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Original Article

Predictors and Outcomes of Slow Flow/No Reflow in Acute Myocardial Infarction Patients Treated with Pharmacoinvasive Strategies

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Abstract

Objectives: This study aimed to determine the incidence, predictors, and clinical outcomes of slow flow and no reflow (SF/NR) in patients undergoing a pharmacoinvasive strategy following full-dose thrombolytic therapy for acute myocardial infarction (AMI).

Methodology: We conducted a prospective observational study at the Department of Cardiology, Hayatabad Medical Complex, Peshawar, from February 2022 to February 2023. The study cohort comprised 130 patients who received percutaneous coronary intervention (PCI) after thrombolytic therapy. Comprehensive data on patient demographics, clinical presentations, procedural details, and outcomes were systematically collected. Multivariate logistic regression was employed to identify independent predictors of SF/NR.

Results: The incidence of SF/NR was 13.8%. Significant predictors included hypertension (Odds Ratio [OR]: 2.31, 95% Confidence Interval [CI]: 1.01-5.29, $p = 0.047$), high thrombus burden (OR: 3.14, 95% CI: 1.38-7.15, $p = 0.006$), and longer lesion length (OR: 1.29 per mm increase, 95% CI: 1.11-1.50, $p < 0.001$). Patients with SF/NR experienced significantly higher in-hospital mortality (16.7% vs. 2.7%, $p = 0.012$), cardiogenic shock (27.8% vs. 5.4%, $p < 0.001$), heart failure (33.3% vs. 7.1%, $p < 0.001$), and major adverse cardiac events (MACE) (44.4% vs. 11.6%, $p < 0.001$). At 30 days post-discharge, the mortality rate was 22.2% in the SF/NR group compared to 4.5% in the normal flow group ($p = 0.004$).

Conclusion: The study highlights a significant incidence of SF/NR in patients undergoing PCI after thrombolytic therapy for AMI. Identified predictors—hypertension, high thrombus burden, and longer lesion length—underscore the need for targeted risk stratification and management strategies to enhance patient outcomes and mitigate adverse effects.

Keywords: Slow flow, No reflow, Pharmacoinvasive strategy, Thrombolytic therapy, Acute myocardial infarction (AMI)

INTRODUCTION

The occurrence of slow flow and no reflow in patients undergoing pharmacoinvasive treatment after receiving thrombolytic therapy for acute myocardial infarction (AMI) represents a significant challenge in cardiovascular care. Slow flow/no reflow (SF/NR) refers to the inadequate perfusion of the heart muscle despite successful recanalization of the obstructed coronary artery. This phenomenon can lead to severe adverse outcomes, including increased morbidity and mortality. Identifying the predictors, prevalence, and subsequent outcomes of SF/NR is crucial for optimizing patient management and improving clinical outcomes [1-3].

The primary objective of percutaneous coronary intervention (PCI) in AMI is to restore coronary blood flow in the affected artery. However, the issue of no reflow has been a recognized complication since the 1970s, affecting approximately 10-40% of PCI patients. This condition is associated with larger myocardial infarction areas, increased cardiac complications, and higher mortality rates [4]. Recent data from Hayatabad Medical Complex highlighted an SF/NR incidence of 13.8% among 130 patients, with significant predictors including hypertension, high thrombus burden, and prolonged lesion length [5]. Other studies have identified additional risk factors such as renal dysfunction and specific pre-procedural interventions, like balloon predilation, which may exacerbate the risk of distal embolization and SF/NR [6,7].

Further research has underscored other notable predictors, including advanced age, elevated baseline inflammatory markers, and complex angiographic features, such as extensive coronary artery disease [3, 8]. The clinical implications of SF/NR are dire, with patients exhibiting poor outcomes including cardiogenic shock, elevated in-hospital mortality, major adverse cardiac events (MACE), and heart failure. The 30-day mortality rate remains significantly high among these patients [8,9].

Recent advancements in mitigating SF/NR have shown promise. The use of intracoronary agents, such as adenosine, nitroprusside, and epinephrine, has demonstrated potential in enhancing coronary flow post-PCI [1, 10]. Additionally, catheter-directed intracoronary thrombolysis (ICT) and optimized thrombus aspiration techniques have emerged as effective interventions. ICT, in particular, has been associated with reduced thrombus burden and improved myocardial perfusion, contributing to better clinical outcomes [9,11]. Innovative techniques, such as flow-mediated hyperemia and the SALINE method, involve selective intracoronary administration of saline or hyperemic agents to improve myocardial perfusion and address no reflow [12,13]. Recent meta-analyses also suggest the benefits of intracoronary recombinant human prourokinase and early intracoronary nicorandil administration in enhancing coronary flow and reducing SF/NR incidence [1,14].

This study aims to assess the incidence of SF/NR in patients undergoing PCI following full-dose thrombolytic therapy for AMI. It hypothesizes that hypertension, high thrombus burden, and longer lesion length are significant predictors of SF/NR. Additionally, the study seeks to evaluate the clinical outcomes associated with SF/NR, including in-hospital mortality, cardiogenic shock, heart failure, and major adverse cardiac events (MACE).

METHODOLOGY

Study Design: This study was a prospective observational research project aimed at assessing the incidence, predictive factors, and clinical outcomes of slow flow and no reflow phenomena in patients who underwent a pharmacoinvasive approach following thrombolytic therapy for acute myocardial infarction (AMI). The study was meticulously designed to minimize biases and ensure that the findings would be applicable to a broader patient population.

Setting: The study was conducted in the Cardiology Department of Hayatabad Medical Complex, Peshawar, a tertiary care hospital equipped with advanced interventional cardiology facilities. The research spanned a period of one year, from February 2022 to February 2023, allowing for a comprehensive analysis of patient outcomes over time.

Ethical Considerations: The study was conducted in accordance with the ethical standards set by the Hayatabad Medical Complex Ethical Review Committee, which approved the study protocol. All participants provided written informed consent prior to enrollment. Patient confidentiality was maintained by anonymizing the data, and all research procedures were conducted following ethical guidelines.

Participants: A total of 130 patients, diagnosed with AMI and treated with thrombolytic therapy followed by percutaneous coronary intervention (PCI), were enrolled in the study. Specific inclusion and exclusion criteria were applied to ensure the study population was representative and to control for confounding variables.

- **Inclusion Criteria:** The inclusion criteria for this study encompassed patients aged 18 years or older, regardless of gender, who presented with acute myocardial infarction (AMI) and received a full dose of thrombolytic therapy. Only those who underwent percutaneous coronary intervention (PCI) within 24 hours of thrombolytic therapy, had complete and accessible medical records, and provided informed consent were eligible for participation.
- **Exclusion Criteria:** Patients with known contraindications to PCI, such as severe aortic stenosis or significant comorbid conditions, were excluded from the study. Additionally, individuals with a history of coronary artery bypass grafting (CABG) or major cardiac surgeries, those who received partial or incomplete thrombolytic therapy, or those who experienced pre-PCI complications like stroke or major bleeding were not included. Patients who could not be followed for at least 30 days post-discharge or were lost to follow-up were also excluded to ensure comprehensive data collection.

Variables: The primary outcome of interest was the occurrence of slow flow or no reflow, defined as a TIMI (Thrombolysis in Myocardial Infarction) flow grade of 0-2 after PCI. Secondary outcomes included the identification of predictive factors for slow flow/no reflow and their impact on clinical outcomes.

- **Independent Variables:** The study's independent variables included a range of demographic and clinical factors. Demographic variables such as age, sex, and BMI were recorded to understand their potential impact on outcomes. Clinical presentation variables encompassed the time from symptom onset to hospitalization and the type of thrombolytics administered. Procedural variables involved the type of stent used and any adjunctive medications administered during the percutaneous coronary intervention (PCI). Additionally, the presence of comorbid conditions like hypertension, diabetes, and smoking status were considered to assess their influence on the study outcomes.
- **Dependent Variables:** The dependent variables focused on assessing the primary and secondary outcomes of the intervention. The primary outcome was the TIMI flow grade recorded post-PCI, which indicated the adequacy of coronary artery blood flow. Secondary outcomes included the incidence of slow flow or no reflow phenomena, as well as broader clinical outcomes such as mortality and major adverse cardiac events (MACE). These variables were analyzed to evaluate the effectiveness and safety of the pharmacoinvasive approach used in the study.

Data Sources/Measurement: Data were collected using a standardized form developed specifically for this study. The form was designed to capture comprehensive information on patient demographics, clinical presentation, and procedural details. Medical records were thoroughly reviewed to ensure accuracy and completeness. TIMI flow grades were assessed by experienced interventional cardiologists immediately after PCI to determine the adequacy of coronary artery blood flow.

Bias: To minimize selection bias, strict inclusion and exclusion criteria were applied. Additionally, data collection was standardized to reduce information bias. The study design accounted for potential confounding factors by including them in the multivariate analysis, thereby isolating the effect of the primary variables of interest.

Study Size: The sample size of 130 patients was determined based on previous studies assessing the incidence of slow flow/no reflow phenomena. The sample size was deemed sufficient to detect statistically significant differences in outcomes and predictive factors while allowing for a robust multivariate analysis.

Quantitative Variables: Continuous variables, such as age and BMI, were reported as mean ± standard deviation (SD). Categorical variables, including the incidence of slow flow/no reflow, were expressed as frequencies and proportions. The statistical analysis focused on identifying predictive factors for slow flow/no reflow and their association with clinical outcomes.

Statistical Methods: Data were analyzed using SPSS version 25.0. Univariate analysis was performed to identify potential predictors of slow flow/no reflow, with a significance level set at $p < 0.1$. Variables identified as significant in the univariate analysis were included in a multivariate logistic regression model to determine independent predictors of slow flow/no reflow. Results were presented as odds ratios (OR) with 95% confidence intervals (CI). A p-value of < 0.05 was considered statistically significant.

RESULTS

Participants: The study included 130 patients diagnosed with acute myocardial infarction (AMI) who underwent percutaneous coronary intervention (PCI) following thrombolytic therapy. The cohort had a mean age of 58.6 ± 11.3 years, with a predominance of male patients (77%). The baseline characteristics of the study population are detailed in Table 1 and summarized as follows: 45% of the patients had hypertension, 30% had diabetes mellitus, 25% were current smokers, 20% had a history of prior myocardial infarction, and 15% had renal dysfunction. The mean body mass index (BMI) was 27.5 ± 3.4 kg/m².

Table 1: Baseline Characteristics of the Study Population

Parameter	Value
Mean Age (years)	58.6 ± 11.3
Male (%)	77
Hypertension (%)	45
Diabetes Mellitus (%)	30
Current Smokers (%)	25
Prior Myocardial Infarction (%)	20
Renal Dysfunction (%)	15
Body Mass Index (BMI, kg/m²)	27.5 ± 3.4

Descriptive Data: The incidence of slow flow/no reflow (SFNR) was observed in 13.8% (18 out of 130) of the patients. SFNR was defined by a TIMI flow grade of 0-2 following PCI, indicating suboptimal coronary blood flow despite successful revascularization. Descriptive statistics for key variables associated with SFNR are illustrated in Table 1 and Table 2.

Outcome Data: The analysis revealed significant differences in clinical outcomes between patients with SFNR and those with normal coronary flow. The clinical outcomes for patients with SFNR versus those with normal flow are detailed in Table 4. Patients with SFNR had notably higher in-hospital mortality (16.7% vs. 2.7%, p = 0.012), a greater incidence of cardiogenic shock (27.8% vs. 5.4%, $p < 0.001$), and a higher occurrence of heart failure (33.3% vs. 7.1%, $p < 0.001$). Additionally, the 30-day mortality rate was significantly elevated in the SFNR group (22.2% vs. 4.5%, p = 0.004).

Table 1: Univariable Analysis of Potential Predictors of SFNR

Predictor	Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
Age (years)	1.03	0.99 - 1.07	0.101
Male gender	1.2	0.45 - 3.22	0.715
Hypertension	2.34	1.02 - 5.37	0.046
Diabetes Mellitus	1.73	0.71 - 4.22	0.232
High Thrombus Burden	3.61	1.56 - 8.38	0.003
Lesion Length (mm)	1.22	1.10 - 1.35	<0.001
Renal Dysfunction	2.89	1.12 - 7.46	0.028
BMI (kg/m²)	1.15	0.96 - 1.39	0.134
Prior MI	1.65	0.63 - 4.31	0.308

Main Results: Univariable logistic regression analysis identified several predictors of SFNR, including hypertension, high thrombus burden, lesion length, and renal dysfunction. These results are presented in Table 2. Multivariable logistic regression analysis further confirmed that hypertension (adjusted OR 2.31, 95% CI 1.01-5.29, p = 0.047), high thrombus burden (adjusted OR 3.14, 95% CI 1.38-7.15, p = 0.006), longer lesion length (adjusted OR 1.29 per mm, 95% CI 1.11-1.50, $p < 0.001$), and renal dysfunction (adjusted OR 2.77, 95% CI 1.03-7.48, p = 0.044) were independently associated with an increased risk of SFNR, as shown in Table 3. These findings highlight the critical factors influencing the occurrence of SFNR and underscore the need for careful management of these risk factors to improve clinical outcomes in AMI patients undergoing PCI.

Table 2: Multivariable Logistic Regression Analysis of Independent Predictors of SFNR

Predictor	Adjusted Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
Hypertension	2.31	1.01 - 5.29	0.047
High Thrombus Burden	3.14	1.38 - 7.15	0.006
Lesion Length (per mm)	1.29	1.11 - 1.50	<0.001
Renal Dysfunction	2.77	1.03 - 7.48	0.044

DISCUSSION

This study aimed to determine the incidence of slow flow/no reflow (SF/NRF), identify independent predictors, and assess the clinical consequences in

patients with acute myocardial infarction (AMI) who received a pharmacoinvasive strategy following thrombolytic therapy. Our findings revealed that SF/NRF occurred in 13.8% of patients, with hypertension, high thrombus burden, and longer lesion length being significant predictors. These results align with existing literature, highlighting the adverse impact of SF/NRF on patient outcomes, including higher in-hospital mortality, cardiogenic shock, heart failure, and major adverse cardiac events (MACE).

Table 3: Clinical Outcomes of Patients with SFNR vs. Normal Flow

Outcome	SFNR (%)	Normal Flow (%)	P-value
In-hospital Mortality	16.7	2.7	0.012
Cardiogenic Shock	27.8	5.4	<0.001
Heart Failure	33.3	7.1	<0.001
Major Adverse Cardiac Events (MACE)	44.4	11.6	<0.001
30-day Mortality	22.2	4.5	0.004

Our observed SF/NRF rate is consistent with previous studies. For example, Babapoor et al. (2022) [15] reported an incidence of 12.9% for slow flow and 17.1% for no reflow in a comparable patient population undergoing primary PCI. Similarly, Savic et al. (2022) [6] documented an approximate incidence of 11.9% for SF/NRF, supporting the reliability of our findings across different clinical settings.

Our study identified hypertension, high thrombus burden, and longer lesion length as significant predictors of SF/NRF. These predictors are corroborated by previous research. Khan et al. (2023) [5] and Sondergaard et al. (2022) [8] observed that patients with higher thrombus burdens and extensive lesion lengths face increased risks of SF/NRF. Additionally, renal dysfunction emerged as a critical predictor of no reflow, consistent with findings by Khan et al. (2023) [5] and Savic et al. (2022) [6], who highlighted the elevated risk associated with impaired renal function.

The adverse clinical outcomes associated with SF/NRF, including elevated in-hospital mortality and increased rates of cardiogenic shock and heart failure, are in agreement with earlier studies. Sondergaard et al. (2022) [8] and Singh et al. (2022) [9] reported that SF/NRF significantly worsens patient prognosis following PCI. Furthermore, our findings regarding 30-day post-discharge mortality align with Godinez Cordova et al. (2022) [16], who found that no reflow correlates with higher short-term mortality rates.

Recent advancements in managing SF/NRF show promise. The use of intracoronary agents such as adenosine and epinephrine has been demonstrated to improve coronary flow and patient outcomes. Studies by Darwish et al. (2022) [17] and Jafari Afshar et al. (2023) [10] support these agents' efficacy in mitigating no reflow effects. Additionally, optimized thrombus aspiration techniques and catheter-directed intracoronary thrombolysis have proven effective in reducing thrombus burden and enhancing myocardial perfusion, leading to improved clinical outcomes.

Limitations

Several limitations affect the interpretation of this study's findings. The single-center design restricts the generalizability of the results to other settings and populations. The sample size of 130 patients, while significant, may not encompass all potential predictors of SF/NRF. The observational nature of the study limits the ability to establish causality between predictors and outcomes. Furthermore, potential biases in data collection, such as recall and selection biases, could impact the accuracy of the findings. The follow-up period of 30 days post-discharge may not fully capture long-term outcomes and complications associated with SF/NRF.

To build on these findings, multicenter studies involving larger and more diverse populations are needed to enhance the generalizability of results. Longitudinal studies with extended follow-up durations would provide deeper insights into the long-term outcomes of SF/NRF. Randomized controlled trials are essential to confirm causal relationships and evaluate the efficacy of various management strategies. Additionally, advancements in imaging techniques could refine the assessment of thrombus burden and lesion characteristics, facilitating better risk stratification and personalized treatment plans. Exploring new pharmacological and mechanical interventions aimed at reducing the incidence and severity of SF/NRF, as well as investigating genetic and molecular mechanisms, could lead to significant improvements in patient care and outcomes

CONCLUSION

This study reveals a notable incidence of slow flow/no reflow (SF/NRF) in patients undergoing percutaneous coronary intervention (PCI) following thrombolytic therapy for acute myocardial infarction (AMI). Key predictors of SF/NRF identified include hypertension, high thrombus burden, longer lesion length, and renal dysfunction. These findings highlight the critical need for early risk assessment and targeted interventions to mitigate the adverse outcomes associated with SF/NRF. Despite these insights, the study's observational design and relatively short follow-up period limit the generalizability and depth of our conclusions. Future research should aim to validate these predictors in larger, more diverse populations and investigate the long-term outcomes associated with SF/NRF.

AUTHORS' CONTRIBUTION

FU, MI, EU, IU, ZA, and WF: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. FU, MI, EU, IU, ZA, and WF: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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