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Predictors and Clinical Outcomes of Coronary Slow-Flow and No-Reflow Phenomenon Following Primary Percutaneous Coronary Intervention in Acute Myocardial Infarction: A Prospective Observational Study

Dr. Ajinkya Jayaji Pandhare[1], Dr. Prashant Prabhakar Udgire[2], Dr. Anantrao Laxman Phad[3], Dr. Bilal Khan[4]

[1]Senior Resident, Department of Cardiology, MGM Medical College and Hospital, Chhatrapati Sambhajinagar, Maharashtra, India (Corresponding Author)

[2]Professor and Head, Department of Cardiology, MGM Medical College and Hospital, Chhatrapati Sambhajinagar, Maharashtra, India

[3]Senior Resident, Department of Cardiology, MGM Medical College and Hospital, Chhatrapati Sambhajinagar, Maharashtra, India

[4]Senior Resident, Department of Cardiology, MGM Medical College and Hospital, Chhatrapati Sambhajinagar, Maharashtra, India

Abstract: ***Background**: Coronary slow-flow and no-reflow phenomena remain important complications of primary percutaneous coronary intervention (PCI) in patients with acute myocardial infarction (AMI). These conditions are associated with impaired myocardial perfusion despite successful epicardial coronary artery recanalization and are linked to adverse clinical outcomes. **Materials and Methods**: This prospective observational study was conducted at a tertiary-care cardiac center over 18 months. One hundred consecutive AMI patients undergoing primary PCI were enrolled. Patients were classified according to final TIMI flow grade into normal flow, slow-flow, and no-reflow groups. Clinical characteristics, laboratory parameters, echocardiographic findings, angiographic characteristics, and procedural variables were compared among groups. **Results**: Among 100 patients, 50 had normal flow, 42 had slow-flow, and 8 had no-reflow following PCI. Severe thrombus burden and higher TIMI thrombus grades were significantly associated with slow-flow/no-reflow. Patients with Killip class ≥2, elevated inflammatory markers, renal insufficiency, septal wall hypokinesia, LAD culprit vessel involvement, and severe thrombus burden demonstrated significantly higher rates of slow-flow/no-reflow. In-hospital mortality was significantly higher among patients with slow-flow/no-reflow compared with those with normal coronary flow. **Conclusion**: Coronary slow-flow/no-reflow remains a frequent complication of primary PCI. Clinical severity, inflammatory status, renal dysfunction, LAD involvement, and thrombus burden are important predictors. Early identification of high-risk patients may facilitate preventive strategies and improve outcomes.*

Keywords: No-reflow phenomenon; Slow-flow phenomenon; Primary PCI; STEMI; Acute myocardial infarction; TIMI flow; Thrombus burden

1. Introduction

India is undergoing a rapid transition with rising burden of coronary artery disease. ST elevation myocardial infarction (STEMI), a potentially fatal medical emergency brought on by a sudden, occlusive thrombus in the coronary artery, is one of the serious manifestation of CAD. There is noticeable decrease in mortality and morbidity when STEMI patients receive prompt reperfusion therapy.[1]

The second-most populous country in the world, India is incredibly diverse in terms of geography, race, culture, literacy, infrastructure, and economy. All of these elements present significant management difficulties for acute illnesses like STEMI.[1] According to World Health Organization (WHO) data, the incidence of coronary artery disease (CAD) is rapidly undergoing an "epidemiological transition" in India. It is now India's leading cause of death, surpassing communicable diseases. According to predictions, CAD mortality rates for men and women in India will rise by 117 percent and 105 percent, respectively, between 1990 and 2020.[2] STEMI is defined as myocardial ischemia with persistent ST segment elevation on electrocardiogram (ECG) and subsequent release of myocardial damage biomarkers. Non-ST segment elevation MI (NSTEMI). is defined as increased biomarkers alone in the absence of ST segment elevation.[1]

For patients with STEMI, percutaneous coronary intervention (PCI) is the recommended course of treatment .[3]

Since the invention of percutaneous coronary angioplasty in 1978, PCI, which produces better angiographic reperfusion states at 90 minutes than pharmacological reperfusion, has been the preferred reperfusion strategy in the context of STEMI.[4]

Despite the restoration of epicardial flow in the treated vessel, a sizable portion of patients do not experience adequate microvascular reperfusion; this is known as the slow flow phenomenon. No reflow is described as suboptimal myocardial reperfusion through a portion of the coronary circulation without angiographic evidence of

mechanical vessel obstruction by Kloner RA et al.[5]

Depending on the features of the population under study and the method used for its diagnosis, the incidence of slow flow or no reflow phenomenon ranges from 10% to 54% of procedures. It is linked to a poor clinical outcome, which includes a faster short- and long-term progression to heart failure and higher mortality.[7-10]

There is still much to learn about this unusual phenomenon. Thoughts have been developed in an effort to explain it, though. It was initially believed that prolonged ischemia and significant myocardial damage resulted in micro-vascular (capillary bed) damage and insufficient reperfusion. The development of no-reflow has recently been linked to additional factors, including distal embolization of the plaque or thrombus after balloon inflation. This theory was confirmed by the finding that patients with no flow have significantly more embolic material trapped in the distal protection device than patients with normal reflow (platelet-fibrin complexes, cholesterol crystals, and macrophages).[11] Systemic inflammatory response, platelet endothelial activation, micro vascular vasoconstriction, myocardial oedema, oxygen-derived free radicals, and calcium overload are additional factors that contribute, at least in part, to the pathogenesis of no reflow. The observation that elevated serum levels, of C-reactive protein (CRP) are associated with impaired coronary micro- vascular response to endothelium-independent vasodilator stimuli, suggests that systemic activation of inflammatory cells may enhance no-reflow.[12]

Additionally, these patients have increased cardiac neutrophil activation.[13] Numerous mechanisms, such as micro vascular obstruction by platelet aggregates and release of vasoactive and chemotactic mediators derived from platelets, may link platelets to no-reflow.[14]

By examining the TIMI (Thrombolysis in Myocardial Infarction) flow grade, the diagnosis of no reflow is made. We lack any proven treatment modalities because pathogenesis is still not fully understood. With varying degrees of success, medications such as nitroprusside, diltiazem, adenosine, nitroglycerin, mifebradil, nebivolol, dipyridamole, and statins have been tried.[15] Several authors have found a strong correlation between this phenomenon and the plasma levels of various markers or with specific IVUS (Intravascular ultrasound) visible atherosclerotic plaque features.[16-23]

However, because these sophisticated techniques are not always accessible in the emergency setting of an AMI (acute myocardial infarction), the utility of these diagnostic techniques is constrained. The goal of the current study was to identify the clinical factors, biochemical markers, angiographic findings, and procedural characteristics that predispose patients with AMI to no-reflow after PCI

2. Aim and Objectives

Aim

To study coronary slow flow and no reflow phenomenon after primary percutaneous intervention.

Objectives

1) To identify clinical, biochemical, angiographic and angioplasty procedural variables associated with slow flow or no reflow phenomenon in patient of acute myocardial ischemia (AMI) undergoing primary percutaneous coronary intervention (PCI).
2) To compare in-hospital mortality in these patients with normal flow patients.
3) To identify predictors of slow flow and no reflow phenomenon after primary percutaneous coronary intervention (PCI).

3. Materials and Methods

Study Design

The study will be a cross sectional prospective observational study

Study Duration

The study was conducted over a period of **18 months**.

Study Population

A total of **100 patients** eligible for primary percutaneous coronary intervention (PCI) were included in the study. The study population included patients admitted through:

- Emergency Department
- Intensive Cardiac Care Unit (ICCU)
- Cardiology OPD

Inclusion Criteria

All patients above 18 years, eligible for primary percutaneous coronary intervention (PCI) were included in the study.

Exclusion Criteria:

- Patients in whom no stenting will be done for various reasons such as unsuitable anatomy or Insignificant lesion in coronary angiogram.
- Chronic valvular heart disease
- No stenotic lesion (recanalized vessel)

Method for Data Collection

The study was conducted in patients undergoing primary PCI. A detailed history and physical examination was carried out. Necessary Investigations were done before procedure and patients were managed as per protocol of department. Door to balloon time, time of presentation to the hospital, angiographic procedure details were recorded.

4. Results

Classification of patients

	Frequency	Percent
Normal flow	50	50.0
Slow flow	42	42.0
No reflow	8	8.0
Total	100	100.0

Groupwise gender distribution

	Gender	Frequency	Percent
Normal flow	Female	14	28.0
	Male	36	72.0
Slow flow	Female	7	16.7
	Male	35	83.3
No reflow	Female	2	25.0
	Male	6	75.0

Alcohol and smoking status

	Frequency	Percent
Smoking	37	37.0
Alcohol	31	31.0

Co-morbidities and family history

	Frequency	Percent
Hypertension	32	32.0
Diabetes mellitus	63	63.0
Family history of CAD	13	13.0

Symptoms

	Frequency	Percent
Chest pain	93	93.0
Sweating	49	49.0
Dyspnoea	39	39.0
Giddiness	7	7.0

Dyspnoea NYHA Class

	Frequency	Percent
I	3	7.7
II	22	56.4
III	6	15.4
IV	8	20.5
Total	39	100.0

Infarct location (RWMA)

	Frequency	Percent
Anterior wall	50	50.0
Apex	49	49.0
Septum	59	59.0
Postero - lateral	26	26.0
Inferior	40	40.0
Lateral	1	1.0
Global	2	2.0

Echocardiography findings

		Frequency	Percent
Akinesia		20	20.0
Hypokinesia		76	76.0
Diastolic dysfunction	Grade I	48	48.0
	Grade II	5	5.0
	No	47	47.0

Distribution of patients as per LVEF

LVEF - %	Frequency	Percent
15-20	3	3.0
20-25	4	4.0
25-30	5	5.0
30-35	22	22.0
35-40	25	25.0
40-45	25	25.0
45-50	11	11.0
50-55	1	1.0
55-60	4	4.0
Total	100	100.0

TIMI flow grade

		Frequency	Percent
TIMI flow	TIMI I	5	5.0
	TIMI II	37	37.0
	TIMI III	50	50.0
	TIMI 0	8	8.0

Post dilatation

	Frequency	Percent
Post dilatation	50	50.0

Mortality

	Frequency	Percent
In hospital mortality	19	19.0

Association with demographic, co-morbidities and history

The association of slow flow/no-reflow phenomenon with demographic parameters, co-morbidities and family and past history of CAD was assessed using Chi-square test. We found no significant association between these parameters among the groups viz. normal flow, slow flow and no-reflow.

Association with symptoms

The association of slow flow/no-reflow phenomenon with symptoms and KILLIP classification was also assessed using Chi-square test. We found no significant association with any of the symptoms with as per groups of slow flow/no-reflow phenomena. According to KILLIP classification significant difference in distribution of patients among the groups viz. normal flow, slow flow and no-reflow was reported with p value of <0.001.

Association with haematological and biochemical parameters

The means of haematological and biochemical parameters were compared between the 3 study groups based on slow flow/no-reflow phenomena. There was no significant difference in the levels of TLC, NLR, random blood sugar reported between the group. While level of blood urea, serum creatinine and CRP were significantly higher in slow flow and no-reflow group compared to normal flow group

Association with infarct location

Similarly, we found significant association of infarct location at anterior wall with slow flow and no-reflow compared to normal flow. While similar significance was reported for inferior site of infarct but with normal flow than slow flow and no-reflow. No other infarct location was found to be associated with groups as per slow flow/no-reflow phenomena.

Association with Echocardiography findings – Akinesia, Hypokinesia, LVEF and Diastolic dysfunction

The association of slow flow/no-reflow phenomenon with echocardiography findings i.e. akinesia, hypokinesia, ejection function and diastolic dysfunction was assessed. We found no significant association between these parameters among the groups viz. normal flow, slow flow and no-reflow.

Distribution of patients as per presence or absence of thrombolysis status

The distribution of patients as per presence of thrombolysis

status was compared among the groups according to slow flow/no-flow phenomenon. There was no significant difference in the distribution of patients as per thrombolysis status was found between the groups viz. normal flow, slow flow and no-reflow. The distribution of patients is shown in Table 19 and presented graphically.

Comparison of door to balloon time as per slow flow/no-reflow phenomenon

		Mean	SD	p value
Door to balloon time	Normal flow	161.66	230.75	0.721
	Slow flow	131.79	90.06	
	No-reflow	150.88	101.24	

Association with artery involved

The association of patients distribution among study groups with artery involved, revealed association of only left anterior descending artery (LAD) (p=0.02), with more number of patients in slow flow and no-reflow compared to normal flow group. While involvement of no other artery was associated with patient distribution in study groups.

Comparison of lesion location and lesion length as per slow flow/no-flow phenomenon

The lesion location and lesion length among the study population were compared using Chi-square test. The lesion location as well as lesion length did not differ significantly between the study groups, viz. normal flow, slow flow and no-reflow.

Association with thrombus burden, multi vessel disease and TIMI thrombus grade

The thrombus burden, TIMI thrombus grade were significantly associated with the slow flow/no-reflow phenomenon, with significantly higher number of patients having severe TIMI thrombus grade in slow flow and no-reflow groups compared to patients with normal flow. While the patients with slow flow were more with higher grade of TIMI thrombus grade than normal flow patients. We found no significant association between multivessel disease and slow flow/no-reflow phenomenon.

Association with TIMI flow

The TIMI flow grade were significantly associated with the slow flow/no- reflow phenomenon. Regarding TIMI flow grade, all patients with normal flow belonged to grade III while there were 37 and 5 patients in grade II and I, respectively in slow flow group, and all 8 in no-reflow group belonged to TIMI 0 group.

Distribution of patients as per aspiration thrombectomy, and post dilatation status

The distribution of patients as per patients who underwent aspiration thrombectomy and post dilatation were compared among the groups according to slow flow/no-flow phenomenon. No significant difference were found among patients who underwent aspiration thrombectomy and post dilatation with slow flow/no-reflow phenomenon.

Association with mortality

In the study population, significantly higher mortality was reported among patients with slow flow and no-reflow as compared to normal flow patients.

5. Summary and Conclusion

The present prospective study was conducted to identify clinical, biochemical, radiological, angiographic, and angioplasty procedural variables associated with the slow flow or no-reflow phenomenon in patients with AMI undergoing primary PCI, and to compare in-hospital mortality in these patients with that of normal flow patients. A total of 100 patients eligible for primary PCI were included in the study.

The thrombus burden, TIMI thrombus grade, and flow grade were significantly associated with the slow flow/no-reflow phenomenon, with a significantly higher number of patients having a severe TIMI thrombus grade in the slow flow and no reflow groups compared to patients with normal flow. Slow flow patients had a higher grade of TIMI thrombus than normal flow patients.

Clinical risk factor Killip class 2 or above , raised inflammatory markers, renal insufficiency, septal wall hypokinesia, LAD as culprit vessel, with severe thrombus burden are strong and significant predictors of slow flow/no-reflow phenomenon in our study.

Patients with slow flow and no reflow had a significantly higher death rate than patients with normal flow.

6. Discussion

The present study demonstrated that coronary slow-flow/no-reflow occurred in 50% of patients undergoing primary PCI (42% slow-flow and 8% no-reflow). The findings support previous studies showing that thrombus burden and impaired microvascular perfusion are major contributors to this phenomenon.

Severe thrombus burden emerged as one of the strongest angiographic predictors. Distal embolization of thrombotic material during PCI can lead to microvascular obstruction and impaired myocardial reperfusion. These findings are consistent with those reported by Alidoosti et al., Sharma et al., and Fajar et al., who identified thrombus burden as a major determinant of no-reflow

Clinical factors including Killip class ≥2, renal dysfunction, inflammatory activation, and LAD culprit vessel involvement were also associated with higher risk. LAD infarctions typically involve larger myocardial territories, resulting in more extensive ischemic injury and greater susceptibility to microvascular dysfunction.

Importantly, slow-flow/no-reflow was associated with significantly higher mortality. These findings reinforce previous evidence that impaired myocardial reperfusion remains an independent predictor of adverse outcomes despite successful epicardial vessel recanalization.

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