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Incidence and Variables of no-reflow phenomenon in patients undergoing primary percutaneous coronary intervention: An observational study from a tertiary care centre of South India

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Abstract

Background: Angiographic no-reflow phenomenon after Primary percutaneous coronary intervention predicts poor ventricular functional recovery and survival in STEMI. The investigation of no-reflow phenomenon after primary percutaneous coronary intervention (PPCI) in patients with acute ST-segment–elevation myocardial infarction (STEMI) has therapeutic implications.

Aim of the study: The study was designed to determine the relation between various clinical, laboratory and angiographic variables and the occurrence of no reflow phenomenon in patients with STEMI undergoing primary PCI.

Methodology: We studied prospectively 120 patients with STEMI presenting to Thanjavur Medical College and Hospital from April 2024 to September 2024, and eligible for Primary PCI according to European Society of Cardiology (ESC) guidelines. Patients were divided into 2 groups according to no-reflow phenomenon. Group I : 99 patients with normal flow and Group II: 21 patients with no reflow phenomenon.

Results: Out of 120 STEMI patients undergoing primary PCI, 21 (17.5%) showed no-reflow phenomenon. The group with no reflow showed significantly older age (62.29 ± 7.90 *vs*. 56.30 ±

10.34, p=0.014), increased time to reperfusion (15.90 ± 7.87 *vs*. 6.08 ± 3.82, p<0.001), decreased LV ejection fraction, increased blood glucose, increased blood creatinine, initial TIMI flow grade 0 and high thrombus burden.

Conclusion: Older age, increased time to reperfusion, decreased LV ejection fraction, increased blood glucose, increased blood creatinine, initial TIMI flow grade 0 and high thrombus burden were associated with no-reflow phenomenon after primary PCI. Therefore strong attention should be paid to patients with one or more of these variables, to protect them from the deleterious effects of no reflow.

Keywords: Myocardial Infarction, Primary percutaneous coronary intervention, No reflow phenomenon.

Introduction:

Coronary artery disease (CAD) is the foremost cause of disability and death in the world and is one of the top five causes of death in India. [1] One of the serious complications of CAD is ST-elevation myocardial infarction (STEMI), a life threatening medical emergency that results from a sudden, occlusive thrombus in the coronary artery. When STEMI patients treated promptly with reperfusion therapy, significant reduction in mortality and morbidity has been observed. [2] Primary percutaneous coronary intervention (PPCI) has been established as the most effective management strategy to restore antegrade blood flow in ST-elevation myocardial infarction (STEMI). The no-reflow phenomenon occurs in a considerable number of patients with acute STEMI (11%–41%) undergoing primary PCI. [3,4] The phenomenon of no-reflow is defined as inadequate myocardial perfusion (TIMI flow grade ≤ 2) through a given segment of the coronary circulation without angiographic evidence of mechanical vessel obstruction [5]. Suggested mechanisms for no-reflow or slow flow include coronary microcirculation disturbances, such as distal embolization of thrombus and plaque debris, microvascular damage, and reperfusion injury.[3,4] A number of clinical, serologic, and angiographic parameters have been shown to be associated with no-reflow.[4] Experimental and clinical studies have shown that the no-reflow phenomenon is associated with large myocardial necrosis and high mortality.[6,7] Early detection, preventive measures and treatment of no reflow may alter the final outcome of PCI [8].

The study was designed to determine the relation between various clinical, laboratory and angiographic variables and the occurrence of no reflow phenomenon in patients with STEMI undergoing primary PCI.

Materials and Methods:

This prospective observational study was conducted on 120 patients with STEMI presenting to Thanjavur Medical College and Hospital from April 2024 to September 2024, and eligible for Primary PCI according to European Society of Cardiology (ESC) guidelines.

Patients were divided into 2 groups according to no-reflow phenomenon. Group I: 99 patients with normal flow phenomenon. Group II: 21 patients with no reflow phenomenon.

Inclusion criteria were patients presenting with STEMI within 24 hours of symptoms and treated with primary PCI.

Exclusion criteria were patients presenting after 24 hours of symptoms and patients who received thrombolytic therapy. Patients with coronary dissection (whether spontaneous or procedure related), and patients in whom stenting was not done for various reasons such as unsuitable anatomy or insignificant lesions in coronary angiogram.

STEMI was defined as the new ST elevation at the J-point in at least two contiguous leads or new onset left bundle branch block:

- In leads V2–V3:
  - ✓ ≥2.5 mm in men <40 years,
  - ✓ ≥2 mm in men 40 - 45 years,
  - ✓ ≥1.5 mm in women regardless of age
- In other leads:

≥ 1 mm (in the absence of left ventricular [LV] hypertrophy or left bundle branch block [LBBB]).

Normal flow was defined as a Thrombolysis in Myocardial Infarction (TIMI) score of 3 after stenting with or without postdilatation. No-reflow was defined as TIMI flow grade ≤ 2.

Sample size:

120 patients selected through convenient sampling.

Ethical Considerations

Institutional ethical committee approval was obtained before conducting the study. Informed written consent was obtained from the patients included in the study. Subjects were informed about the purpose and procedure of the study and benefits of sharing in it. Ethical considerations of the study were carried out according to that of Declaration of Helsinki.

Research design:

All patients were subjected to history taking including personal history: Age, sex, risk factors including Hypertension (HTN), Diabetes Mellitus (DM), smoking, renal impairment, family history of premature coronary artery disease (men under 55 years and women under 65 years), past medical history of prior MI, PCI or Coronary Artery Bypass Graft (CABG) and medications history. Hypertension was defined as systemic blood pressure ≥140/90 mm Hg or the use of antihypertensive treatment. Diabetes mellitus was defined as fasting blood sugar ≥126 mg/dL or the use of specific treatment.

Clinical examination including vital signs: e.g.: Heart rate, blood pressure, Body Mass Index (BMI), signs of heart failure, hemodynamic instability according to Killip classification, signs of co- morbidities: Renal or hepatic insufficiency, diabetes, cardiac examination, twelve leads surface Electrocardiogram (ECG), echocardiography including measurement of ejection fraction, dimensions and segmental wall motion abnormalities were recorded. Blood tests including complete blood count, lipid profile (total cholesterol, HDL, LDL, triglycerides), random blood sugar on admission, blood urea and creatinine.

Patients were subjected to diagnostic coronary angiography and primary PCI with door to balloon time less than 90 minutes. Total ischemic time (time to reperfusion) was defined as time from onset of symptom to first balloon inflation in hours. The collected angiographic data included the details of the culprit vessel and lesion, such as thrombus burden (low or high), lesion location (proximal, mid, or distal lesion), and TIMI flow grade before the procedure. Thrombus burden was classified as low if the TIMI thrombus class was ≤3 and high if the TIMI thrombus class was >3. Patients were divided into normal flow and no-reflow groups according to the coronary flow assessed in coronary angiogram following stenting and postdilatation. Predilatation and postdilatation were done according to operators' discretion. Reperfusion success was measured by TIMI blood flow grade: Reperfusion was considered successful (TIMI 3) or abnormal (TIMI 0-1-2) according to the TIMI blood flow grade **[9]**.

Data analysis:

Data was entered in MS excel sheet. Statistical presentation and analysis of the present study was conducted, using the mean, standard deviation and chi-square test by SPSS V.20. Numerical variables like age, SBP, DBP, pulse rate, ejection fraction, time to reperfusion, blood parameters like serum creatinine, blood glucose were expressed as mean (SD). Categorical variables like gender, smoking status, co-morbidity status, thrombus burden were expressed as number and percentages. When the chi- squared test was not appropriate, the likelihood ratio test was applied. The level of significance was adopted at $p<0.05$.

Results:

The patients were divided into two groups according to the final TIMI flow after the primary PCI as follows: **Group I:** Patients with normal flow after Primary PCI. **Group II:** Patients with no reflow after Primary PCI .

Demographic data:

Regarding the gender, Group I included 75 males (75.8%) and 24 females (24.2%), Group II included 13 males (61.9%) and 8 females (38.1%). There was statistically no significant difference between the two groups as regarding the gender (*p*- value=0.192).

In group I, the age of the patients ranged from 29 to 81 years with a mean age of 56.30±10.34 years. In group II the age ranged from 44 to 78 years with a mean age of 62.29±7.90 years. There was statistically significant difference between the two groups as regarding the age (*p*- value 0.014).

Table 1. Distribution of the studied groups.

	No	**%**
Normal flow(group I)	99	82.5
No reflow (group II)	21	17.5

Table 2. Comparison between the studied groups as regard to demographic data.

	Group I (n=99)		**Group II (n=21)**		**Test of sig.**	**p**
	No	**%**	**No**	**%**		
Sex						
Male	75	75.8	13	61.9	χ^2=1.700	0.192*
Female	24	24.2	8	38.1		
Age						
Min. – Max.	29.0 – 81.0		44.0 – 78.0		t=2.498	0.014**
Mean ± SD	56.30 ± 10.34		62.29 ± 7.90			

*p value by chi-square test of association; **p value by independent t test

Risk factors:

There was statistically no significant difference regarding Diabetes, HTN, Smoking, Dyslipidemia and family history of CAD.

Clinical characteristics:

There was a statistically significant difference between the two studied groups as regard to Ejection Fraction and time to reperfusion. However, there was statistically no significant difference regarding systolic BP, diastolic BP and heart rate.

There was a statistically significant difference between the two studied groups as regard to blood sugar at admission and creatinine. Also, there was a statistically significant difference between the two studied groups as regard to initial TIMI flow and thrombus burden.

Table 3. Comparison between the studied groups as regard to risk factors.

	Group I (n=99)		**Group II (n=21)**		**χ^2**	**p**
	No	**%**	**No**	**%**		

Diabetes						
Non diabetic	62	62.6	9	42.9	2.803	MCp=0.094
Diabetic	37	37.4	12	57.1		
Hypertension	48	48.5	7	33.3	1.602	0.206
Smoking						
Non smoker	43	43.4	11	52.4	0.560	0.454
Smoker	52	52.5	9	42.9	0.648	0.421
Ex-smoker	4	4.0	1	4.8	0.023	FEp=1.000
Dyslipidemia	54	54.5	15	71.4	2.021	0.155
Family History of CAD	17	17.1	2	9.5	0.760	FEp=0.521

Table 4. Comparison between the studied groups as regard to clinical characteristics.

	Group I (n=99)	**Group II (n=21)**	**t**	**p**
SBP				
Min. – Max.	50.0-200.0	70.0-160.0	1.971	0.051
Mean ± SD	129.29 ± 27.93	116.67 ± 19.32		
DBP				
Min. – Max.	30.0-120.0	40.0-90.0	1.870	0.064
Mean ± SD	81.06 ± 15.62	74.29 ± 12.07		

Pulse				
Min. – Max.	41.0-120.0	60.0-130.0	0.069	0.945
Mean ± SD	84.56 ± 16.33	84.29 ± 15.69		
Ejection fraction(%):				
Min.-max.	30.0-70.0	31.0-60.0	2.336*	0.025*
Mean ± SD	49.80±7.76	45.45±9.26		

Table 5. Comparison between the studied groups as regard to time to reperfusion.

	Group I (n=99)	**Group II (n=21)**	**Z**	**P (by independent t test)**
Time to reperfusion(hours)				
Min. – Max.	1.0-19.0	1.0-30.0	4.999*	<0.001*
Mean ± SD	6.08 ± 3.82	15.90 ± 7.87		
Median	5.0	17.0		

Table 6. Comparison between the studied groups as regard to laboratory parameters on admission.

	Group I (n=99)	**Group II (n=21)**	**Test of sig.**	**P (by independent t test/ Z test)**
Creatinine(mg/dl)				
Min. – Max.	0.60-2.30	0.40-1.80	*t*=2.855*	0.005*
Mean ± SD	1.09±0.26	1.25±0.30		
Median	1.0	1.20		

Blood glucose				
Min. – Max.	84.0-442.0	104.0-440.0	Z=3.377*	0.001*
Mean ± SD	186.38 ± 84.65	275.29 ± 104.11		
Median	150.0	280.0		

Table 7. Comparison between the studied groups as regard to angiographic characteristics.

	Group I (n=99)		**Group II (n=21)**		**Test of sig.**	**P (by chi-square test)**
	No	**%**	**No**	**%**		
Thrombus burden						
Low	66	66.4	3	13.8	χ^2 =26.020*	<0.001*
High	33	33.6	18	86.2		
Initial TIMI flow						
0	73	73.7	21	100	χ^2 =9.457*	0.002*
1-3	26	26.3	0	0		

Discussion:

The rate of no-reflow phenomenon after primary PCI in the present study (17.5%) was similar to that (12%-25%) reported previously in Piana et al. [10] and Morishima et al. [5].

In our study, we found that the groups with no reflow have shown significantly older age, decreased left ventricular ejection fraction, increased plasma glucose, increased blood creatinine, increased time to reperfusion, initial TIMI flow grade 0 and high thrombus burden.

Ndrepepa G et al. [7], found that initial TIMI 0 flow in the infarct-related artery (P<0.001), initial perfusion defect (P<0.03), and previous history of myocardial infarction (P<0.013) as independent predictors of no reflow.

Hyperglycemia is associated with impairment of microvascular function and can cause angiographic slow flow. Iwakura K *et al.* [11], found that hyperglycemia (>160 mg/dl) during admission was an independent prognostic factor for no reflow, along with older age, male gender, absence of pre-infarction angina, complete occlusion of the culprit lesion, and anterior STEMI.

Prolonged ischemia leads to edema of distal capillary beds, swelling of myocardial cells, neutrophil plugging, and alterations of capillary integrity. Delayed reperfusion can result in an older, more organized intracoronary thrombus, which may increase the risk of distal embolization during PPCI and increase the chance of no-reflow as reported by Nagata Y et al.[12]

Previous studies have shown that LV ejection fraction <50%, cardiogenic shock, and tachycardia are independent predictors of final TIMI ≤ 2 flow.[13-15] Patients with LV systolic dysfunction resulting from larger infarction can have large microvascular injury, increased LV end-diastolic pressure, and decreased coronary perfusion pressure, leading to suboptimal coronary flow.

Sabin et al. [16] in their study which was conducted on 181 patients with STEMI who underwent primary PCI from August 2014 to February 2015, found that predictors of no reflow were age >60 years, reperfusion time >6h, low initial TIMI flow (1), a high thrombus burden, a long target lesion, Killip Class III/IV and overlap stenting.

Zhou et al. [17] identified that age >65years, long time from onset to reperfusion >6 hours, low SBP on admission <100 mmHg, IABP use before PCI, low (" 1) TIMI flow grade before primary PCI, high thrombus burden, and long target lesion on angiography were independent predictors of no-reflow.

Conclusion :

Older age, increased time to reperfusion, decreased LV ejection fraction, increased blood glucose, increased blood creatinine, initial TIMI flow grade 0 and high thrombus burden were associated with no-reflow phenomenon after primary PCI. Therefore strong attention should be paid to patients with one or more of these variables, to protect them from the deleterious effects of no reflow.

Study limitations :

The study has some limitations: First, this is a single-center experience and represents a limited number of patients. Second, the evaluation of no- reflow was done by the TIMI flow grade only. As microvascular perfusion may also be reduced in patients with TIMI flow grade 3. Third, Patients were not followed up to see clinical outcomes.

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