ORIGINAL ARTICLE

# CLINICAL CHARACTERISTICS OF PATENTS WHO DEVELOPED SLOW FLOW/ NO-REFLOW AFTER POST-DILATATION WITH NON-COMPLIANT BALLOON DURING PRIMARY PERCUTANEOUS CORONARY INTERVENTION

**Chandar Parkash[1], Vashu Mal[1], Asim Shaikh[1], Dileep Kumar[1], Rameez Ahmed[1], Sara Masood[1], Jehanghir Ali Shah[1], Bashir Ahmed[1], Naveedullah Khan[1], Jawaid Akbar Sial[1]**

[1]National Institute of Cardiovascular Diseases, Karachi, Pakistan

**Objectives:** Post-dilatation with non-compliant (NC) balloons is a commonly used strategy to improve inadequate stent expansion but this strategy carries an increased risk of slow flow/no-reflow (SF/NR) due to distal embolization. Therefore, our objective was to evaluate the demographic, clinical, angiographic, and procedure characteristics among patients undergoing primary percutaneous coronary intervention (PCI) who developed slow flow/no-reflow (SF/NR) after post-dilatation with non-compliant (NC) balloons.

**Methodology:** In this cross-sectional observational study, we included consecutive patients with SF/NR after post-dilatation using NC balloon post stent deployment during primary PCI. The demographic, clinical, angiographic, and procedure characteristics were evaluated.

**Results:** In the sample of 107 patients, male were 77.6% (83) and mean age was 56.94 ± 10.47 years. The median chest pain to ER (emergency room) arrival time was 292 [180-394] minutes. A majority of the patients (66.4%) had multi-vessel disease. Mean length NC balloon was 10.57±1.98 mm and diameter was 3.5±0.26 mm. The mean number of inflation were 3.62±1.08, at mean maximal pressure of 20.43±2.49 mmHg, proximal edge pressure of 19.25±2.74 mmHg, and distal edge pressure of 14.64±2.01 mmHg. A total of 5.6% (6) patients developed adverse events and final TIMI (thrombolysis in myocardial infarction) III flow was achieved in 89.7% (96) of the patients.

**Conclusion:** SF/NR after post-dilatation during primary PCI is associated with a significant rate of adverse events and sub-optimal (<III) final TIMI flow. The detrimental effects of high pressure, short length, and increased number of inflations on post NC SF/NR need further investigations.

**Keywords**: ST-segment elevation myocardial infarction (STEMI), primary percutaneous coronary intervention (PCI), non-compliant (NC) balloon, slow flow/no-reflow (SF/NR)

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## INTRODUCTION

Primary percutaneous coronary intervention (PCI), is a recommended and treatment of choice for the prompt restoration of myocardium by reopening of the infarct-related coronary artery for the patients with acute ST-elevation myocardial infarction (STEMI).[1, 2] Yet sub-optimal flow even after the mechanical opening of the lesion due to micro-vascular obstruction, known as "slow flow/no-reflow", remained a major complications that reduces benefits of percutaneous revascularization.[3-5] Even though, pathophysiology of slow flow/no-reflow is not well explained, the phenomenon is considered to be a multifactorial with multiple possible etiologies including "micro-vascular obstruction of thrombus fragments", "micro-vascular spasm,", and/or "endothelial swelling due to ischemic/reperfusion injury" to name a few.[6-8]

Unlike any other population, the clinical data for primary PCI from Pakistan reported an incidence rate of slow flow/no-reflow ranging from 4.1% to as high as 36.6%, [4,5,9,10] as against 2.3% to 41% in other regions.[3] The incidence of slow flow/no-reflow has been observed to be associated with various factors including prolonged ischemic time, advanced age, low pre-procedure Thrombolysis in Myocardial Infarction (TIMI) flow grade, longer lesion length, and high thrombus burden.[3,4,11-14]

Under-expansion and stent malapposition increases the risk of in-stent restenosis (ISR), [15] post-dilatation using non-compliant (NC) balloons is a commonly used strategy by the interventionist to effectively improve inadequate stent expansion and position but this strategy carries an increased risk of slow flow/no-reflow due to distal embolization,[16-18] and resulting in higher risk of short- and long-term adverse cardiovascular events.[19] Owing to these concerns, the adjunctive post-dilatation remains at operators' discretion in primary PCI settings.[20]

Hence, it is important to understand the factors that may potentially leads to distal embolization resulting in slow flow/no-reflow after post-dilatation. A cautious use of NC balloons can improve its efficacy in the setting of primary PCI. Therefore, in this study our aim was to evaluate the demographic, clinical, angiographic, and procedure characteristics among patients undergoing primary PCI who developed "slow flow/no-reflow" after post-dilatation with NC balloons.

## METHODOLOGY

This cross-sectional study was conducted during study period of December 2021 to July 2022 after approval from ethical review committee of the National Institute of Cardiovascular Disease (NICVD), Karachi, Pakistan. Consecutive consenting patients with "slow flow/no-reflow" after post-dilatation using non-compliant (NC) balloon post stent deployment during primary PCI were included in this study. The specified inclusion criteria were patients shifted to catheterization laboratory for primary PCI with diagnosis of STEMI, stent deployed in the infarct related artery along with post-dilatation with NC balloon, and developed "slow flow/no-reflow". Non-consenting patients and patients in whom either stent was not deployed or post dilation was not performed by the primary operator were excluded from the study.

Diagnosis of STEMI was made based on "history of typical chest pain for at least 20 minutes" and "presenting 12-lead ECG showing ST elevation in at least two contiguous leads >2mm in men or >1mm in women in leads V2 to V3 and/or >1mm in other contiguous chest leads or limb leads". Data for this observational study were collected using a structured proforma which included demographic variables (gender age) and associated co-morbid conditions such as hypertension ("history of diagnosis or using anti-hypertensive medication for over 6 months"), diabetes ("history of diagnosis or using anti-hyperglycemic medication for over 6 months"), smoker ("history of or currently smoking 1 pack a year"), ischemic heart diseases (IHD), positive family history ("history of IHD in first blood relatives of under 45 years male and 55 years female"), and obesity ("body mass index ≥ 30 kg/m$^2$"). Type of myocardial infarction (MI), duration from onset of chest pain to emergency room arrival time (minutes), door to balloon time (minutes), presentation status including killip class, random blood sugar, blood pressure, heart rate, arrhythmias, and cardiac arrest were recorded for all the patients.

Primary PCI procedures were performed as per the standard guidelines, angiographic findings such as number of diseased vessels, culprit segment, TIMI flow, length of lesion, stent diameter, and procedure related characteristics such as use of export catheter, pre-dilatation, and detailing regarding post-dilatation including diameter and length of NC balloon, number of inflations, maximal pressure, proximal and distal edge pressure, and adverse events after no-reflow and final TIMI flow were recorded. As per the institutional protocol, drug-eluting stent (DES) was deployed in all the patients. The slow flow/no-reflow was defined "TIMI flow grade of <III in the infarct-related artery" after post-dilatation with NC balloon. Slow flow/no-reflow was treated with the use of intracoronary medication as per the institutional protocol and discretion of the primary operator.

Collected data were summarized with the help of mean ± standard deviation (SD) or median [interquartile range (IQR)] for quantitative characteristics while the qualitative characteristics were summarized as frequency (%). Data were analyzed using IBM SPSS version 21.

## RESULTS

In this study were summarized demographic, clinical and procedural characteristics of 107 patients who developed "slow flow/no-reflow" after post-dilatation with NC balloons during primary PCI. Male were 77.6% (83) of the total study sample and mean age was 56.94 ± 10.47 years. The median chest pain to ER (emergency room) arrival time was 292 [180-394] minutes. Arrhythmias were observed in 6.5% (7), 5.6% (6) had right bundle branch block, and thee patients (2.8%) were post-CPR (cardiopulmonary resuscitation). The baseline demographic characteristics, presentation, and clinical characteristics of the patients who developed "slow flow/no-reflow" after post-dilatation with NC balloons during primary PCI are presented in Table 1. The distribution of angiographic and procedural characteristics of patients who developed "slow flow/no-reflow" after post-dilatation with NC balloons during primary PCI are presented in Table 2.

A majority of the patients (66.4%) had multi-vessel disease with mean left ventricular end-diastolic pressure (LVEDP) of 17.49 ± 4.09 mmHg. Pre-dilatation was done in 52.3% (56), dottering with balloon in 2.8% (3), and export catheter was used in only one patient (0.9%).

**Table 1: Baseline demographic characteristics, presentation, and clinical characteristics**

| | Summary |
|---|---|
| **Total (N)** | **107** |
| **Sex** | |
| Male | 77.6% (83) |
| Female | 22.4% (24) |
| **Age (years)** | 56.94 ± 10.47 |
| **Type of MI** | |
| Anterior wall MI | 64.5% (69) |
| Inferior wall MI | 28% (30) |
| Posterior wall MI | 3.7% (4) |
| Anterior wall MI + RVI | 0.9% (1) |
| Lateral wall MI | 2.8% (3) |
| Chest pain to ER arrival time (min) | 292 [180-394] |
| Door to balloon time (min) | 100 [70-120] |
| **Killip Class** | |
| I | 77.6% (83) |
| II | 15.9% (17) |
| III | 5.6% (6) |
| IV | 0.9% (1) |
| Random blood sugar (mg/dL) | 180 [145-220] |
| Systolic blood pressure (mmHg) | 128.5 ± 23.35 |
| Heart rate (bpm) | 87.03 ± 16.24 |
| **Co-morbid conditions** | |
| Hypertension | 60.7% (65) |
| Diabetes | 43% (46) |
| Smoker | 30.8% (33) |
| Ischemic heart diseases | 4.7% (5) |
| Positive family history | 1.9% (2) |
| Obesity | 0.9% (1) |
| **Arrhythmia** | 6.5% (7) |
| AV dissociation | 0.9% (1) |
| Complete heart block | 1.9% (2) |
| Ventricular tachycardia | 3.7% (4) |

*MI: myocardial infarction, ER: emergency room, RVI: right ventricular infarction, AV: atrioventricular*

**Table 2: The distribution of angiographic and procedural characteristics**

| | Summary |
|---|---|
| **Total (N)** | **107** |
| **LVEF (%)** | 38.88 ± 6.88 |
| **LVEDP (mmHg)** | 17.49 ± 4.09 |
| **No of vessel diseased** | |
| Single vessel disease | 33.6% (36) |
| Two vessel disease | 42.1% (45) |
| Three vessel disease | 24.3% (26) |
| **Culprit coronary artery** | |
| Left anterior descending artery | 64.5% (69) |
| Right coronary artery | 20.6% (22) |
| Left circumflex | 14% (15) |
| Ramus | 0.9% (1) |
| **Maximum stent diameter (mm)** | 3.2 ± 0.29 |
| **Total stent length (mm)** | 27.79 ± 9.12 |
| **Pre-procedure TIMI flow** | |
| 0 | 48.6% (52) |
| I | 6.5% (7) |
| II | 28% (30) |
| III | 16.8% (18) |

*LVEF: left ventricular ejection fraction, LVEDP: left ventricular end-diastolic pressure, TIMI: thrombolysis in myocardial infarction*

Post-dilatation was done using NC balloon with mean length of 10.57 ± 1.98 mm and diameter of 3.5 ± 0.26 mm. The mean number of inflation were 3.62 ± 1.08, at mean maximal pressure of 20.43 ± 2.49 mmHg, proximal edge pressure of 19.25 ± 2.74 mmHg, and distal edge pressure of 14.64 ± 2.01 mmHg (Table 3). Slow flow was treated in all the patients with the help of intracoronary medication. A total of 5.6% (6) patients developed adverse events after slow flow/no-reflow, out of which 2 patient each developed atrial fibrillation and bradycardia and one patient each developed acute pulmonary edema and ventricular tachycardia (Table 3). An optimal final TIMI flow grade of III was achieved in a total of 89.7% (96) of the patients (Table 3).

**Table 3: Details of post-dilatation, associated complications, and final TIMI (thrombolysis in myocardial infarction) flow**

| | Summary |
|---|---|
| **Total (N)** | **107** |
| **TIMI flow before NC** | |
| 0 | 0% (0) |
| I | 0.9% (1) |
| II | 12.1% (13) |
| III | 86.9% (93) |
| Average number of inflation NC | 3.62 ± 1.08 |
| Average NC diameter (mm) | 3.5 ± 0.26 |
| Average NC length (mm) | 10.57 ± 1.98 |
| Average maximal pressure (mmHg) | 20.43 ± 2.49 |
| Average proximal edge pressure (mmHg) | 19.25 ± 2.74 |
| Average distal edge pressure (mmHg) | 14.64 ± 2.01 |
| **TIMI flow post NC** | |
| 0 | 19.6% (21) |
| I | 44.9% (48) |
| II | 35.5% (38) |
| III | 0% (0) |
| **Adverse event after slow flow** | 5.6% (6) |
| Atrial fibrillation | 1.9% (2) |
| Acute pulmonary edema | 0.9% (1) |
| Bradycardia | 1.9% (2) |
| Ventricular tachycardia | 0.9% (1) |
| **Final TIMI Flow** | |
| 0 | 0% (0) |
| I | 0% (0) |
| II | 10.3% (11) |
| III | 89.7% (96) |

*TIMI: thrombolysis in myocardial infarction, NC: non-compliant balloon*

## DISCUSSION

Post-dilatation with NC balloon after stent deployment is a common clinical practice to improve stent

expansion and position, intravascular ultrasound (IVUS) based studies revealed that without post-dilatation, optimal stent expansion can be achieved in only 15%-29% of the cases.[21] However, it has been also commonly observed to be associated with increased incidence of slow flow/no-reflow.[16-18] Hence, identification of factors associated with an increased risk of post-dilatation slow flow/no-reflow is of paramount importance. Therefore, in this study we have evaluated the demographic, clinical, angiographic, and procedure characteristics of patients who developed slow flow/no-reflow after post-dilatation with NC balloons during primary PCI. The clinical profile of these patients include, predominantly male patients, mostly in their 60$^{th}$ year of life, presented with anterior wall MI, mostly presented to ER after 4 hours of symptoms, and few (6.5%) in killip class III/IV, and with hypertension and diabetes as main co-morbid conditions. Post-dilatation was done using NC balloon with mean length of 10.57 ± 1.98 mm and diameter of 3.5 ± 0.26 mm. The mean number of inflation were 3.62 ± 1.08, at mean maximal pressure of 20.43 ± 2.49 mmHg, proximal edge pressure of 19.25 ± 2.74 mmHg, and distal edge pressure of 14.64 ± 2.01 mmHg. And in most of these patients (89.7%) TIMI III flow was achieved after intracoronary medication.

The post-dilatation does not only increase the risk of slow flow/no-reflow, but it also found to be associated with an increased risk of in-stent restenosis (ISR) and target vessel revascularization (TVR).[18] In an observational study by Gao P et al.,[18] ISR rate up to 1 year was 14.4% vs. 6.0%; p=0.02 with an adjusted odds ratio of 3.08 [1.20 to 7.91] for post-dilatation patients compared to non-post-dilatation patients.[18] Similarly, TVR rate was observed to be 5.6% vs. 0.8%, p=0.03 for post-dilatation patients compared to non-post-dilatation patients.[18] The association of post-dilatation with slow flow/no-reflow has been also reported by Soylu K et al.[17] in their study of 62 patients each randomized to post-dilatation and non-post-dilatation group. The slow flow/no-reflow rate was 35.5% vs. 14.5%; p=0.007 for patients with and without post-dilatation. They further reported that the post-dilation was independent predictor of slow flow/no-reflow on multivariable analysis along with female gender, TIMI flow after wire insertion.[17] The prognostic role of post-dilatation along with increased risk of slow flow/no-reflow has been also endorsed by other studies too.[19] In addition to post-dilatation, various other clinical and laboratory parameters are reported to be associated with the development of slow flow/no-reflow in these patients that included, older age, ischemic time, hypotension, blood sugar level, creatinine, platelet volume, neutrophil to lymphocyte ratio, high-density lipoprotein level, post-wiring flow, thrombus burden, and lesion type.[3, 4, 11-14, 17]

It has been postulated that inability of achieving post-dilatation with NC balloon within the stent boundary can result in edge dissection, coronary perforation, microvascular injuries, and distal embolization, resulting in slow flow/no-reflow.[18, 22] A single-center, randomized, single blinded, pilot trial of 50 patients with 30 cases and 20 controls by Ma M et al., [23] compared conventional rapid inflation/deflation strategy with prolonged balloon inflation strategy and reported the prolonged balloon inflation strategy to be associated with lower incidence of slow flow/no-reflow and improved myocardial perfusion.

To the best of our knowledge, in this study we are reporting the clinical profile of largest cohort of patients who developed slow flow/no-reflow after post-dilatation with NC balloons during primary PCI. Our study has certain limitation, first and foremost, lack of comparative control group of patents without slow flow/no-reflow. Secondly, the steps and technique of post-dilatation not strictly same for multiple operators due to observational nature of the study. And finally, the observational nature and single center experience remain the key limitations of this study. Further multicenter, randomized studies are warranted to identify the endogenous factors for the development of slow flow/no-reflow in these patients.

## CONCLUSION

In conclusion, slow flow/no-reflow after post-dilatation during primary PCI is associated with a significant rate of adverse events such as atrial fibrillation, bradycardia, acute pulmonary edema, and ventricular tachycardia along with sub-optimal (<III) final TIMI flow. The detrimental effects of high pressure, short length, and increased number of inflations on post NC SF/NR need further investigations. Further studies are warranted for the identification of endogenous risk factors for the development of slow flow/no-reflow after post-dilatation.

## AUTHORS' CONTRIBUTION

CP and VM: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. AS, DK, RA, SM, JALS, BA, NUK, and JAS: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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## Address for Correspondence:

**Dr. Vashu Mal,** Post Fellow Interventional Cardiology at National Institute of Cardiovascular Diseases (NICVD), Karachi, Pakistan.
**Email:** vm.lohana@gmail.com