Original Article

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# Study of Incidence, Outcome and Relevant Factors of No Reflow and Slow Flow After Primary Percutaneous Coronary Intervention in Acute Myocardial Infarction

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## Abstract

**Background:** Early primary percutaneous transluminal coronary angioplasty (PTCA) is a cornerstone therapy for patients with ST elevation myocardial infarction(STEMI). However, the no-reflow and slow flow phenomena occur in nearly one-third of primary PTCA cases. This study aims to investigate the incidence and outcome of no-reflow/slow flow and the clinical, angiographic, and interventional characteristics associated with these phenomena.

**Methods:** This retrospective study analyzed a prospectively maintained database from October 2022 to September 2023, enrolling 118 STEMI patients who underwent primary PTCA. We evaluated various clinical, angiographic, and interventional factors correlated with the occurrence of no-reflow phenomena.

**Results:** Among the 118 STEMI patients, no-reflow/slow flow was observed in 39 patients (33.1%). In the no-reflow/slow flow group, 66% had diabetes, and 77% were current smokers, compared to 40% and 54%, respectively, in the reflow group. The left anterior descending (LAD) artery was the culprit in 69% of the no-reflow/slow flow cases and was associated with longer target lesion lengths. Ventricular tachycardia (VT) occurred in 18% of the no-reflow group versus 3.7% of the reflow group.

**Conclusion:** There is a high incidence of no-reflow/slow flow in our study, likely due to late presentation to the emergency room. Refractory no-reflow during primary PTCA is associated with an increased risk of major adverse cardiovascular events, underscoring the need for prompt intervention.

**Keywords:** Cardiovascular events, No-reflow phenomena, Primary PTCA, STEMI

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## Introduction

Acute myocardial infarction (MI) with ST-segment elevation is caused by plaque rupture or erosion of an atherosclerotic plaque that leads to thrombotic occlusion of the epicardial coronary artery[1]. Primary percutaneous transluminal coronary angioplasty (PTCA) of infarct related artery (IRA) is the best treatment modality to open the occluded coronary artery promptly[2]. Microvascular obstruction (MVO) and distal embolization reduce the beneficial effects of a successful recanalization of the infarct-related artery[1].

No-reflow phenomenon is a serious complication that occurs after opening of an infarct related artery and manifests as inadequate myocardial perfusion through a given segment of the coronary circulation without angiographic evidence of mechanical vessel obstruction[1,3]. It results in worse outcome of these patients; therefore no-reflow must be treated to avoid the adverse consequences[1].

Prevalence of no reflow is upto 32% in primary PTCA of ST elevation myocardial infarction (STEMI) patients and is associated with different clinical, angiographic and procedural risk factors[4]. Older age, comorbid status, prior MI, delayed presentation, and large thrombus burden are predominant risk factors[2]. It may occur due to incomplete stent expansion, vasospasm, use of multiple stents, longer stent length, dissection or in situ thrombosis[2].

Mechanism of no-reflow is multifactorial, but ischemia–reperfusion injury plays a key role[1,5]. Early detection, preventive measures, and treatment of no-reflow are crucial, and the drugs used for this purpose dilate the microcirculation, such as adenosine, glyceryl trinitrate, verapamil, and adrenaline[1,7,8].

In this study, we aimed to investigate the clinical, angiographic and procedural factors related with no reflow or slow flow in patients undergoing PTCA for acute STEMI.

## Materials and Methods

This was a retrospective study of prospectively maintained database over a period of one year at the Department of Cardiology, Manmohan Cardio-thoracic Vascular and Transplant Center (MCVTC). A prior approval from Institutional Review Committee {IRC number: 337(6-11)E2} was gained. Keeping in consideration the inclusion and exclusion criteria in study protocol, one hundred and eighteen STEMI patients who had undergone primary PTCA in the cardiac catheterization lab of MCVTC from October 2022 to September 2023 were enrolled and evaluated:

### Inclusion Criteria

- Acute STEMI patients who have undergone primary PCI

### Exclusion Criteria

- Patients who underwent plain old balloon angioplasty (POBA)
- Patients with unsuccessful primary PCI and pretreatment with fibrinolysis before primary PCI
- Acute non ST elevation MI (NSETMI) patients who have indications for primary PCI were not included
- Patients with severe liver or renal disease, neoplasms

Diagnosis of STEMI was based on 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR guidelines for the evaluation and diagnosis of chest pain. Significant coronary artery disease was defined as the presence of at least 70% stenosis in at least one epicardial artery. No reflow and slow flow were graded according to the TIMI grades. No reflow was defined as TIMI flow 0 or 1 and slow flow was graded as TIMI flow 2. TIMI 3 flow was considered reflow group.[4]

Data collection was limited to existing records, as no face-to-face interactions were conducted with patients or their families. The information about demographic profile, risk factors, clinical characters and examination findings were collected from in-patient files obtained from medical record section. Details regarding angiographic information and intervention and final in-hospital outcome were obtained from procedural notes, in-patient files and video recordings that were accessed from cardiac catheterization lab.

All of the patients received 300 mg of aspirin, 600 mg of clopidogrel and 40 mg of rosuvastatin immediately at emergency room and 10,000 U of intravenous heparin before PTCA. PTCA was performed using standard radial or femoral artery approach and IRA was successfully revascularised after angiography. Intracoronary medications were used as adjunctive pharmacotherapy to alleviate no reflow/slow flow as per operator choice. Manual aspiration thrombectomy was performed as bail-out procedure and GpIIb/IIIa inhibitors were used in patients with TIMI flow less than or equal to one.

Patients were divided into two groups based on post-procedural TIMI flow grades. Patients with TIMI score of 2 or less were categorized as no reflow or slow flow group and those with TIMI flow 3 were categorized as reflow group. Collected data was analyzed using IBM SPSS (version 21). Distribution of baseline characteristics categorized as continuous variables and categorical variables were expressed as mean ± standard deviation (SD) as frequency percentages (%) respectively. Comparison of demographic profile, risk factors, clinical characters and angiographic profile between no-reflow/slow flow and reflow group was done by conducting appropriate independent sample t-test/ Chi-square and Fischer's exact test. P-value ≤0.05 was taken as criteria for statistical significance.

## Results

During the period of study, total of 136 patients underwent primary PCI among which eight cases underwent POBA only. Similarly six NSTEMI patients and four chronic kidney disease (CKD) patients were also excluded from the study. After excluding these eighteen patients, a total of 118 patients were included for analysis among which 73 were men (61.9%) and rest were women (38.1%) with a mean age of 58±13. There were 39 cases in no reflow/slow flow group (33.1%) and 79 cases in reflow group (66.9%).

Table 1 shows the stratified data of baseline and presenting characteristics among no-reflow/slow flow versus reflow groups. No-reflow phenomena most commonly occurred in patients who were current smokers and who had underlying diabetes and the association was statistically significant with p-value <0.05.

In no-reflow/slow flow group diabetes was found in 66% of patients versus 40% in reflow group. Similarly, in no-reflow group 77% of patients were current smokers whereas in reflow group only 54% were current smokers. In addition, they were older in age, had co-existent hypertension and presented late in emergency room as compared to patients in reflow group. However statistically significant difference was noted only in patients with diabetes (p-value 0.011) and current smokers group (p-value 0.026).

**Table 1:** Baseline and presenting characteristics among study patients of no-reflow/slow flow and reflow groups

| Variables | Reflow(n=79) | No reflow and slow flow(n=39) | P-value |
|---|---|---|---|
| Age | 57.70+/-12.84 | 59.72+/-14.72 | 0.467*** |
| Male | 49 | 24 | 1.000* |
| Duration(hours) | 19.06+/-25.66 | 23.59+/-22.28 | 0.326*** |
| **Co-morbidities** | | | |
| Diabetes | 32 | 26 | 0.011* |
| Hypertension | 37 | 21 | 0.056* |
| Dyslipidemia | 19 | 4 | 0.088* |
| Hypothyroidism | 8 | 3 | 0.751* |
| Chronic Kidney Disease | 2 | 0 | 1.000** |
| Chronic Obstructive Airway Disease | 2 | 1 | 1.000** |
| **Prior History** | | | |
| Prior stroke | 3 | 0 | 0.550** |
| Prior Myocardial Infarction | 7 | 0 | 0.094** |
| Prior CABG | 1 | 1 | 1.000** |
| Prior PTCA | 5 | 0 | 0.169** |
| **Risk factors** | | | |
| Smoking | 43 | 30 | 0.026* |
| Alcohol | 24 | 18 | 0.105* |
| Chewing Tobacco | 6 | 4 | 0.728** |
| Substance abuse | 0 | 1 | 0.331** |
| **Clinical characters** | | | |
| Chest Pain | 62 | 33 | 0.471* |
| Dyspnoea | 19 | 18 | 0.020* |
| Syncope | 9 | 3 | 0.748* |
| Systolic BP(mm Hg) | 123.52+/-28.6 | 109.4+/-28.23 | 0.013*** |
| Heart Rate(bpm) | 79.78+/-21.15 | 90.51+/-20.78 | 0.010*** |
| LVEF(%) | 43.73+/-9.04 | 38.04+/-6.04 | 0.001*** |
| **Killip Class** | | | |
| Class I | 27 | 12 | 0.123* |
| Class II | 34 | 11 | |
| Class III | 12 | 8 | |
| Class IV | 6 | 8 | |
| **Territory by ECG** | | | |
| Anterior wall STEMI | 35 | 26 | 0.099** |
| Inferior wall STEMI | 36 | 12 | |
| Posterior wall STEMI | 4 | 1 | |
| Antero-lateral wall STEMI | 4 | 0 | |
| **In Hospital Complications and outcome** | | | |
| Ventricular Tachy-cardia | 3 | 7 | 0.015* |
| S/P DC shock | 3 | 7 | 0.015** |
| S/P CPR | 2 | 3 | 0.330** |
| Mortality | 4 | 4 | 0.437** |
| Repeat Vascular-ization | 2 | 2 | 0.598** |
| Stroke | 2 | 0 | 1.000** |
| Complete Heart Block | 10 | 3 | 0.541** |
| Heart Failure | 14 | 9 | 0.622* |
| Vascular Compli-cations | 6 | 3 | 1.000** |

*BP: Blood pressure; CABG: Coronary artery bypass graft; CPR: Cardio-pulmonary resuscitation; DC: Direct Current; LVEF: Left ventricular ejection fraction; PTCA: Percutaneous coronary intervention; STEMI: ST elevation myocardial infarction*

*=Chi-square **= Fischer ***=T-test

Dyspnea was the presenting complaint in most of the patients in no-reflow/slow flow group and had tachycardia, low blood pressure and low ejection fraction at baseline compared to reflow group. Heart failure was observed in 23% of no reflow/slow flow group versus 17.7% in reflow group. In no-reflow group, 20.5% of patients presented in Killip class IV versus 7.5% in reflow group. No-reflow/slow flow mostly occurred in anterior wall STEMI however the association was not statistically significant (p-value 0.099).

In no-reflow group , GP IIb/IIIa was used in six cases along with other intracoronary medication like adrenaline, glyceryl trinitrate and verapamil. Check CAG was done before discharge of these six cases which revealed TIMI 3 flow in three cases, TIMI 2 flow in two cases and TIMI 1 flow in one case. Thrombus aspiration was also done in one case along with use of GP IIb/IIIa inhibitors.

None of the patients with history of prior MI and prior PTCA developed no-reflow phenomena. Patients in no-reflow/slow flow group developed sustained ventricular tachycardia requiring DC shock, which is significantly higher in comparison to reflow group (18% versus 3.4%) with p-value 0.015. Mortality rate was 10.2% in no-reflow/slow flow group compared to 5% in reflow group, however the difference was not statistically significant.

In reference to angiographic and interventional data depicted at Table 2; left anterior descending artery was the culprit IRA in majority of the patients exhibiting no-reflow phenomena and the association was statistically significant (p-value 0.03). No-reflow/slow flow was noted in many cases when the target lesion was more proximal , longer in length and had high thrombus burden but the results was statistically significant only for target lesion length (p-value 0.031). The lesion was located proximally in 59% of patients in no-reflow group versus 37% in reflow group. Similarly, two stents were used in 15.4% of patients in no-reflow group versus 7.6% in reflow group.

**Table 2:** Comparison of angiographic and interventional findings among no-reflow/slow flow and reflow groups

| Variables | Reflow (n=79) | No reflow and slow flow (n=39) | P-value |
|---|---|---|---|
| Number of vessels | | | |
| Single vessel disease | 33 | 18 | 0.692* |
| Double vessel disease | 28 | 15 | |
| Triple vessel disease | 18 | 6 | |
| Infarct related coronary artery | | | |
| LAD | 32 | 27 | 0.030** |
| RCA | 32 | 10 | |
| LCx | 10 | 1 | |
| Major OM | 3 | 0 | |
| RI | 1 | 1 | |
| D1 | 1 | 0 | |
| Initial TIMI flow grade | | | |
| 0 | 44 | 23 | 0.964* |
| 1 | 20 | 9 | |
| 2 | 15 | 7 | |
| Target lesion location | | | |
| Proximal | 29 | 23 | 0.078* |
| Mid | 37 | 12 | |
| Distal | 13 | 4 | |
| Thrombus Burden | | | |
| Low( Grade 0 and 1) | 0 | 0 | 0.471* |
| Intermediate( Grade 2 and 3) | 17 | 6 | |
| High( Grade 4 and 5) | 62 | 33 | |
| Target lesion length(mm) | 18.87+/-8.20 | 22.69+/-10.13 | 0.031*** |
| Number of stents | | | |
| 1 | 73 | 33 | 0.207** |
| 2 | 6 | 6 | |
| Stent Length(mm) | 27.20+/-7.92 | 28.28+/-7.93 | 0.489*** |
| Stent Diameter(mm) | 2.99+/-0.41 | 3.06+/-0.37 | 0.348*** |
| Pre-dilation | 68 | 36 | 0.383** |
| Post-dilation | 59 | 33 | 0.248* |
| Final TIMI | | | |
| 1 | 0 | 15 | <0.001* |
| 2 | 0 | 24 | |
| 3 | 79 | 0 | |
| Check CAG at discharge | 0 | 6 | <0.001** |

*CAG: Coronary angiography; D1: 1st diagonal; LAD: Left anterior descending; LCx: Left circumflex; OM: Obtuse marginal; RCA: Right coronary artery; RI: Ramus intermedius; TIMI: Thrombolysis in myocardial infarction*

*=Chi-square **= Fischer ***=T-test

Multivariate logistic regression analysis was done with the variables that had significant statistical association between either of the groups. However, significant association was noted only with tachycardia at presentation (p-value 0.034) and in-hospital complication of ventricular tachycardia (p-value 0.018) as shown in Table 3.

**Table 3:** Independent associations for no-reflow/slow flow phenomena after primary PTCA

| Variable | Odds ratio | Confidence Interval | P-value |
|---|---|---|---|
| Diabetes | 2.520 | 0.987-6.42 | 0.053 |
| Smoking | 2.424 | 0.909-6.464 | 0.077 |
| Dyspnoea | 0.657 | 0.164-2.629 | 0.552 |
| Systolic BP | 0.992 | 0.973-1.011 | 0.40 |
| Heart rate | 1.028 | 1.002-1.054 | 0.034 |
| LVEF(%) | 0.940 | 0.854-1.034 | 0.200 |
| Target lesion length | 0.119 | 0.00-3.091 | 0.994 |
| Ventricular tachycardia | 5.542 | 1.347-22.793 | 0.018 |
| S/P DC shock | 2.091 | 0.387-11.288 | 0.391 |

*BP: Blood pressure; DC: Direct current; LVEF: Left ventricular ejection fraction*

## Discussion

Incidence of no-reflow/slow flow phenomena during primary PTCA of STEMI patients in our study is 33.1 % and is significantly associated with older age, smoking habit, co-existent diabetes, decreased LVEF at presentation, longer target lesion length and LAD being the culprit artery. Similarly, patients presenting with dyspnea, tachycardia and hypotension were significantly predisposed to develop no-reflow. Complication like ventricular tachycardia, need of DC shock and cardio-pulmonary resuscitation were also higher in no-reflow group indicating the increased incidence of major adverse cardiovascular events associated with refractory no flow. The incidence of no-reflow/slow flow phenomena in our study is comparable to studies conducted by Shahin et al. and Rezkella et al with reported incidence of 32.8% and 32% respectively[2,5,8]. In the study done by Harrison R. et al and Goutam D. et al , the incidence of no-reflow was 2.3% and 7.75% respectively[2,5]. Variable incidence of no reflow phenomena among different studies is supposed to be only due to different sample sizes, difference in duration of presentation and inclusion/exclusion criteria for selection of study populations.

There was increased propensity of no-reflow phenomena in older patients, diabetics, current smokers and late presenting patients in our study and similar results have been observed in many studies done earlier[4,6,8]. The mean age of patients in no reflow group was 59.72± 14.72 years and in reflow group was 57.70±12.84 years and this consistent with study done by Kumar D. et al[1]. Diabetes and smoking which are the major factors responsible for endothelial and micro-vascular dysfunction has been associated with no-reflow phenomena in our study and likewise depicted in study by Goutam D. et al. Endothelial dysfunction, micro-thrombosis, chronic inflammation and platelet dysfunction occurred predominantly in patients with diabetes and also results from exposure to free radicals and various toxins in smokers that leads to micro-vascular dysfunction and subsequent no-reflow phenomena[2]. We also found that patients presenting with dyspnea, low LVEF, low systolic BP and increased heart rate had higher probability of developing no-reflow phenomena. As there are high chances of no-reflow phenomena in STEMI patients presenting with heart failure and severe LV dysfunction, post-dilation is preferably discouraged and use of intracoronary vasodilators and intravenous anti-platelets is contemplated in this subset of patients.

Among the angiographic and interventional correlates, incidence of no-reflow/slow flow was higher in left anterior descending artery and patients with longer target lesion length which was similar as reported in study by Alidoosti M. et al[4]. They tend to develop more complications during hospital stay like ventricular tachycardia, subsequent DC shock and cardio-pulmonary resuscitation.

We also found that patients with anterior wall STEMI, higher Killip class and those with target lesion located proximally had higher incidence of no-reflow/slow flow although not statistically significant. Alidoosti M. et al. reported significant association between no-reflow phenomena and lesser TIMI flow at presentation and higher TIMI thrombus grades but in our study there was no significant association which is only supposed to be due to low sample size in our study[4].

There is complex association of various mechanisms that results in occurrence of no-reflow after primary PTCA. Among the vessel related etiologies; endothelial and microvascular dysfunction, distal embolization of thrombus, vessel spasm, excess post-dilation and reperfusion injuries contributes for major causes[7].

In addition, types of stent, length and diameter of stents, length and diameter of balloon, and balloon inflation pressure has been associated with no reflow phenomena. Pre-dilation and post-dilation status has no significant association with no-reflow phenomena in our study similar to results of Alidoosti M. et al[4]. No-reflow phenomena was significantly higher in patients in whom stents of longer length and wider diameter were used as reported in study done by Babapour B. et al. and Alidoosti M. et al[4,6]. However in our study, although there was higher incidence of no-reflow in patients in whom stents of longer length and diameter were used, the results were not statistically significant which also could be due to small sample size of our study and association of confounding factors like diabetes, smoking, vascular territory, thrombus burden and duration of symptoms that intricate the result .

However there were few limitations in our study like small sample size, derivation of data only from medical records rather than face to face interview, and analysis of in-hospital outcome only.

## Conclusion

This study depicts the higher risk groups that are not likely to benefit from primary PTCA. However, since the imaging modality in these acute conditions are not recommended before the procedure, the findings are best used to counsel the patients regarding the possible complications. Therefore, we need to be aware of the possible risk factors that are associated with the no-flow or slow-flow phenomenon.

### Declaration of patient consent

The authors certify that they have obtained consent from the parent for publication of clinical information and investigation report.

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### Conflicts of interest

There are no conflicts of interest.

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