Original Article

PREDICTORS AND IN-HOSPITAL MORTALITY OF SLOW FLOW/NO-REFLOW AFTER PERCUTANEOUS CORONARY INTERVENTION IN PATIENTS WITH ST-ELEVATION MYOCARDIAL INFARCTION

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ABSTRACT

Background: To detect the frequency of slow flow/no-reflow in patients with ST-elevation myocardial infarction (STEMI) after the primary percutaneous coronary intervention (P-PCI), determine its association with various clinical, echocardiographic & angiographic factors and detect in-hospital mortality in these patients.

Material and Methods: It was a descriptive, cross-sectional study in which 153 STEMI patients were included by convenient sampling at the Rawalpindi Institute of Cardiology. After approval from the Hospital's ethics committee, the study was conducted from March 2022 to August 2022. After obtaining informed written consent, all the patients underwent P-PCI. The statistical analysis was done with the Statistical Package for the Social Sciences version 25.

Results: Slow flow/no-reflow occurred in 19(12.4%) patients. It had a significant association with age groups (p-value = 0.03), prior myocardial infarction (MI) (p-value = 0.000), time to treatment initiation (p-value = 0.000), Killip class (p-value = 0.000), MI type (p-value = 0.036), target lesion length (p-value = 0.000), occlusion site (p-value = 0.004) and thrombus grade (p-value = 0.031). Out of 153 patients, 13(8.5%) patients died with 8(61.5%) of them with slow/no-reflow.

Conclusion: Slow flow/no-reflow is a frequent complication (12.4%) in patients who underwent P-PCI for STEMI. Its significant predictors are advanced age, prior MI, longer time to treatment initiation, higher Killip class, anterior wall MI, longer target lesions, proximal occlusion site and high thrombus burden. The in-hospital mortality is much higher in these patients.

Key Words: ST Elevation Myocardial Infarction, Patients, Coronary artery disease

doi: https://doi.org/10.51127/JAMDCV5I3OA05

How to cite this:
Shah M, Mohsin M, Satti KN, Shah MU. Predictors and in-hospital mortality of slow flow/no-reflow after percutaneous coronary intervention in patients with st-elevation myocardial infarction JAMDC. 2023;5(3): 144-151
doi: https://doi.org/10.51127/JAMDCV5I3OA05

INTRODUCTION

Coronary artery disease (CAD) affects 126 million people annually worldwide, with an estimated 9 million deaths in 2017. This figure is projected to increase to 23.6 million by 2030.[1] In addition, it is also a significant financial burden for countries. The financial cost attributed to CVD was US$863 billion globally, which will rise to > US$1 trillion by 2030.[1] ST elevation myocardial infarction (STEMI) is a common clinical manifestation of CAD responsible for a major proportion of cardiovascular mortality, morbidity, and disability.[2]

Treatment in STEMI aims to achieve adequate and early revascularization of the

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Date of submission 18-05-2023
Date of review 24-05-2023
Date of acceptance 13-10-2023

ischemic coronary artery. The primary treatment option, P-PCI, restores coronary blood flow with a high success rate. But in some cases, the phenomenon of slow flow or no-reflow occurs.[3] No reflow is characterized by hypoperfusion of the myocardial tissue. However, the epicardial coronary arteries are patent, provided that other hypoperfusion causes, such as spasm, thrombus, dissection, and residual stenosis, have been ruled out. Slow reflow is defined as less decrease in coronary blood flow.[4] This is attributed to failure to attain reperfusion in the ischemic myocardium resulting from microvascular obstruction. No reflow/slow-flow pathogenesis involves ischemic reperfusion injury, endothelial swelling, myocardial edema, capillary obstruction, inflammation, oxygen-free radical generation, calcium overload, and distal coronary embolization.[5,6] The Thrombolysis in Myocardial Infarction (TIMI) flow grade determines coronary reperfusion achieved after P-PCI, with TIMI grade 3 showing complete reperfusion.[7] TIMI grade 0-1 indicate no reflow and TIMI grade 2 shows slow flow. The lesser the TIMI grade flow, the higher the chances of cardiovascular deaths and major adverse cardiovascular events (MACE).[8]

Despite the advances in Interventional Cardiology, no-flow/slow reflow occur in some patients after P-PCI, with the reported cases ranging from 12%-32.8%. According to the literature, various factors predispose to slow/no-reflow, such as gender, age, Killip class, hypertension, diabetes mellitus, creatinine, peak creatine kinase, blood glucose, C reactive protein, initial TIMI grade, delay in initiating treatment, lesion length and thrombus burden.[9,10]

Various clinical, echocardiographic, and angiographic parameters are linked to no reflow/slow flow, but the association of no-reflow/slow flow with various risk factors has not been fully established. Identifying predictors of this phenomenon will help interventional cardiologists guide and modify interventional strategies to prevent slow flow/no-reflow and improve outcomes.

MATERIAL AND METHODS

It was a descriptive, cross-sectional study in which a nonprobability convenient sampling technique included 153 patients presenting with STEMI at the Rawalpindi Institute of Cardiology, Rawalpindi. After approval from the Hospital's ethics committee, the study was conducted from March 2022 to August 2022. After obtaining informed written consent, the patient's details were noted on a Proforma. The clinical manifestations, electrocardiogram (ECG), elevated cardiac markers (Troponin and Creatine kinase), and coronary angiography confirmed the diagnosis of STEMI. Oral aspirin, clopidogrel, and intravenous heparin were administered in all patients before P-PCI. All the patients underwent P-PCI within 24 hours of symptoms using a standard radial approach. The exclusion criteria were the patients with severe kidney or liver disease, hematological disorders, previous coronary artery bypass grafting (CABG) or Unsuccessful P-PCI, time to treatment initiation > 24 hours, or those who received fibrinolytic treatment/glycoprotein IIb/IIIa inhibitors before undergoing PCI. TIMI flow grade 3 indicated complete reperfusion, grade 0-1 no-reflow, and TIMI grade 2 showed slow flow. Patients with normal flow were included in one group and those with slow/no-reflow were allocated to another group. The relation of various clinical, echocardiographic, and angiographic factors was compared between the two groups. The factors evaluated in our study were patient age, gender, time to initiation of treatment, Killip class, diabetes mellitus (DM), smoking, hypertension (HTN), hyperlipidemia, obesity, prior myocardial infarction (MI), family history of CAD, type of MI, coronary artery involved, target lesion length, site of lesion, number of diseased vessels, initial TIMI flow grade,

thrombus grade and left ventricular ejection fraction (LVEF).

The results were based on statistical analysis with the Statistical Package for the Social Sciences (SPSS) version 25. Quantitative variables such as age were presented as mean & standard deviation and qualitative variables including gender, Hypertension and diabetes were shown using frequency & percentage. A Pearson Chi-square test determined the relation of various variables between patients with slow/no-reflow and normal flow. A significant p value was ≤ 0.05.

RESULTS

Patients had a mean age of 52.64±10.30, ranging from 20 to 77 years.

Out of 153 patients, slow flow/no-reflow occurred in 19(12.4%) patients and 134(87.6%) patients had normal flow.

Thirteen patients (68.4%) developed no-reflow and 6(31.6%) had slow flow. The relation of slow/no-reflow with various risk factors showed statistically significant results for age groups, time to treatment initiation, Killip class and prior MI. Patients with advanced age are prone to experience slow flow/no-reflow. The greater the time to treatment initiation, the higher the chances of slow flow/no-reflow. Higher Killip classes (III and IV) and previous MI episodes are associated with the phenomena. Table 1 shows these results.

Table 1: Association of Slow Flow/No-Reflow with Various Risk Factors

Parameter	Slow/No-Reflow	Normal Flow	Total	Chi-Square Statistic	p-value
Age groups				26.445	**0.03***
<30	0	2	2		
30-40	0	16	16		
41-50	2	45	47		
51-60	5	49	54		
61-70	10	18	28		
71-80	2	4	6		
Total	19	134	153		
Gender				1.967	0.579
Male	14	113	127		
Female	5	21	26		
Total	19	134	153		
Time to treatment initiation				66.370	**0.000***
<3 hours	0	32	32		
<6 hours	4	60	64		
<9 hours	5	26	31		
<12 hours	4	11	15		
<15 hours	4	2	6		
< 18 hours	1	2	3		
< 21 hours	1	1	2		
Total	19	134	153		
Killip class				57.274	**0.000***
I	2	84	90		
II	4	38	42		
III	8	10	15		
IV	5	2	6		
Total	19	134	153		
Hypertension				1.971	0.578
Nonhypertensive	13	80	93		
Hypertensive	6	54	60		
Total	19	134	150		
Diabetes mellitus				1.604	0.658
Nondiabetic	14	100	114		
Diabetic	5	34	39		
Total	19	134	153		
Smoking				2.110	0.550

Nonsmoker	12	101	113		
Smoker	7	33	40		
Total	19	134	153		
Hyperlipidemia					
Absent	15	114	129	6.707	0.08
Present	4	20	24		
Total	19	134	153		
Obesity					
Nonobese	19	122	141		
Obese	0	12	12	1.846	0.605
Total	19	134	153		
Prior MI					
Absent	12	126	138		
Present	7	8	15	33.467	**0.000***
Total	19	134	153		
Family History of CAD					
Present	15	127	142		
Absent	4	7	11	7.187	0.06
Total	19	134	153		

***Statistically Significant**

The relation of slow flow or no-reflow with echocardiographic and angiographic parameters was also determined. It significantly correlates with the type of MI, target lesion length, occlusion site, and thrombus grade. Anterior wall MI and high thrombus burden were related to a high frequency of slow or no-reflow. The phenomenon was more common in patients with diffuse target lesions followed by tubular lesions (Table 2).

Table 2: Association of Slow Flow/No-Reflow with Echocardiographic and Angiographic Parameters

Parameter	Slow/No-Reflow	Normal Flow	Total	Chi-Square Statistic	p-value
Type of MI					
Anterior	14	63	77		
Lateral	3	12	15	13.497	**0.036***
Inferior	2	59	61		
Total	19	134	153		
Coronary artery involved					
Left anterior descending (LAD)	10	76	86		
Left circumflex artery (LCX)	2	20	22	5.265	0.510
Right coronary artery (RCA)	7	38	45		
Total	19	134	153		
Number of diseased vessels					
Single vessel disease (SVD)	9	72	81		
Double vessel disease (DVD)	8	44	52	3.348	0.764
Triple vessel disease (TVD)	2	18	20		
Total	19	134	153		
Target lesion length					
Focal (<10 mm)	5	104	109		
Tubular (10-20 mm)	6	26	30	47.111	**0.000***
Diffuse (>20 mm)	8	6	14		

Total	19	134	153		
Site of occlusion					
Proximal	9	19	28	18.981	**0.004***
Mid	3	55	58		
Distal	7	60	67		
Total	19	134	153		
Initial TIMI flow grade					
TIMI flow grade 0-2	18	117	135	8.012	0.533
TIMI flow grade 3	1	7	18		
Total	19	134	153		
Thrombus grade					
Low	2	65	67	26.704 **0.031***	
High	17	69	86		
Total	19	134	153		
LVEF					
20%-29%	0	6	6	7.314	0.604
30%-39%	7	55	62		
40%-49%	8	61	69		
50%-59%	4	12	16		
Total	19	134	153		

***Statistically Significant**

Out of 153 patients, 13(8.5%) patients died with 8(61.5%) patients with slow flow/no-reflow group and 5(38.5%) patients with normal flow. The rest of 140(91.5%) patients were discharged, 11(7.85%) with slow flow/no-reflow and 129(92.15%) with normal flow. The p-value was statistically significant (0.000).

DISCUSSION

Slow flow/no-reflow is common after P-PCI and is associated with worse outcomes of higher mortality and left ventricular dysfunction.[11] In our study, out of a total of 153 patients, 12.4% of patients developed no-reflow/slow flow. In other studies, slow flow/no-reflow occurred in 15.7%, 18%, 22.2%, and 25.9% of the patients.[12-15] Slow flow/no-reflow occurred in 38.9% and 31.3% of the patients in two other studies, respectively.[11,16] Its frequency was much greater in two other studies in Pakistan. In a study by Farahe et al., 25% of the patients developed the phenomenon, whereas, in the other study, the frequency of slow flow/no-reflow was 31.4%.[17,18]

Our results showed a significant association between increased age with slow flow/no reflow. Literature has also reported a significant relation between age with slow/no-reflow, with a greater percentage of older patients developing this phenomenon.[12, 14-16] Other studies done in Pakistan revealed a significant relationship of age with the phenomenon.[17,18] Our study found no significant association of gender with slow flow/no-reflow, similar to two other studies.[16,19] Conversely, Elakabawi et al. and Nizami et al. revealed its association with the female gender.[14,18] In our study, slow flow/no-reflow had no relationship with diabetes mellitus, smoking, hypertension, hyperlipidemia, obesity, and a family history of CAD. The phenomenon was only associated with prior MI episodes. Kakar et al. revealed that prior MI episodes were significantly correlated with slow/no-reflow.[13] A study did not link slow/no-reflow with risk factors.[16] In a study by Elakabawi et al., no significant association was seen with any risk factors except smoking.[14] Farahe et al. and Rajesh et al. found a significant link between slow flow/no-reflow with diabetes mellitus.[17,20]

Our study revealed a significant relation between slow flow/no-reflow and anterior wall MI, similar to the studies by Kakar et

al. and Alidoosti et al.[13,16] On the other hand, no association was seen by Zhang et al.[21] Our study showed no relation between slow flow/no-reflow and coronary artery involved whereas, Alidoosti et al. and Nizami et al. found significant results with LAD involvement common in slow flow/no-reflow.[16,18] No significant relationship between the coronary artery and slow flow/no-reflow was observed.[13,14] Our study showed a significant correlation between target lesion length, lesion site, thrombus grade, Killip class & time to treatment interval and slow/no-reflow. The phenomenon is associated with longer lengths of target lesions.[15,16] In contrast, a study showed no relation between the two.[22] Kakar et al. and Rajesh et al. have demonstrated its relation with the site of lesion, with more cases in patients with proximal lesions[13,20,] whereas other studies found no association.[14,16] A statistically higher proportion of patients with high thrombus burden developed slow/no-reflow than patients having low thrombus burden in various studies.[13,14,16,17] In studies by Kakar et al., Elakabawi et al., and Sabin et al., slow flow/no-reflow was related to the high Killip class.[13-15] A significant association was seen between slow flow/no-reflow and longer time to treatment interval.[15,18,19] Soeda et al. and Kakar et al. found no association between the two parameters.[11,13] There was no association of the phenomenon with TIMI flow. Similar results were reported by Kakar et al.[13] In contrast, Nizami et al. reported a correlation of the phenomena with initial low TIMI flow.[18] Similarly, in other studies, most patients with an initial low TIMI flow developed slow/no reflow.[14,15,19] Conversely, an initial higher TIMI flow was associated with a high frequency of slow/no-reflow in another study.[16]

There was no relation between slow/no-reflow and the number of diseased vessels. A similar finding was observed in several other studies.[13,14,16] Our results showed no link of the phenomenon with LVEF. In contrast, Kumar et al. and Farahe et al. revealed statistically significant results with LVEF.[10,17]

In our study, 8.5% of in-hospital deaths occurred after P-PCI, 61.5% of these patients had slow/no-reflow, and 38.5% had normal flow. The results were statistically significant. Rajesh et al. also reported that slow flow/no-reflow was linked with increased in-hospital deaths.[20] A study revealed a higher prevalence of deaths and MACE at 30 days in patients with slow/no-reflow.[14] The limitations of this study are that prognosis of patients with slow flow or no flow was only reported in terms of in-hospital mortality. Loss of follow-up is the limitation of our study. Other prognostic parameters such as 30-day mortality, MACE, and LVEF were not determined.

CONCLUSION

Slow flow/no-reflow is a frequent complication (12.4%) in patients who underwent P-PCI for STEMI. Its significant predictors are advanced age, prior MI episodes, longer time to treatment initiation, higher Killip class, anterior wall MI, longer target lesions, proximal occlusion site, and high thrombus burden. The in-hospital mortality is much higher in these patients.

Financial Disclosure: None
Conflict of interest: None

AUTHOR'S CONTRIBUTION

MS: Conception of idea and manuscript writing
MM: Data collection and analysis
KNS: Data collection and analysis
MUS: Manuscript writing

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