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FREQUENCY OF NO-REFLOW IN PRIMARY PCI WITH PRE-DILATATION AND WITHOUT PRE-DILATATION: A RETROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: No-reflow following primary percutaneous coronary intervention (PCI) remains a clinically significant complication, associated with adverse myocardial outcomes despite successful epicardial vessel recanalization. Data on its contemporary frequency and the influence of procedural strategy in real-world settings remain limited.

Objectives: To determine the frequency of no-reflow in a consecutive cohort of patients undergoing primary PCI, and to evaluate the impact of direct stenting versus balloon pre-dilatation on reflow outcomes.

Methods: This retrospective observational study included 72 consecutive patients presenting with acute ST-elevation myocardial infarction (STEMI) requiring primary PCI at Army Cardiac Hospital, Lahore. All procedures used 6-French access and third-generation drug-eluting stents. Procedural strategy was operator-determined. Reflow was classified as Type A (normal, TIMI 3), Type B (transient no-reflow, requiring intracoronary vasodilators), or Type C (persistent no-reflow, TIMI ≤2 at procedure end).

Results: Mean age was 56.5 years; 88.9% were male. The LAD was the most frequent target vessel (44.4%). Pre-dilatation was used in 53 cases (73.6%) and direct stenting in 19 (26.4%). Normal reflow was achieved in 55 patients (76.4%). The overall no-reflow rate was 23.6%, comprising transient no-reflow in 6 cases (8.3%) and persistent no-reflow in 11 (15.3%). No-reflow occurred in 28.3% of the pre-dilatation group versus 10.5% in the direct stenting group, with persistent no-reflow exclusively in the pre-dilatation arm (20.8% vs 0%).

Conclusion: No-reflow occurred in nearly one in four patients undergoing primary PCI in this cohort. Direct stenting was associated with substantially lower no-reflow rates compared to pre-dilatation and may represent a preferable strategy in suitable lesions to reduce microvascular injury during primary PCI.

KEYWORDS: no-reflow, primary PCI, STEMI, direct stenting, microvascular obstruction

INTRODUCTION

ST-segment elevation myocardial infarction (STEMI) is a leading cause of morbidity and mortality worldwide, and primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy when performed in a timely manner [1,2]. Despite successful restoration of epicardial coronary flow in most cases, a substantial proportion of patients develop impaired microvascular perfusion, a problem known as the no-reflow phenomenon. First described in experimental models and later confirmed in humans, no-reflow is characterized by inadequate tissue-level reperfusion despite a patent epicardial artery, and it is associated with larger infarct sizes, adverse ventricular remodeling, heart failure, and higher short- and long-term mortality [3–5].

The incidence of no-reflow in primary PCI for STEMI varies widely across studies, typically ranging from 10% to 30%, depending on how it is defined (angiographic TIMI flow, myocardial blush grade, or cardiac magnetic resonance), patient populations, and procedural factors [6–9]. Reported rates include approximately 10.9% in a large angiographic core laboratory analysis of the TOTAL trial, 18% in a Chinese STEMI cohort using a nomogram model, and up to 28.8% in a contemporary South Asian real-world series [4,10,11]. This variability reflects the multifactorial nature of the phenomenon, driven by distal embolization of thrombus or plaque debris, microvascular spasm, endothelial dysfunction, reperfusion injury, and inflammatory responses [12,13].

Established predictors of no-reflow include high thrombus burden (TIMI thrombus grade ≥4), low pre-PCI TIMI flow (0–1), prolonged symptom-to-balloon time, diabetes mellitus, cardiogenic shock, older age, and lesion characteristics such as long lesions or small vessel diameter [14–16]. The choice of revascularization strategy, direct stenting versus

balloon pre-dilatation, is a potentially modifiable factor. Direct stenting may reduce distal embolization by minimizing balloon-induced thrombus dislodgement, and observational data as well as some meta-analyses suggest lower no-reflow rates compared with conventional stenting after pre-dilatation [17–19]. Randomized evidence, however, remains mixed, and real-world adoption varies based on operator preference and lesion complexity.

Management of established no-reflow relies primarily on intracoronary vasodilators (adenosine, verapamil, nitroprusside, epinephrine) and glycoprotein IIb/IIIa inhibitors, with recent network meta-analyses supporting epinephrine and verapamil for improving final TIMI 3 flow [20,21]. Preventive strategies, including thrombus aspiration (though large trials like TOTAL showed no overall benefit), deferred stenting, and optimized pharmacotherapy, continue to be investigated. Despite these advances, no-reflow remains a significant unmet clinical need, particularly in resource-limited or high-thrombus-burden settings.

The present retrospective observational study was conducted to determine the contemporary frequency of no-reflow (classified as transient Type B or persistent Type C) in a consecutive cohort of 72 patients undergoing primary PCI, and to evaluate the impact of procedural strategy (pre-dilatation versus direct stenting) on reflow outcomes. Real-world data from a standardized protocol using third-generation drug-eluting stents and 6-French access are reported to inform procedural decision-making and identify opportunities for risk mitigation in routine clinical practice.

METHODS

Study Design and Population

This study was a retrospective, observational analysis conducted to evaluate the frequency of the no-reflow phenomenon in patients undergoing primary percutaneous coronary intervention (PCI). The study population consisted of 72 consecutive patients presenting for emergency revascularization. Patients were included if they presented with clinical and electrocardiographic evidence of acute myocardial infarction requiring primary PCI. Standard procedural data were prospectively recorded in a digital registry, which was subsequently reviewed for this analysis.

Procedural Protocol

All procedures were performed via a 6-French arterial access using standard femoral or radial techniques. Prior to the intervention, all patients received a standardized pharmacological loading regimen consisting of 300 mg of Clopidogrel and 300 mg of Aspirin, supplemented by an intravenous bolus of 10,000 IU of Heparin to maintain therapeutic anticoagulation.

The choice of revascularization strategy, either direct stenting or stenting following balloon pre-dilatation, was at the discretion of the interventional cardiologist based on lesion morphology and thrombus burden. Lesions were crossed using high-performance steerable coronary guide wires, including both hydrophilic-coated and non-hydrophilic workhorse wires. For patients in the pre-dilatation group, semi-compliant or non-compliant balloons were used for lesion preparation prior to stent delivery. Revascularization was performed using third-generation drug-eluting stents (DES) featuring bioresorbable or durable polymer technologies.

Angiographic Assessment and Definitions

Coronary angiograms were reviewed to assess vessel diameter, lesion length, and flow dynamics. The primary endpoint was the occurrence of the no-reflow phenomenon, which was classified into three distinct categories based on Thrombolysis in Myocardial Infarction (TIMI) flow grades and clinical response:

1. **Normal Reflow (Type A):** Defined as the achievement of an excellent angiographic result with TIMI 3 flow and no residual stenosis.
2. **Transient No-Reflow (Type B):** Defined as a temporary reduction in antegrade flow (slow flow or damping) that required the administration of intracoronary vasodilators, such as Adenosine or Nitroglycerin, to restore normal flow.
3. **Persistent No-Reflow (Type C):** Defined as persistent flow impairment (TIMI ≤ 2), "hazy" flow, or the complete absence of antegrade flow (no-reflow) that remained unresolved by the end of the procedure.

Cases where persistent no-reflow occurred immediately following balloon inflation, preventing the successful delivery or deployment of a stent, were recorded as "no stenting" procedures and included in the persistent no-reflow analysis.

Statistical Analysis

Continuous variables were expressed as means with standard deviations or medians with ranges, while categorical variables were presented as frequencies and percentages. The study specifically compared the incidence of Type A, B, and C reflow between the direct stenting and pre-dilatation cohorts to identify procedural factors associated with microvascular obstruction.

RESULTS

Demographics and Baseline Clinical Data

The study included 72 patients who underwent primary percutaneous coronary intervention. The mean age of the study population was 56.5 years, with ages ranging from 35 to 88 years. The cohort was predominantly male (n=64, 88.9%) compared to female (n=8, 11.1%). Pharmacological loading was near-uniform across the cohort, with all patients receiving 300 mg of Clopidogrel and 10,000 IU of Heparin as the standard antithrombotic and antiplatelet regimen; one patient (1.4%) did not receive Aspirin loading due to procedural status.

Procedural Characteristics and Vessel Involvement

The Left Anterior Descending (LAD) artery was the most frequent target vessel, involved in 32 cases (44.4%), followed by the Right Coronary Artery (RCA) in 26 cases (36.1%) and the Left Circumflex (LCX) artery in 14 cases (19.4%). The mean reference vessel diameter recorded was 3.1 mm. Procedural strategies were categorized into two groups: Pre-dilatation and Direct Stenting. Pre-dilatation was utilized in 53 cases (73.6%), while Direct Stenting was performed in 19 cases (26.4%).

In the pre-dilatation group, balloon inflation pressures ranged from 10 to 22 Bars, with a median pressure of 14 Bars. Standard 6 French guide catheters were used in all cases. Lesions were crossed using high-performance steerable guide wires, including both hydrophilic-coated and non-hydrophilic workhorse wires. Third-generation drug-eluting stents (DES) featuring bioresorbable or durable polymers were used for revascularization, with stent lengths ranging from 10 mm to 48 mm.

Baseline patient and procedural characteristics are summarized in ***Table 1***.

Table 1: Baseline Patient and Procedural Characteristics

Variable	Total Population (N=72)
Age (years), Mean (Range)	56.5 (35–88)
Gender (Male), n (%)	64 (88.9%)
Pharmacology, n (%)	
Clopidogrel (300 mg)	72 (100%)
Aspirin (300 mg)	71 (98.6%)*
Heparin (10,000 IU)	72 (100%)
Target Vessel, n (%)	
Left Anterior Descending (LAD)	32 (44.4%)
Right Coronary Artery (RCA)	26 (36.1%)
Left Circumflex (LCX)	14 (19.4%)
Procedural Strategy, n (%)	
Pre-dilatation	53 (73.6%)
Direct Stenting	19 (26.4%)
Vessel Metrics, Mean	
Reference Vessel Diameter (mm)	3.1
Guide Catheter Size	6 French

**One patient recorded as not receiving Aspirin loading due to procedural status.*

Incidence and Classification of Reflow Outcomes

Normal reflow (Type A) was achieved in 55 cases (76.4%). The overall frequency of no-reflow (combined Type B and Type C) was 23.6% (17 cases). Transient no-reflow (Type B), characterized by slow flow requiring adenosine or nitroglycerin, occurred in 6 cases (8.3%). Persistent no-reflow (Type C), characterized by TIMI 2 flow or "hazy" flow at the end of the procedure, was observed in 11 cases (15.3%).

Reflow outcomes stratified by procedural strategy are detailed in ***Table 2***.

Table 2: Reflow Outcomes by Procedural Strategy

Reflow Classification	Total (N=72)	Pre-dilatation (n=53)	Direct Stenting (n=19)
Normal Reflow (Type A)	55 (76.4%)	38 (71.7%)	17 (89.5%)
No-Reflow (Combined)	17 (23.6%)	15 (28.3%)	2 (10.5%)
Transient (Type B)	6 (8.3%)	4 (7.5%)	2 (10.5%)
Persistent (Type C)	11 (15.3%)	11 (20.8%)	0 (0%)
Procedural Failure: No Stenting (Post-Balloon)	5 (6.9%)	5 (9.4%)	0 (0%)

Impact of Procedural Strategy on Reflow Frequency

A significant disparity in reflow outcomes was observed between the two procedural strategies. In the Direct Stenting group, 17 of the 19 patients (89.5%) achieved normal reflow, with the remaining 2 cases (10.5%) experiencing only transient no-reflow (Type B). No cases of persistent no-reflow (Type C) occurred in the Direct Stenting group.

In contrast, the Pre-dilatation group demonstrated a higher frequency of flow disturbances. Only 38 of the 53 patients (71.7%) achieved normal reflow. All 11 cases of persistent no-reflow (100% of Type C outcomes) occurred within the pre-dilatation cohort. Notably, within this persistent no-reflow subset, 5 cases resulted in a final procedural status of "no stenting" because the target vessel developed persistent flow impairment immediately following balloon pre-dilatation and lesion preparation.

Analysis of balloon pressures indicated that pre-dilatation at or above 18 Bars was more frequently documented in cases that subsequently developed Type B or Type C reflow compared to those treated with lower inflation pressures.

DISCUSSION

Key Findings and Comparison with Literature

In this cohort of 72 consecutive patients undergoing primary PCI for STEMI, the overall incidence of no-reflow (combined transient and persistent) was 23.6% (17/72), with normal reflow (Type A) achieved in 76.4%. This rate is consistent with the 10–30% range reported in contemporary literature and comparable to rates in other real-world registries (e.g., 18–28.8%) [6,10,11]. Classifying outcomes into transient (Type B: 8.3%) and persistent (Type C: 15.3%) no-reflow revealed a clear procedural pattern: all 11 persistent cases (and all 5 procedural failures with no stenting) occurred exclusively in the pre-dilatation arm (n=53), while the direct stenting arm (n=19) had only transient no-reflow in 2 patients (10.5%) and no persistent events or procedural failures.

These findings are consistent with prior evidence favoring direct stenting. In the TOTAL trial angiographic sub-study, direct stenting was independently associated with lower no-reflow risk (adjusted OR 0.66), and thrombectomy provided additional benefit specifically in direct-stenting patients [4]. A 2015 meta-analysis and more recent observational data similarly suggest reduced embolization and better myocardial blush with direct stenting, particularly in high-thrombus lesions [17,19]. The complete absence of persistent no-reflow in our direct-stenting group (0% vs 20.8% in the pre-dilatation group) supports the hypothesis that avoiding balloon pre-dilatation limits distal thrombus embolization and microvascular plugging. Pre-dilatation pressures of 18 Bars or above were more frequently documented in patients who subsequently developed Type B or C no-reflow, which further implicates aggressive lesion preparation as a contributor to microvascular injury.

Baseline characteristics (mean age 56.5 years, 88.9% male, predominant LAD involvement) were typical of STEMI populations undergoing primary PCI. The high rate of pre-dilatation (73.6%) reflects real-world practice where operators often opt for lesion preparation in complex or thrombotic lesions, yet our data suggest this strategy may carry a higher risk of refractory no-reflow and even inability to deliver a stent (9.4% no-stenting rate in pre-dilatation arm). Pharmacologic loading was nearly universal (aspirin exception in 1.4% due to procedural status), consistent with guideline-directed care [2].

Clinical Implications

The association between pre-dilatation and adverse reflow outcomes has direct procedural implications. When anatomically feasible (e.g., visible thrombus, non-calcified lesions, adequate vessel visualization), direct stenting should be the preferred approach to reduce microvascular obstruction risk. For cases where pre-dilatation is necessary, operators should use lower inflation pressures, consider aspiration thrombectomy despite mixed trial evidence, or administer prophylactic intracoronary vasodilators before balloon inflation. Recent network meta-analyses support the routine availability of intracoronary epinephrine and verapamil for both prevention and treatment of no-reflow, given their effectiveness in restoring TIMI 3 flow [20]. In this cohort, transient cases responded to adenosine or nitroglycerin, while persistent cases did not resolve, which underscores the importance of upstream prevention.

Persistent no-reflow carried real procedural consequences; impairment was linked to procedural failure in nearly half of Type C cases, with the attendant risks of larger infarcts and worse clinical outcomes. Large registry data show no-reflow is associated with roughly doubled in-hospital mortality and higher rates of heart failure and cardiogenic shock [5,14]. In resource-constrained settings or centers managing high volumes of STEMI, these data support investments in training for direct-stenting techniques and the development of standardized no-reflow protocols.

LIMITATIONS

This study has several limitations. First, its retrospective, single-center design limits generalizability and precludes causal inference. Second, the modest sample size (N=72) and imbalance between arms (53 vs 19) reduce statistical power for subgroup analyses; no multivariable adjustment was performed, although the stark difference in persistent no-reflow (100% in pre-dilatation) is unlikely to be fully explained by confounding. Third, angiographic assessment was operator-reported without independent core laboratory adjudication, potentially introducing bias in TIMI flow

and no-reflow classification. Fourth, long-term clinical outcomes (mortality, heart failure, recurrent MI) were not captured, precluding correlation of reflow status with prognosis. Fifth, advanced intravascular imaging (IVUS or OCT) to quantify thrombus burden or plaque characteristics was not routinely used, which might have better stratified risk. Finally, the study period and specific stent platforms may not reflect the very latest technologies or pharmacotherapies.

Strengths and Future Directions

Strengths include consecutive patient inclusion, standardized pharmacological and procedural protocols, detailed classification of no-reflow into clinically actionable subtypes (transient vs persistent), and real-world applicability. The clear signal favoring direct stenting adds to the growing body of evidence supporting this strategy in primary PCI [4,17,19].

Future research should include adequately powered randomized trials comparing direct stenting versus pre-dilatation with modern stents and antithrombotic regimens, ideally stratified by thrombus burden (e.g., using OCT). Integration of risk scores (such as the recently validated no-reflow prediction score incorporating cardiogenic shock, delayed presentation, and lesion features) into pre-procedural planning could identify patients most likely to benefit from direct stenting or adjunctive therapies [6]. Novel approaches including deferred stenting, distal protection devices, and targeted anti-inflammatory agents warrant further investigation. Large multicenter registries with core-lab adjudication and long-term follow-up would better define the prognostic impact of no-reflow subtypes and refine preventive algorithms.

CONCLUSION

In this cohort, no-reflow occurred in nearly one-quarter of primary PCI procedures, with a markedly higher burden of persistent no-reflow and procedural failure confined to the pre-dilatation strategy. Direct stenting was associated with favorable reflow outcomes and may represent a straightforward, cost-effective approach to limiting microvascular obstruction when anatomically suitable. These findings support greater use of direct stenting in primary PCI, alongside careful attention to thrombus burden and balloon inflation parameters. Continued efforts to prevent and promptly treat no-reflow remain important for improving outcomes in patients with STEMI.

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