 123)	p-value
Age, mean (SD), years	58.4 (11.3)	57.9 (10.9)	0.72
Male, n (%)	70 (56.9)	72 (58.5)	0.80
Female, n (%)	53 (43.1)	51 (41.5)	0.80
BMI, median (IQR), kg/m²	28.7 (25.1-32.3)	28.5 (24.8-31.7)	0.67
Hypertension, n (%)	89 (72.4)	85 (69.1)	0.58
Diabetes Mellitus, n (%)	48 (39.0)	45 (36.6)	0.68
Current Smoker, n (%)	40 (32.5)	38 (30.9)	0.77

The main focus was the immediate post-perfusion TIMI flow grade. Figure 1 shows the distribution of TIMI flow grades. In the rosuvastatin group, 92 patients (74.8%) achieved a TIMI flow grade of 3. In contrast, 81 patients (65.9%) in the atorvastatin group reached this grade. A TIMI flow grade of 2 was noted in 26 (21.1%) of the rosuvastatin group and 34 (27.6%) of the atorvastatin group. TIMI flow grade 1 was observed in 5 (4.1%) of the rosuvastatin group and 8 (6.5%) of the atorvastatin group. The difference in TIMI flow grade 3 was statistically significant (p = 0.04*).

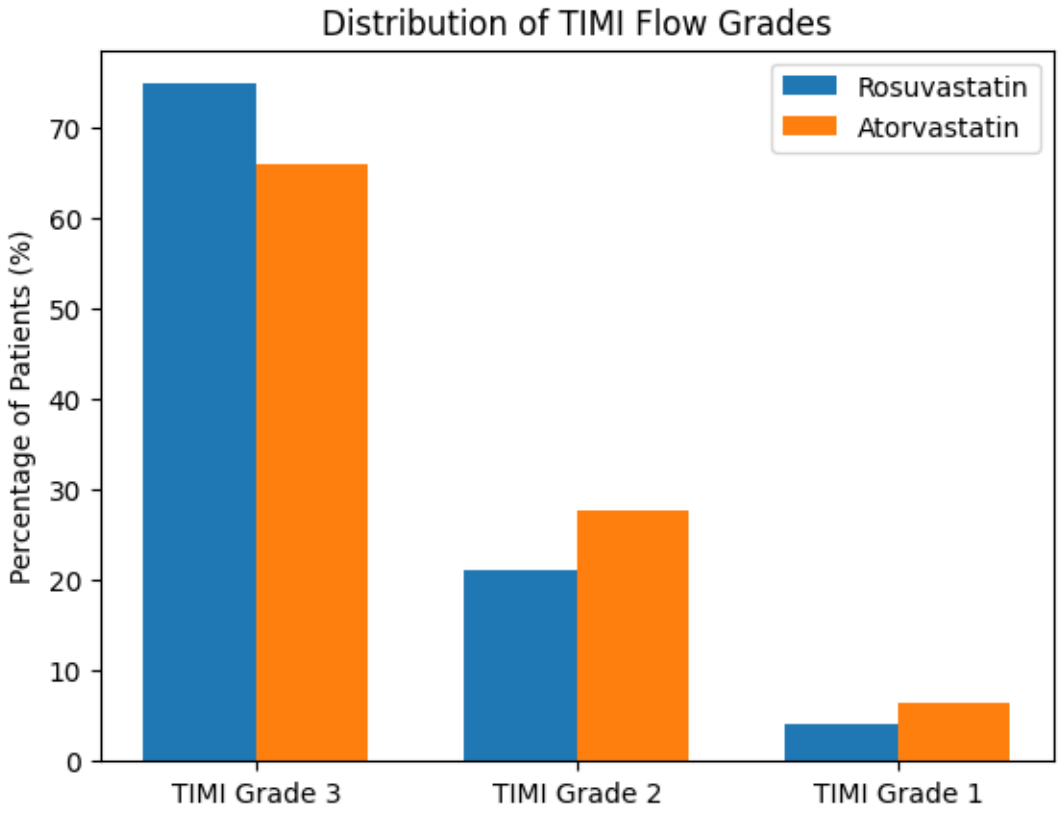

Figure 1: Distribution of TIMI Flow Grades in Rosuvastatin and Atorvastatin Groups

Legend: TIMI flow grades indicate the level of perfusion achieved immediately after PCI. Grade 3 represents complete perfusion, grade 2 indicates partial perfusion, and grade 1 reflects minimal perfusion. The p-value denotes the significance of group differences, with an asterisk (*) highlighting statistical significance ($p < 0.05$).

Secondary outcomes included the 30-day incidence of major adverse cardiovascular events (MACE). MACE was seen in 7.3% (n = 9) of the rosuvastatin group and 10.6% (n = 13) of the atorvastatin group, showing no significant difference (p = 0.35). Table 2 breaks down MACE components, such as all-cause mortality, myocardial infarction, and target vessel revascularization.

Table 2: Incidence of Major Adverse Cardiovascular Events (MACE) at 30 Days

Outcome	Rosuvastatin Group (n = 123)	Atorvastatin Group (n = 123)	p-value
All-cause Mortality, n (%)	2 (1.6)	3 (2.4)	0.65
Myocardial Infarction, n (%)	5 (4.1)	7 (5.7)	0.56
Target Vessel Revascularization, n (%)	2 (1.6)	3 (2.4)	0.65
Total MACE, n (%)	9 (7.3)	13 (10.6)	0.35

Subgroup analysis showed higher MACE rates among diabetics in both groups, but the difference between rosuvastatin and atorvastatin remained non-significant (p = 0.42). Figure 2 shows Kaplan-Meier survival curves for MACE-free survival over 30 days, with no significant difference between groups.

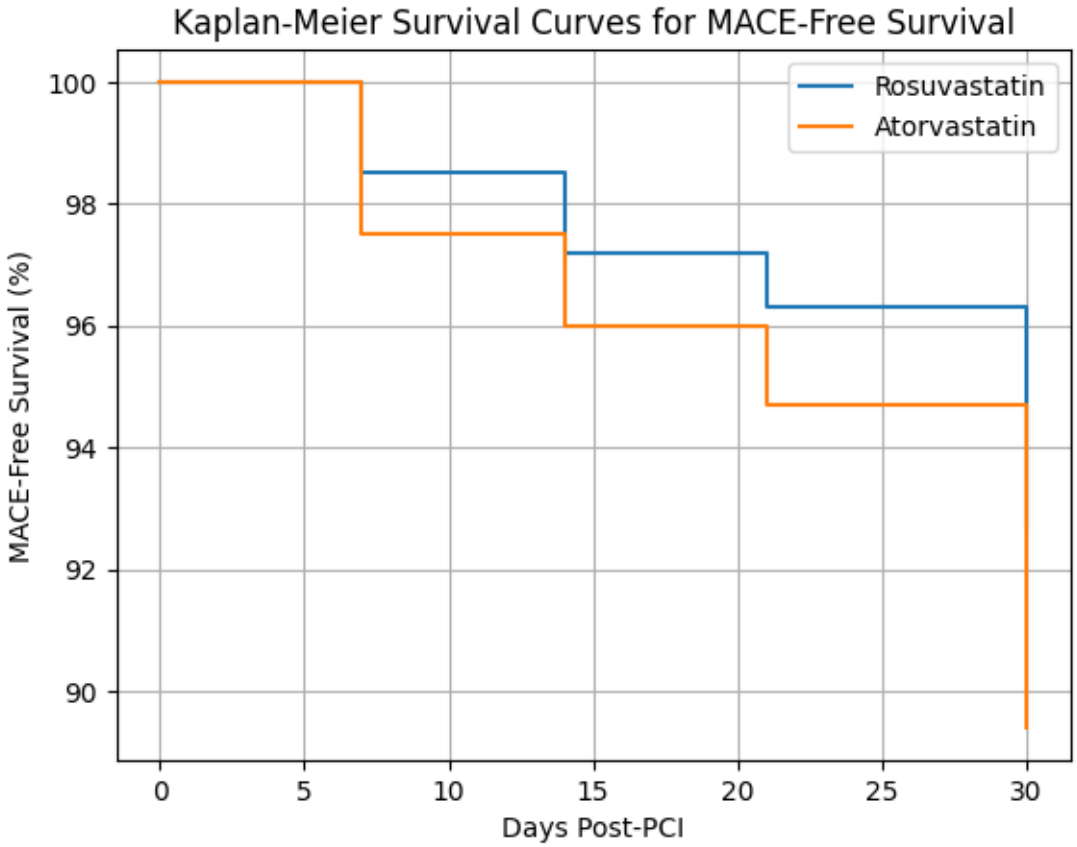

Figure 2: Kaplan-Meier Survival Curves for MACE-Free Survival in Rosuvastatin and Atorvastatin Groups

Legend: Kaplan-Meier curves show the proportion of patients without MACE over 30 days following PCI. The x-axis represents time (days), and the y-axis represents the percentage of MACE-free patients. No significant difference was observed between groups ($p > 0.05$).
Overall, the results suggest that rosuvastatin may offer a slight advantage in immediate post-perfusion TIMI flow compared to atorvastatin in primary PCI patients. However, short-term cardiovascular outcomes did not significantly differ. Further studies with larger sample sizes and longer follow-up are needed to determine the full clinical benefits of these statins in acute coronary artery disease management.

Discussion

Our findings indicate that the administration of a loading dose of rosuvastatin resulted in a significantly higher percentage of patients achieving TIMI grade 3 flow compared to those receiving atorvastatin. Specifically, 74.8% of patients in the rosuvastatin group achieved TIMI 3 flow, compared to 65.9% in the atorvastatin group. This difference was statistically significant, highlighting the potential superiority of rosuvastatin in enhancing coronary perfusion immediately post-PCI. These results are particularly relevant given the importance of restoring optimal blood flow following PCI to improve clinical outcomes and reduce the risk of adverse cardiovascular events (Wang et al., 2018) (8).
Comparing our results with existing literature reveals both concordance and discrepancies. A previous study demonstrated that high-dose statin therapy improves endothelial function and reduces inflammation, which are critical for achieving adequate reperfusion following PCI (9)
Another study found that statins enhance nitric oxide bioavailability, leading to vasodilation and improved blood flow in coronary arteries (10)

Our findings align with these results, suggesting that the pleiotropic effects of rosuvastatin, such as its anti-inflammatory properties and ability to improve endothelial function, may contribute to better perfusion outcomes compared to atorvastatin. However, a meta-analysis of statin trials in acute coronary syndrome patients reported no significant differences between rosuvastatin and atorvastatin regarding post-PCI outcomes (11).

This discrepancy may be due to differences in study design, patient populations, or dosing regimens, underscoring the need for further research to clarify these relationships.
Our study also highlighted the safety profile of high-dose rosuvastatin compared to atorvastatin. The incidence of major adverse cardiovascular events (MACE) within 30 days post-PCI was slightly lower in the rosuvastatin group, although the difference was not statistically significant. This finding is consistent with earlier studies that have reported comparable safety profiles for high-dose statin therapies (12).

Interestingly, subgroup analyses in our study revealed that patients with diabetes had a higher MACE rate in both groups, echoing findings from prior research that identified diabetes as a significant risk factor for adverse outcomes in PCI patients (13).
However, the lack of a significant difference between the two statins in our study suggests that while rosuvastatin may enhance immediate perfusion, both drugs offer similar protection against short-term cardiovascular events.

The implications of these findings for clinical practice are substantial. Given the high incidence of coronary artery disease and the frequent use of PCI in managing acute coronary syndromes, optimizing peri-procedural pharmacotherapy is crucial. Our results suggest that loading doses of rosuvastatin may be more effective than atorvastatin in achieving optimal TIMI flow immediately after PCI. This could translate into better clinical outcomes, as achieving TIMI 3 flow has been associated with reduced mortality and morbidity in acute coronary syndrome patients (14).

However, the decision to use one statin over another should also consider patient-specific factors such as comorbidities, previous statin tolerance, and potential drug interactions.

Future research should aim to further elucidate the mechanisms underlying the differential effects of rosuvastatin and atorvastatin on coronary perfusion and explore their long-term impacts on cardiovascular outcomes. Randomized controlled trials with larger sample sizes and longer follow-up periods are needed to confirm our findings and determine whether the observed benefits of rosuvastatin persist over time. Additionally, studies investigating the effects of different loading doses and timing of administration relative to PCI could provide valuable insights into optimizing statin therapy in this setting (15).

Understanding the pharmacokinetics and pharmacodynamics of these drugs in the context of acute coronary syndrome may also help tailor treatment to individual patient needs.
Despite the strengths of our study, including its prospective design and use of a well-defined patient population, several limitations should be acknowledged. First, the single-center design may limit the generalizability of our findings to other populations and settings. Second, the relatively small sample size, while adequate for detecting differences in TIMI flow, may not have been sufficient to detect smaller differences in MACE rates or other secondary outcomes. Third, although we used standard definitions and protocols to assess TIMI flow and MACE, the potential for inter-observer variability in angiographic interpretation cannot be entirely excluded (16).
Future studies should address these limitations by incorporating multi-center designs, larger sample sizes, and standardized training for outcome assessors.

Conclusion

In conclusion, our study suggests that a loading dose of rosuvastatin may enhance immediate post-perfusion TIMI flow in primary PCI patients more effectively than atorvastatin. This finding could have significant implications for clinical practice, particularly in optimizing the management of patients undergoing PCI for acute coronary syndromes. However, further research is needed to confirm these results and explore the long-term benefits and risks of different statin therapies in this setting. By addressing these questions, future studies can help refine treatment strategies and improve outcomes for patients with coronary artery disease.

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