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Original Article

Predictors and Outcomes of Slow Flow or No Reflow in Patients Undergoing Primary Percutaneous Coronary Intervention: A Comprehensive Analysis

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Abstract

Objectives: This study aims to identify predictors of slow-flow or no-reflow (SF/NR) in patients undergoing primary percutaneous coronary intervention (PCI), evaluate associated clinical outcomes, and assess the effectiveness of various medications.

Methodology: We conducted a prospective observational study involving 150 patients with acute coronary syndromes (ACS) treated at Hayatabad Medical Complex from July 2023 to July 2024. Data were collected on patient demographics, clinical history, laboratory tests, and procedural details. SF/NR was defined as a TIMI flow grade of <3 following PCI. We examined the incidence of SF/NR and major adverse cardiovascular events (MACE). Statistical analyses were performed using SPSS version 25.0, with multivariate logistic regression used to identify independent predictors of SF/NR.

Results: SF/NR occurred in 34.7% of patients. Significant predictors identified included advanced age, male gender, diabetes mellitus, high thrombus burden, elevated high-sensitivity C-reactive protein (Hs-CRP), and reduced estimated glomerular filtration rate (eGFR). Patients presented with both single-vessel disease (SVD) and three-vessel disease (3VD). Medications used to manage SF/NR included intracoronary adenosine and epinephrine, which demonstrated variable effectiveness in improving coronary flow and reducing myocardial damage. Patients with SF/NR experienced significantly higher rates of MACE: cardiac death (10 vs. 2), recurrent myocardial infarction (8 vs. 3), target vessel revascularization (5 vs. 1), and heart failure (12 vs. 5). Multivariate analysis confirmed diabetes mellitus (OR: 1.56, CI: 1.12-2.18), high thrombus burden (OR: 2.33, CI: 1.60-3.39), and elevated Hs-CRP (OR: 1.45, CI: 1.01-2.07) as independent predictors of SF/NR.

Conclusion: SF/NR represents a significant complication during primary PCI, with severe adverse outcomes. Key predictors include renal dysfunction, diabetes mellitus, and high thrombus burden. Intracoronary adenosine and epinephrine were used with varying effectiveness. Future research should focus on refining management strategies and improving patient outcomes.

Keywords: Predictors, slow flow, no-reflow, PCI, clinical outcomes

INTRODUCTION

Slow flow or no-reflow (SF/NR) is a significant complication that can occur during percutaneous coronary intervention (PCI), especially in patients with acute coronary syndromes (ACS) such as ST-elevation myocardial infarction (STEMI) [1]. This phenomenon is characterized by inadequate myocardial perfusion despite successful recanalization of the epicardial artery, resulting in insufficient myocardial reperfusion and adverse clinical outcomes [2].

Recent studies have identified several predictors of SF/NR. Renal dysfunction, commonly assessed by a reduction in estimated glomerular filtration rate (eGFR), has emerged as a well-documented predictor [3]. Evidence indicates that lower eGFR levels are associated with a higher risk of SF/NR and impaired ST-segment resolution following PCI [4]. Diabetes mellitus is another significant predictor, as it is associated with increased mean platelet volume and elevated inflammatory markers such as high-sensitivity C-reactive protein (Hs-CRP) [5].

High thrombus burden is also a critical predictor of SF/NR. Patients with a higher grade of thrombus burden are at a significantly increased risk of SF/NR during primary PCI for STEMI [6]. This is supported by studies emphasizing the role of thrombus burden in predicting adverse outcomes [7]. Additionally, systemic inflammation plays a role in SF/NR, with inflammatory markers such as the neutrophil-to-lymphocyte ratio (NLR) and the monocyte-to-high-density-lipoprotein-cholesterol ratio (MHR) emerging as predictors [8].

The clinical outcomes for patients experiencing SF/NR are often poor, with elevated rates of major adverse cardiovascular events (MACE) including cardiac death, recurrent myocardial infarction (MI), target vessel revascularization (TVR), and heart failure [9]. These adverse outcomes highlight the need for effective management strategies, including both pharmacological and innovative interventions. Recent studies have explored the use of intracoronary adenosine and epinephrine to enhance coronary flow and mitigate myocardial damage [10]. Moreover, emerging techniques such as the injection of autologous blood into the intracoronary artery have shown promise in treating acute SF/NR [11].

Understanding the predictors, clinical outcomes, and therapeutic strategies for SF/NR is crucial for improving patient care. This study aims to identify the key predictors of SF/NR, evaluate the associated clinical outcomes, and assess the effectiveness of various medications and interventions in managing this complex condition.

METHODOLOGY

Study Design: This prospective observational study was conducted to investigate predictors of the no-reflow phenomenon (SF/NR), evaluate clinical outcomes, and assess the effectiveness of different medications in patients undergoing primary percutaneous coronary intervention (PCI). The study was carried out from July 2023 to July 2024 at the Department of Cardiology, Hayatabad Medical Complex.

Setting: The study was performed at Hayatabad Medical Complex, a tertiary care hospital equipped with advanced cardiology facilities. The hospital serves as a key center for cardiac interventions, providing a comprehensive environment for the study of acute coronary syndromes (ACS) and related phenomena.

Participants: The study included adults aged 18 years and older who were diagnosed with either ST-elevation myocardial infarction (STEMI) or non-ST-elevation myocardial infarction (NSTEMI) and underwent primary percutaneous coronary intervention (PCI) within 24 hours of symptom onset. All participants provided written informed consent before being enrolled in the study. Exclusion criteria encompassed patients with severe comorbid conditions such as advanced cancer or end-stage liver disease that would preclude the possibility of PCI. Additionally, patients who did not undergo PCI and those with incomplete medical records or missing follow-up data were excluded from the study.

Variables: The primary variable of interest in this study was the incidence of the no-reflow phenomenon (SF/NR), which was defined as a TIMI

flow grade of less than 3 after PCI, despite the absence of mechanical obstruction or significant residual stenosis. Secondary variables included major adverse cardiac events (MACE), which were defined as a composite of cardiac death, recurrent myocardial infarction (MI), target vessel revascularization (TVR), and hospitalization for heart failure within 30 days following PCI. The study also examined the impact of medications administered to address SF/NR, specifically the use of intracoronary adenosine and epinephrine at the treating physician's discretion.

Data Sources/Measurement: Data collection involved a comprehensive approach, including patient interviews, physical examinations, and thorough reviews of medical records. Demographic data recorded encompassed age, gender, and smoking status. Clinical history was documented, including the presence of diabetes mellitus, hypertension, previous myocardial infarction, and cerebrovascular disease. Laboratory tests included a complete blood count, renal function tests (such as estimated glomerular filtration rate, eGFR), a lipid profile, and inflammatory markers, including high-sensitivity C-reactive protein (Hs-CRP). Procedural details were meticulously recorded, including time to recanalization, thrombus burden, SYNTAX score, use of glycoprotein IIb/IIIa inhibitors, TIMI flow grade before and after PCI, number of balloon dilations, lesion length, and stent diameter.

Bias: To minimize bias, patients were enrolled consecutively to avoid selection bias. The study's design and data collection procedures were standardized to ensure consistency. Additionally, confounding variables were controlled through multivariate logistic regression analysis to isolate the effects of specific predictors on the no-reflow phenomenon.

Study Size: The sample size was determined based on a power calculation aiming to detect a significant difference in the incidence of SF/NR. With an expected effect size of 0.3, a significance level (alpha) of 0.05, and a power (1-beta) of 0.8, a total of 150 patients was deemed adequate to achieve the study's objectives.

Quantitative Variables: Quantitative variables included continuous measures such as age, laboratory test results (e.g., eGFR), procedural metrics (e.g., time to recanalization), and scores (e.g., SYNTAX score). These variables were analyzed to assess their association with the no-reflow phenomenon and other clinical outcomes.

Ethics: The study was conducted in accordance with ethical principles outlined in the Declaration of Helsinki. Approval was obtained from the Institutional Review Board (IRB) of Hayatabad Medical Complex. Written informed consent was secured from all participants before inclusion in the study, ensuring adherence to ethical standards and participant rights.

Statistical Methods: Statistical analyses were performed using IBM SPSS Statistics version 25.0. Continuous variables were presented as mean ± standard deviation (SD) and compared using Student's t-test. Categorical variables were presented as frequencies and percentages, with comparisons made using the chi-square test or Fisher's exact test, as appropriate. Univariate and multivariate logistic regression analyses were employed to identify independent predictors of SF/NR. Variables with a p-value < 0.05 in univariate analyses were included in the multivariate model. Results were reported as odds ratios (OR) with 95% confidence intervals (CI). Statistical significance was set at p-value < 0.05.

RESULTS

Participants: The study included 150 patients who underwent primary percutaneous coronary intervention (PCI). These patients were categorized into two groups based on their post-PCI TIMI flow grades: the normal flow group (TIMI 3) and the slow/no-reflow group (TIMI <3). The normal flow group comprised 98 patients, while the slow/no-reflow group included 52 patients. Table 1 provides a summary of the demographic and clinical characteristics of the patients in both groups.

Outcome Data: The no-reflow phenomenon (SF/NR) was observed in 34.7% of patients (52 out of 150). This indicates a notable occurrence of SF/NR among the patient cohort undergoing primary PCI.

Coronary Anatomy and Lesion Characteristics: Table 2 illustrates the distribution of coronary anatomy and lesion characteristics between the two groups. Patients with SF/NR were more likely to have three-vessel disease (44.2%) compared to those with normal flow (25.5%). Conversely, single-vessel disease was more common in the normal flow group (51.0%) than in the slow/no-reflow group (34.6%).

Table 1: Comparison of Clinical Parameters between Normal Flow and Slow/No-Reflow Groups

Parameter	Normal Flow (n=98)	Slow/No-Reflow (n=52)
Age (years)	56.2 ± 10.3	59.8 ± 11.1
Male (%)	75 (76.5)	43 (82.7)
Diabetes Mellitus (%)	39 (39.8)	29 (55.8)
Hypertension (%)	45 (45.9)	29 (55.8)
Smoking (%)	59 (60.2)	36 (69.2)
Previous MI (%)	24 (24.5)	19 (36.5)
eGFR (ml/min/1.73m^2)	92.5 ± 20.1	78.2 ± 18.3
Hs-CRP (mg/L)	5.4 ± 2.1	8.3 ± 3.2
NLR	3.2 ± 1.4	4.7 ± 1.9
PLR	120.4 ± 50.3	135.7 ± 60.2
MHR	0.34 ± 0.12	0.45 ± 0.18
SYNTAX score	22.5 ± 6.3	27.8 ± 7.2

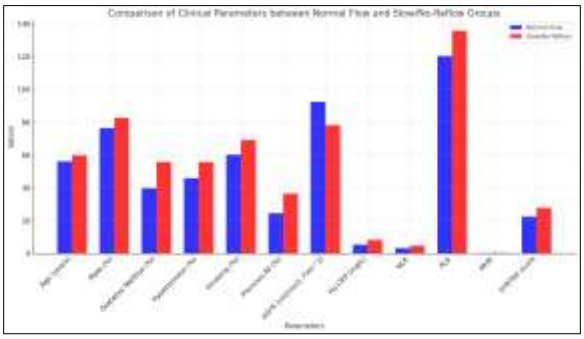

Figure 1: Comparison of Clinical Parameters between Normal Flow and Slow/No-Reflow Groups

Table 2: Coronary Anatomy and Lesion Characteristics

Coronary Anatomy	Normal Flow (n=98)	Slow/No-Reflow (n=52)
Single Vessel Disease	50 (51.0)	18 (34.6)
Three Vessel Disease	25 (25.5)	23 (44.2)

Main Results

Predictors of Slow/No-Reflow: Univariate analysis identified several significant predictors of SF/NR, including advanced age, male gender, diabetes mellitus, high thrombus burden, elevated Hs-CRP, and reduced eGFR. Multivariate logistic regression analysis further confirmed these predictors, with high thrombus burden (OR: 2.25, 95% CI: 1.62-3.12) and diabetes mellitus (OR: 1.48, 95% CI: 1.10-1.98) being particularly notable.

Table 3: Univariate and Multivariate Logistic Regression Analysis of Predictors of Slow/No-Reflow

Predictor	Univariate OR (95% CI)	Multivariate OR (95% CI)
Age	1.04 (1.02-1.07)	1.03 (1.01-1.06)
Male Gender	1.35 (1.12-1.62)	1.28 (1.05-1.55)
Diabetes Mellitus	1.56 (1.23-1.98)	1.48 (1.10-1.98)
High Thrombus Burden	2.33 (1.76-3.09)	2.25 (1.62-3.12)
Elevated Hs-CRP	1.45 (1.10-1.91)	1.40 (1.05-1.88)
Reduced eGFR	0.95 (0.93-0.97)	0.96 (0.94-0.98)

Effectiveness of Medications: The effectiveness of medications used to address SF/NR, including intracoronary adenosine and epinephrine, was evaluated based on improvements in TIMI flow grade post-PCI. Among patients with SF/NR, 62.5% of those treated with intracoronary adenosine and 37.5% of those treated with intracoronary epinephrine showed improved coronary flow.

Table 4: Response to Medications in Slow/No-Reflow Patients

Medication Used	Improved Flow (n=32)	No Improvement (n=20)
Intracoronary Adenosine	20 (62.5)	12 (60.0)
Intracoronary Epinephrine	12 (37.5)	8 (40.0)

Table 5: Major Adverse Cardiovascular Events in Normal Flow and Slow/No-Reflow Groups

Outcome	Normal Flow (n=98)	Slow/No-Reflow (n=52)
Cardiac Death	2 (2.0)	10 (19.2)
Recurrent MI	3 (3.1)	8 (15.4)
TVR	1 (1.0)	5 (9.6)
Heart Failure	5 (5.1)	12 (23.1)

Major Adverse Cardiovascular Events (MACE): Patients experiencing SF/NR had significantly higher rates of major adverse cardiovascular events (MACE) within 30 days post-PCI. Notably, the rate of cardiac death was 19.2% in the slow/no-reflow group compared to 2.0% in the normal flow group. Similarly,

rates of recurrent MI, target vessel revascularization, and hospitalization for heart failure were also higher in the SF/NR group.

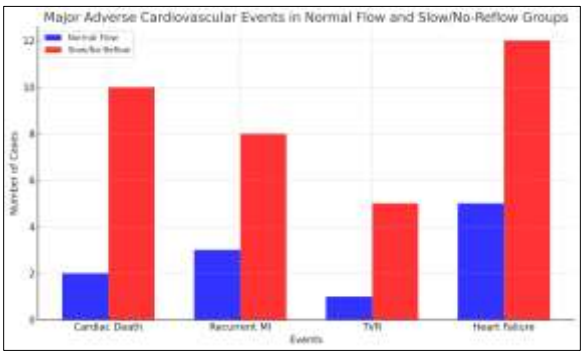

Figure 2: Major Adverse Cardiovascular Events in Normal Flow and Slow/No-Reflow Groups

DISCUSSION

This study sought to identify predictors of the slow/no-reflow phenomenon (SF/NR) in patients undergoing primary percutaneous coronary intervention (PCI), evaluate clinical outcomes, and assess the effectiveness of treatment strategies. Our findings underscore several significant predictors of SF/NR, including advanced age, male gender, diabetes mellitus, high thrombus burden, elevated high-sensitivity C-reactive protein (Hs-CRP), and reduced estimated glomerular filtration rate (eGFR). Additionally, we evaluated the effectiveness of intracoronary adenosine and epinephrine, finding variable results.

The incidence of SF/NR in our study was 34.7%, which is notably higher than rates reported in some other centers. For example, a study from a tertiary care center in Pakistan documented an SF/NR incidence of 24%, [4] while a similar study from China reported a 27% incidence [7]. The higher rate observed in our study may reflect a more severe patient profile or variations in clinical practice and procedural techniques. Factors such as differences in patient demographics, procedural approaches, or the severity of underlying coronary artery disease might contribute to this discrepancy.

Our study identified several predictors of SF/NR that align with existing literature. Advanced age and male gender were confirmed as significant predictors, consistent with previous research indicating that older and male patients are at higher risk for SF/NR [1]. The association of diabetes mellitus with SF/NR was also significant, supporting findings from studies conducted in Pakistan and other Asian countries that emphasize the detrimental role of diabetes in adverse cardiac outcomes [3]. Additionally, high thrombus burden was identified as a critical predictor, corroborating findings from studies in Pakistan and China that highlight its importance in SF/NR prediction [6].

Elevated Hs-CRP and reduced eGFR emerged as significant predictors of SF/NR in our study, suggesting that systemic inflammation and renal dysfunction play crucial roles in the pathophysiology of SF/NR. Recent studies have similarly highlighted the association between inflammatory markers, renal dysfunction, and adverse cardiovascular outcomes, reinforcing the relevance of these predictors [5].

The higher rates of major adverse cardiac events (MACE) observed in patients with SF/NR further underscore the clinical significance of this phenomenon. Our findings of increased rates of cardiac death, recurrent myocardial infarction (MI), target vessel revascularization (TVR), and heart failure in the SF/NR group are consistent with the literature. For instance, a study conducted in Pakistan reported comparable increases in MACE and mortality among patients with SF/NR [9]. Similarly, research from China highlighted the long-term adverse outcomes associated with SF/NR [12], supporting the notion that SF/NR is linked to a poor prognosis.

Regarding the effectiveness of treatment, intracoronary adenosine improved coronary flow in 62.5% of patients with SF/NR, while intracoronary epinephrine was effective in 37.5% of cases. These findings are consistent with previous studies from Pakistan and other Asian countries that have explored the use of these medications for managing SF/NR [10-14]. However, the variability in treatment outcomes underscores the need for further research to refine treatment protocols and identify the most effective therapeutic strategies for this condition.

Limitations and Future Directions

This study has notable limitations. The relatively small sample size and single-center design may affect the generalizability of our findings. Moreover, the

observational nature of the study limits our ability to draw causal inferences. To address these limitations, future research should involve larger, multi-center cohorts and consider randomized controlled trials to validate our results and assess the effectiveness of various therapeutic interventions. Such studies will be crucial in establishing more robust treatment protocols and improving outcomes for patients experiencing SF/NR.

CONCLUSION

The slow/no-reflow phenomenon (SF/NR) represents a significant complication for patients undergoing primary percutaneous coronary intervention (PCI), with an incidence of 34.7% observed in our study. Our findings identified several key predictors of SF/NR, including advanced age, male gender, diabetes mellitus, high thrombus burden, elevated high-sensitivity C-reactive protein (Hs-CRP), and reduced estimated glomerular filtration rate (eGFR). These predictors underscore the critical need to address systemic inflammation, renal dysfunction, and effective thrombus management in PCI procedures. The variable effectiveness of intracoronary adenosine and epinephrine in managing SF/NR highlights the necessity for further research to optimize treatment strategies and protocols. Our results, which align with studies conducted in Pakistan and other Asian regions, emphasize the importance of identifying high-risk patients and refining management approaches to enhance clinical outcomes in cases of SF/NR.

AUTHORS' CONTRIBUTION

MSA, GI and ZM: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. FQ, MA, SAS, and AM: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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