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Original Article

Frequency of No-Flow in Patients Following PCI in Stable Coronary Artery Disease

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ABSTRACT

Background: No-reflow following percutaneous coronary intervention (PCI) is a clinically important complication characterized by impaired myocardial perfusion despite successful epicardial revascularization, and although well studied in acute coronary syndromes, its occurrence and impact in stable coronary artery disease (CAD) remain less clearly defined. Objective: To determine the incidence of no-reflow after elective PCI in stable CAD patients, identify associated clinical and procedural factors, and evaluate short-term clinical outcomes. Methods: This prospective observational study included 100 consecutive patients with stable CAD undergoing elective PCI at a tertiary care center from January to April 2025. No-reflow was defined as final TIMI flow ≤2 in the absence of mechanical obstruction. Baseline clinical, angiographic, and procedural variables were recorded, and patients were followed for 30 days to assess major adverse cardiovascular events. Statistical analysis was performed using SPSS version 22.0, with a p-value <0.05 considered significant. Results: No-reflow occurred in 5% of patients. Higher balloon inflation pressure (16 ± 3 atm vs. 11 ± 2 atm; p=0.01) and use of high-pressure inflation (80% vs. 27.4%; p=0.04) were significantly associated with no-reflow. Post-procedural myocardial infarction was significantly higher in the no-reflow group (60% vs. 2.1%; p=0.03), while re-hospitalization and mortality were numerically higher but not statistically significant. Conclusion: No-reflow is an infrequent but clinically significant complication in stable CAD PCI, strongly associated with procedural factors and increased risk of early adverse outcomes, highlighting the need for careful procedural strategies and early intervention. Keywords: No-reflow, percutaneous coronary intervention, stable coronary artery disease, myocardial infarction, microvascular dysfunction, procedural outcomes.

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INTRODUCTION

Percutaneous coronary intervention (PCI) remains a cornerstone in the management of patients with stable coronary artery disease (CAD), offering symptomatic relief and improved quality of life through restoration of epicardial coronary blood flow. Despite high procedural success rates, a subset of patients experiences impaired myocardial perfusion following technically successful PCI, a phenomenon commonly referred to as no-reflow or no-flow. This condition is characterized by reduced antegrade coronary flow (typically defined as Thrombolysis in Myocardial Infarction [TIMI] flow grade ≤2) in the absence of mechanical obstruction such as dissection, residual stenosis, or spasm, and reflects underlying microvascular dysfunction (1). The pathophysiology of no-reflow is multifactorial, involving distal embolization of atherothrombotic debris, ischemia-reperfusion injury, endothelial dysfunction, and microvascular spasm, all of which contribute to impaired tissue-level perfusion despite restoration of epicardial vessel patency (2).

Although the no-reflow phenomenon has been extensively studied in the context of acute coronary syndromes (ACS), particularly ST-segment elevation myocardial infarction (STEMI), where its incidence may reach 20–30% depending on diagnostic criteria, its occurrence in elective PCI for stable CAD is less well characterized (3). Available evidence suggests that the incidence of no-reflow in stable CAD is considerably lower, generally ranging from 1% to 5%, but remains clinically significant due to its association with adverse short- and long-term outcomes, including peri-procedural myocardial infarction, left ventricular dysfunction, and increased mortality (4). Importantly, even transient impairment in microvascular perfusion during PCI has been linked to worse prognosis, underscoring the need for early recognition and prompt management (5).

Several patient-related, lesion-related, and procedural factors have been implicated in the development of no-reflow. Patient-level risk factors such as diabetes mellitus, hypertension, and prior myocardial infarction are thought to predispose to microvascular dysfunction through chronic endothelial injury and structural remodeling (6). Lesion characteristics including heavy calcification, long lesion length, and high plaque burden increase the likelihood of distal embolization during intervention (7). Procedural variables, particularly high-pressure balloon inflation, multiple stent deployments, and prolonged procedural time, may further exacerbate microvascular injury and contribute to impaired perfusion (8). However, much of the existing literature derives from heterogeneous populations or predominantly ACS cohorts, limiting the generalizability of these findings to stable CAD patients undergoing elective PCI.

Furthermore, there is a relative paucity of prospective data from low- and middle-income settings evaluating the incidence, predictors, and short-term clinical consequences of no-reflow in stable CAD populations. Variations in patient demographics, comorbidity profiles, lesion complexity, and procedural practices may influence both the occurrence and outcomes of this complication. Consequently, there is a need for context-specific evidence to better inform risk stratification and optimize peri-procedural management strategies in such settings (9).

Given this background, the present study was designed to determine the incidence of no-reflow following elective PCI in patients with stable CAD, to explore associated clinical and procedural factors, and to evaluate its impact on short-term clinical outcomes, including post-procedural myocardial infarction, re-hospitalization, and mortality. It is hypothesized that no-reflow, although infrequent in stable CAD, is associated with identifiable risk factors and confers a higher risk of adverse outcomes within 30 days following PCI (10).

METHODS

This prospective observational study was conducted in the Department of Cardiology at Sandeman Provincial Hospital in collaboration with Bolan Medical Complex Hospital, Quetta, from January 2025 to April 2025. The study was designed to determine the incidence of no-reflow following elective percutaneous coronary intervention (PCI) in patients with stable coronary artery disease (CAD), and to evaluate associated clinical, angiographic, and procedural factors as well as short-term outcomes. A prospective design was selected to enable real-time assessment of procedural variables and standardized follow-up, thereby minimizing recall bias and improving temporal relationship assessment between exposure variables and outcomes (11).

A total of 100 consecutive patients diagnosed with stable CAD and scheduled for elective PCI were enrolled using a non-probability consecutive sampling technique. Eligible participants were adults aged between 40 and 80 years with angiographically confirmed stable CAD undergoing their first elective PCI. Patients presenting with acute coronary syndromes, including unstable angina or myocardial infarction, those with severe left ventricular systolic dysfunction (ejection fraction <30%), known contraindications to contrast media or antithrombotic therapy, prior coronary artery bypass grafting, or significant systemic comorbidities that could confound outcome assessment were excluded. All eligible

patients were approached during their pre-procedural evaluation, and written informed consent was obtained prior to inclusion in the study (12).

Baseline demographic and clinical data were collected through structured interviews and review of medical records at the time of admission. Variables included age, sex, history of diabetes mellitus, hypertension, prior myocardial infarction, and relevant medication use. Angiographic and procedural data were recorded during PCI by the operating interventional cardiologist using a standardized data collection proforma. Lesion characteristics, including location, length, and degree of calcification, were assessed based on coronary angiography. Procedural variables such as stent type, balloon inflation pressure (measured in atmospheres), use of high-pressure inflation (defined as ≥14 atm), procedural duration, and adjunctive pharmacological therapies were documented (13).

The primary outcome variable was the occurrence of no-reflow, operationally defined as a final Thrombolysis in Myocardial Infarction (TIMI) flow grade ≤2 in the treated vessel in the absence of mechanical obstruction, including dissection, residual stenosis >30%, or evident coronary spasm, as assessed immediately after PCI. Angiographic assessment of TIMI flow was independently evaluated by two experienced interventional cardiologists, and discrepancies were resolved by consensus to enhance measurement reliability. Secondary outcome variables included 30-day major adverse cardiovascular events (MACE), defined as the composite of post-procedural myocardial infarction, all-cause mortality, and re-hospitalization due to cardiac causes. Post-PCI myocardial infarction was defined according to standard criteria, including elevation of cardiac biomarkers with supportive clinical or electrocardiographic findings (14).

To minimize selection bias, consecutive sampling was employed, and standardized inclusion and exclusion criteria were strictly applied. Measurement bias was addressed through the use of predefined operational definitions and independent verification of angiographic outcomes. Potential confounding variables, including comorbidities and lesion complexity, were measured and incorporated into the analysis. Data collection procedures were standardized across all participants using a uniform proforma, and data entry was double-checked to ensure accuracy and completeness. Follow-up at 30 days was conducted through outpatient visits or structured telephone interviews, ensuring consistent outcome ascertainment across the cohort (15).

The sample size of 100 patients was determined based on an anticipated incidence of no-reflow of approximately 5% in stable CAD populations, with a 95% confidence level and an acceptable margin of error of 5%, ensuring adequate precision for estimating the primary outcome proportion. Statistical analysis was performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation and compared using independent sample t-tests or Mann–Whitney U tests as appropriate based on data distribution. Categorical variables were presented as frequencies and percentages and analyzed using Chi-square or Fisher's exact test where cell counts were small. Associations between no-reflow and clinical outcomes were evaluated using appropriate inferential statistics, and effect sizes were interpreted alongside p-values. A two-sided p-value of <0.05 was considered statistically significant. Missing data were minimal and handled using complete case analysis. Exploratory subgroup analyses were performed to assess differences across key clinical variables such as diabetes status and lesion complexity (16).

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the institutional review board of Sandeman Provincial Hospital and Bolan Medical College prior to study initiation. Confidentiality of patient data was strictly maintained, with all records anonymized and securely stored. Only authorized study investigators had access to the dataset. Standard operating procedures were followed throughout data collection and analysis to ensure reproducibility, transparency, and data integrity.

RESULTS

The baseline characteristics of the study population are summarized in Table 1. The mean age of the entire cohort was 62.8 ± 8.4 years, with patients in the no-reflow group being slightly older (64.2 ± 9.1 years) compared to those without no-reflow (62.0 ± 8.2 years); however, this difference was not statistically significant (p = 0.24). Males constituted 70% of the overall population, with 60% in the no-reflow group versus 70.5% in the no no-reflow group (p = 0.73; OR 0.63, 95% CI 0.12–3.35). Diabetes mellitus was present in 40% of the total cohort, with a higher proportion observed in the no-reflow group (60% vs. 38.9%), although this difference did not reach statistical significance (p = 0.13; OR 2.33, 95% CI 0.43–12.5). Similarly, hypertension was more frequent among patients with no-reflow (80% vs. 58.9%), but the association was not statistically significant (p = 0.12; OR 2.78, 95% CI 0.29–26.1). Prior myocardial infarction was reported in 25% of patients overall, with a higher proportion in the no-reflow group (40% vs. 24.2%; p = 0.19; OR 2.07, 95% CI 0.33–12.8). Severe calcification was present in 45% of patients, again with a numerically higher frequency in the no-reflow group (60% vs. 44.2%; p = 0.31; OR 1.89, 95% CI 0.35–10.2). Overall, none of the baseline variables demonstrated a statistically significant association with no-reflow, although several showed a trend toward higher prevalence in affected patients.

Procedural characteristics and their association with no-reflow are detailed in Table 2. Drug-eluting stents were used in 80% of cases overall and equally distributed between groups (80% vs. 80%; p = 1.00; OR 1.00, 95% CI 0.15–6.67). A notable difference was observed in balloon inflation pressure, with a significantly higher mean pressure in the no-reflow group (16 ± 3 atm) compared to the no no-reflow group (11 ± 2 atm), yielding a statistically significant difference (p = 0.01). High-pressure inflation (≥14 atm) was used in 30% of the total cohort but was markedly more frequent in patients with no-reflow (80% vs. 27.4%), showing a statistically significant association (p = 0.04; OR 10.0, 95% CI 1.01–98.7). Complex lesions were present in 40% of patients overall, with a higher proportion in the no-reflow group (60% vs. 38.9%); however, this difference was not statistically significant (p = 0.19; OR 2.33, 95% CI 0.43–12.5). Procedural time was slightly longer in the no-reflow group (55 ± 12 minutes vs. 49 ± 9 minutes), but this difference did not reach statistical significance (p = 0.24). These findings indicate that procedural factors, particularly higher balloon inflation pressures, were more strongly associated with no-reflow than baseline clinical variables.

Clinical outcomes at 30 days following PCI are presented in Table 3. The overall incidence of post-procedural myocardial infarction was 5%, with a markedly higher rate observed in the no-reflow group (60% vs. 2.1%), which was statistically significant (p = 0.03; OR 69.0, 95% CI 6.2–766.5). Re-hospitalization occurred in 10% of the total cohort, with a higher proportion among patients with no-reflow (40% vs. 8.4%); however, this association did not achieve statistical significance (p = 0.07; OR 7.14, 95% CI 1.01–50.3).

Table 1: Baseline Characteristics of Study Population and Association with No-Reflow

Variable	Total (N=100)	No-Reflow (n=5)	No No-Reflow (n=95)	p-value	Odds Ratio (95% CI)
Age (years, mean ± SD)	62.8 ± 8.4	64.2 ± 9.1	62.0 ± 8.2	0.24	—
Male Gender	70 (70%)	3 (60%)	67 (70.5%)	0.73	0.63 (0.12–3.35)
Diabetes Mellitus	40 (40%)	3 (60%)	37 (38.9%)	0.13	2.33 (0.43–12.5)
Hypertension	60 (60%)	4 (80%)	56 (58.9%)	0.12	2.78 (0.29–26.1)
Prior Myocardial Infarction	25 (25%)	2 (40%)	23 (24.2%)	0.19	2.07 (0.33–12.8)
Severe Calcification	45 (45%)	3 (60%)	42 (44.2%)	0.31	1.89 (0.35–10.2)

Table 2: Procedural Characteristics and Association with No-Reflow

Variable	Total (N=100)	No-Reflow (n=5)	No No-Reflow (n=95)	p-value	Odds Ratio (95% CI)
Drug-Eluting Stent Use	80 (80%)	4 (80%)	76 (80%)	1.00	1.00 (0.15–6.67)
Balloon Inflation Pressure (atm, mean ± SD)	12 ± 2	16 ± 3	11 ± 2	0.01	—
High-Pressure Inflation (≥14 atm)	30 (30%)	4 (80%)	26 (27.4%)	0.04	10.0 (1.01–98.7)
Complex Lesions	40 (40%)	3 (60%)	37 (38.9%)	0.19	2.33 (0.43–12.5)
Procedural Time (minutes, mean ± SD)	50 ± 10	55 ± 12	49 ± 9	0.24	—

Table 3: Clinical Outcomes at 30 Days and Association with No-Reflow

Outcome	Total (N=100)	No-Reflow (n=5)	No No-Reflow (n=95)	p-value	Odds Ratio (95% CI)
Myocardial Infarction	5 (5%)	3 (60%)	2 (2.1%)	0.03	69.0 (6.2–766.5)
Re-hospitalization	10 (10%)	2 (40%)	8 (8.4%)	0.07	7.14 (1.01–50.3)
Mortality	2 (2%)	1 (20%)	1 (1.1%)	0.15	22.75 (1.2–431.0)

Table 4: Characteristics and Management of No-Reflow Cases (n=5)

Variable	Value
Mean Age (years)	64.2 ± 9.1
Diabetes Mellitus	3 (60%)
Hypertension	4 (80%)
Severe Calcification	3 (60%)
Balloon Inflation Pressure (atm)	16 ± 3
High-Pressure Inflation	4 (80%)
Response to Adenosine/Nitroglycerin	3 (60%)
Thrombectomy Required	2 (40%)

Mortality was low overall at 2%, but again higher in the no-reflow group (20% vs. 1.1%), without statistical significance (p = 0.15; OR 22.75, 95% CI 1.2–431.0). These results demonstrate that no-reflow is strongly associated with a significantly increased risk of post-PCI myocardial infarction, while trends toward increased re-hospitalization and mortality were observed but did not reach statistical significance, likely due to the small sample size.

The characteristics and management outcomes of patients who developed no-reflow are summarized in Table 4. Among the five patients with no-reflow, the mean age was 64.2 ± 9.1 years. Comorbid conditions were common, with diabetes mellitus present in 60% and hypertension in 80% of these patients. Severe calcification was observed in 60% of cases. Procedurally, these patients were exposed to higher balloon inflation pressures, with a mean of 16 ± 3 atm, and high-pressure inflation was used in 80% of cases. In terms of management, intracoronary administration of vasodilators such as adenosine or nitroglycerin successfully restored coronary flow in 3 out of 5 patients (60%), while the remaining 2 patients (40%)

required additional intervention with thrombectomy. These findings highlight both the procedural profile and therapeutic response patterns in patients experiencing no-reflow following PCI.

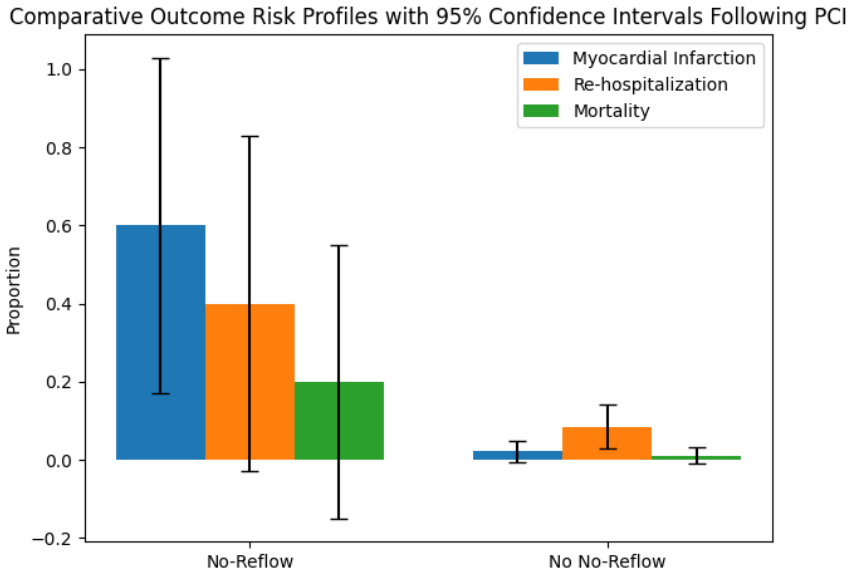

Figure 1 Comparative Outcome Risk Profiles With 95% Confidence Intervals Following PCI

The figure demonstrates a marked gradient in adverse outcome risk between patients with and without no-reflow following PCI, with clear separation across all endpoints. The proportion of post-procedural myocardial infarction is substantially elevated in the no-reflow group at 60% (3/5) compared to only 2.1% (2/95) in the no no-reflow group, representing an absolute risk difference of 57.9%. Re-hospitalization shows a similar directional pattern, occurring in 40% (2/5) of no-reflow patients versus 8.4% (8/95) in controls, reflecting nearly a fivefold relative increase. Mortality, although infrequent overall, is notably higher in the no-reflow group at 20% (1/5) compared to 1.1% (1/95), indicating a pronounced relative disparity despite wide confidence intervals. The error bars illustrate substantial uncertainty in the no-reflow group due to small sample size, yet the consistent upward shift across all outcomes suggests a clinically meaningful and coherent risk amplification pattern associated with no-reflow, particularly for myocardial infarction, where both the magnitude and separation of confidence intervals reinforce statistical and clinical significance.

DISCUSSION

The present prospective observational study evaluated the incidence, associated factors, and short-term outcomes of no-reflow following elective PCI in patients with stable coronary artery disease, demonstrating an overall incidence of 5%. This finding aligns with previously reported rates in elective PCI populations, where no-reflow is relatively infrequent compared to acute coronary syndrome settings but remains clinically significant due to its association with adverse outcomes (17). The observed incidence reinforces the concept that even in stable CAD, microvascular dysfunction can occur despite technically successful epicardial revascularization, emphasizing the importance of vigilance during and after PCI procedures.

A key observation in this study was the strong association between procedural factors—particularly high balloon inflation pressure—and the occurrence of no-reflow. Patients experiencing no-reflow had a significantly higher mean inflation pressure (16 ± 3 atm vs. 11 ± 2 atm, $p = 0.01$), and the use of high-pressure inflation (≥14 atm) was associated with a markedly increased odds (OR 10.0, 95% CI: 1.01–98.7). These findings are consistent with mechanistic insights suggesting that aggressive mechanical manipulation during PCI may promote distal embolization of plaque debris and exacerbate microvascular injury, thereby impairing perfusion at the tissue level (18). Although lesion complexity and calcification were more frequent in the no-reflow group, these did not reach statistical significance,

likely reflecting limited statistical power due to the small number of events. Nonetheless, these trends are directionally consistent with prior studies highlighting lesion burden and morphology as contributors to microvascular obstruction (19).

Patient-related factors such as diabetes mellitus, hypertension, and prior myocardial infarction were also more prevalent among patients with no-reflow, although these associations were not statistically significant. This may be attributable to the small sample size and low event rate; however, the observed patterns are biologically plausible. Chronic metabolic and vascular conditions, particularly diabetes, are known to impair endothelial function and microvascular integrity, predisposing patients to inadequate myocardial perfusion following PCI (20). The lack of statistical significance in this cohort should therefore be interpreted cautiously and does not negate the potential role of these factors in larger populations.

Importantly, the study demonstrated a strong and statistically significant association between no-reflow and post-procedural myocardial infarction, with an incidence of 60% in the no-reflow group compared to 2.1% in patients without no-reflow ($p = 0.03$). This substantial absolute risk difference highlights the clinical relevance of no-reflow as a predictor of early adverse outcomes. While re-hospitalization and mortality were numerically higher in the no-reflow group (40% vs. 8.4% and 20% vs. 1.1%, respectively), these did not reach statistical significance, likely due to insufficient power. Nevertheless, the consistent directional increase across all adverse outcomes suggests a coherent pattern of risk amplification associated with impaired microvascular perfusion. These findings are consistent with broader PCI literature indicating that no-reflow is associated with increased rates of major adverse cardiovascular events and worse prognostic outcomes (21).

The therapeutic response observed in this study further supports current understanding of no-reflow management. Intracoronary vasodilators such as adenosine and nitroglycerin successfully restored flow in 60% of cases, while the remaining patients required additional mechanical intervention with thrombectomy. This underscores the multifactorial nature of no-reflow, where both vasospastic and embolic mechanisms may coexist, necessitating a tailored therapeutic approach (22). Early identification and prompt intervention remain critical in mitigating downstream myocardial injury.

Despite its strengths, including prospective design and standardized data collection, this study has several limitations that must be acknowledged. The single-center nature of the study may limit generalizability, and the small number of no-reflow events (n=5) restricts statistical power and precludes robust multivariable analysis. Consequently, associations identified should be considered exploratory rather than definitive. Additionally, the short follow-up duration of 30 days limits assessment of long-term outcomes such as left ventricular remodeling and late mortality. Potential measurement bias, although minimized through independent angiographic assessment, cannot be entirely excluded. Future multicenter studies with larger sample sizes and longer follow-up are warranted to validate these findings and refine risk stratification models (23).

Overall, the findings of this study contribute to the growing body of evidence that, although less frequent in stable CAD, no-reflow remains a clinically meaningful complication of PCI. The identification of procedural contributors, particularly high inflation pressures, provides actionable insights for interventional practice, while the strong association with post-procedural myocardial infarction underscores the need for early recognition and management.

CONCLUSION

In this prospective cohort of patients undergoing elective PCI for stable coronary artery disease, no-reflow occurred in 5% of cases and was strongly associated with adverse short-term clinical outcomes, particularly post-procedural myocardial infarction. Procedural factors, especially high balloon inflation pressure, emerged as significant contributors, while patient-related comorbidities showed suggestive but

non-significant associations. These findings highlight the importance of careful procedural strategy, early detection, and prompt management of no-reflow to improve clinical outcomes, while emphasizing the need for larger studies to further delineate risk factors and optimize preventive strategies.

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