

## **Original Research Article**

### **Incidence and Predictors of No Reflow Phenomenon in Patient Undergoing Primary Percutaneous Coronary Intervention**

#### **Abstract**

**Objective:** To evaluate the incidence, clinical and angiographic predictors of no reflow phenomenon in patient undergoing primary percutaneous coronary intervention (PCI).

**Methods:** This prospective observational cross-sectional study was carried out on 748 patients who underwent primary coronary angioplasty after acute ST- Segment Elevation Myocardial Infarction (STEMI). Patients were subdivided in to two groups: Group I: (case group) patients with no-reflow phenomenon (NRP) in the absence of dissection, thrombus, spasm or high-grade residual stenosis and group II: (Control group) one consecutive STEMI patient after each case, with TIMI flow III after primary PCI. All patients were subjected to clinical and laboratory examination, electrocardiogram (ECG), echocardiography (ECHO) and PCI.

**Results:** 22.9 % of patients had no-reflow; 10 % had persistent no reflow and 12.9% had transient no reflow. Multivariate analyses identified that age (OR=1.417, 95% CI 1.319–1.521), diabetes mellitus (DM) (OR=10.110, 95% CI 3.950–25.880), hypertension (HTN) (OR=0.326, 95% CI 0.142–0.752), total ischemia time  $\geq 6$  hours (OR=60.511, 95% CI 24.973–146.618), SBP<90 mmHg (OR=0.238, 95% CI 0.091–0.621) , lesion length  $\geq 20$  mm(OR=16.182, 95% CI 5.008–52.287) , high thrombus burden (thrombus grade  $\geq 4$ ) (OR=2.914, 95% CI 1.018–8.338), balloon pre dilatation (OR=0.272, 95% CI 0.093–0.791), stent length  $\geq 20$  mm(OR=7.709, 95%CI 33.346–17.758), balloon post dilatation (OR=5.885, 95% CI 2.571–13.474), CRP (OR=1.016, 95% CI 1.002–1.030) were the independent predictors of the no-flow phenomenon.

**Conclusions:** Clinical and laboratory predictors on admission were associated with higher percentage of no-reflow phenomenon. while angiographic predictors could independently predicts no-reflow after Primary PCI.

**Keywords:** Predictors, No Reflow Phenomenon, Percutaneous Coronary Intervention.

**Total word count:**

**Introduction:**

Timely reperfusion of the infarct-related coronary artery using percutaneous coronary intervention (PCI) is the optimum ST segment elevation myocardial infarction (STEMI) treatment. Yet, despite opening the affected epicardial coronary artery, myocardial perfusion often might not be restored causing no-reflow. <sup>[1, 2]</sup>

No-reflow phenomenon (NRP) is a myocardial hypoperfusion state due to microvascular obstruction in spite of patent epicardial coronary vessels. <sup>[3]</sup>

Patients with impaired flow or no reflow after revascularization will usually suffer from obvious bad outcome like higher incidence of death due to cardiac causes, heart failure symptoms as well as pericardial effusion. <sup>[4]</sup>

Several clinical factors have been found to impact the functional and clinical prognosis of MI cases. Although these factors may have an impact on the development of microvascular dysfunction, their link to the NRP remains unclear. <sup>[5, 6]</sup>

No reflow diagnosis can be suspected initially by patient symptoms and electrocardiography ischemic changes or persistent ST segment elevation in spite of patent coronary culprit vessel. <sup>[7]</sup> Diagnosis of no reflow can be confirmed by different angiographic scores. The thrombolysis in myocardial infarction flow scoring system (TIMI flow score) provides easy tool to evaluate degree of coronary perfusion. <sup>[8]</sup> Also, TIMI frame score can be used for coronary reperfusion and diagnosis of no reflow. <sup>[9]</sup>

this work aimed to evaluate the incidence, clinical and angiographic predictors of no reflow phenomenon in patient undergoing primary PCI.

**Materials and Methods:**

a) **Study design:** This prospective observational cross-sectional trial was carried out at cardiovascular medicine department Tanta university hospitals, Egypt. This trial was conducted in a period of two years starting from October 2019.

b) **study populations:** 748 cases who were subjected to primary coronary angioplasty after acute ST- Segment Elevation Myocardial Infarction (STEMI) according to STEMI guidelines indications to primary PCI <sup>[13]</sup> cases were classified into 2 groups: **Group I: (case group)** patients with NRP in the absence of dissection, thrombus, spasm or high-grade residual stenosis and **group II: (Control group)** one consecutive STEMI patient following every case, with TIMI flow III following primary PCI. Group I were divided in to 2 sub-groups according to treatment response and TIMI flow post primary PCI: **Sub Group A: (persistent No-reflow group)** patients failed to respond to treatment of No-reflow with TIMI flow 0-I post primary PCI in the absence of dissection, thrombus, spasm or high-grade residual stenosis and **sub group B: (Transient No-reflow group)** patients responded to treatment of no reflow with TIMI flow  $\geq$  II post primary PCI in the absence of dissection, thrombus, spasm or high-grade residual stenosis.

**Ethical considerations:** The trial was conducted after approval from the Ethical Committee Tanta University Hospitals. An informed written consent was taken from the cases.

c) **Methods:** All cases were subjected to: history taking, clinical examination, twelve leads surface electrocardiogram (ECG), venous sampling for routine laboratory investigations at hospital admission before primary PCI and Echocardiography by M-mode and modified Simpson method using a GE vivid seven Cardiac ultrasound phased array system with tissue Doppler imaging using M4S transducer 4 M.Hz. were done during admission before PCI to assess LV systolic function, volume and assess Segmental wall motion abnormalities and global wall motion.<sup>[15]</sup>

Primary PCI for infarct related artery (IRA) within 24 hours of presentation, Grade of blood flow after procedure was determined by TIMI blood flow grade classification system. <sup>[16]</sup> IRA was identified according to the culprit lesion on the basis of the infarct location on the admission ECG and the

angiographic findings (target vessel, lesion characteristics). Multivessel disease was defined as presence of  $\geq 1$  lesion with  $>50\%$  stenosis in  $\geq 1$  major epicardial coronary artery or its major branches remote from the IRA. <sup>[17]</sup>

Thrombus grading score was utilized to assess clot burden., <sup>[18]</sup> PCI was immediately performed with a 6-Fr guiding catheter. Thrombus aspiration, balloon pre-dilatation and post-dilatation were performed when indicated. The type of stents (drug-eluting stent or bare metal stent) was left to the surgeon's discretion. Reperfusion success is measured by TIMI blood flow grade: Reperfusion was deemed successful (TIMI 3) or abnormal (TIMI 0-1-2).

Patients with No-reflow received intracoronary medications in the form of nitrates, glycoprotein IIb/IIIa inhibitor, calcium channels blocker, adrenaline.

### **Statistical analysis**

Using IBM SPSS v 20.0, the data were analysed (Armonk, NY: IBM Corp). Quantitative and percentage descriptions were provided for qualitative data. The mean and standard deviation were used to characterise the quantitative data. Chi-square or Fisher's Exact or Monte Carlo correction was used to compare categorical variables between groups, F-test (ANOVA) for normally distributed quantitative variables, to compare between more than two groups, and Post Hoc test (Tukey) for pairwise comparisons and Kruskal Wallis test for abnormally distributed quantitative variables, to compare between more than two studied groups, and Post Hoc (Dunn's multiple comparisons test) for pairwise comparisons. Using univariate and multivariate analysis, independent predictors of the no-reflow phenomena were identified. P value  $\leq 0.05$  was considered statistically significant.

### **Results:**

In our study, 22.9 % of cases developed no-reflow. Patients with persistent no reflow was 10 % and patients with transient no reflow was 12.9%. Table 1

**Table 1: Incidence of No-reflow**

N = 1635	No (%)
<b>Group I (case / no reflow)</b>	374 (22.9 %)
<b>Persistent no reflow</b>	163 (10 %)

<b>Transient no reflow</b>	211 (12.9 %)
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Data are presented as frequency (%). MI: Myocardial infarction

Persistent no reflow and transient no reflow had no significant difference between them regarding age, gender distribution, DM, HTN, smoking, SBP, killip class, STEMI localization, ischemic time, lesion length, number of diseased vessels, lesion localization, IRA, balloon pre dilatation and balloon post dilatation, while persistent no reflow and transient no reflow groups had significantly older cases (>60 years old), higher percentages of males and females, higher percentages of diabetic, hypertensive patients, lower percentages of smokers compared to control group, lower SBP (<90 mmHg), longer Total Ischaemia Time (>6 hrs), longer Lesion length ( $\geq 20$ ), more MVD and higher percentage of balloon predilatation and postdilatation compared to control group ( $P \leq 0.05$ ). Dyslipidemia, family history of previous coronary artery diseases and HR had no significant variation between the studied groups. Killip class was significantly different in Persistent no reflow and transient no reflow groups in which class  $\geq III$  was the predominant classification compared to control group. Location of infarction was significantly different in Persistent no reflow and transient no reflow groups in which the most common infarction was the anterior one followed by the inferior compared to control group. Lesion localization was significantly different in Persistent no reflow and transient no reflow groups as they had more proximal lesions compared to control group. IRA was significantly different in persistent no reflow and transient no reflow groups in which the most common IRA was LAD followed by RCA compared to control group (LAD followed by LCX). Persistent no reflow group had significantly lower pre-procedural TIMI flow score ( $\leq 1$ ) than transient no reflow group. Persistent no reflow group had significantly lower pre-procedural TIMI flow score ( $\leq 1$ ) than control group. Transient no reflow group had significantly higher pre-procedural TIMI flow score ( $>1$ ) than control group. Persistent no reflow group had significantly higher Thrombus grade ( $\geq 4$ ) compared to Transient no reflow and control groups. No significant difference was found between transient no flow and control groups. Persistent no reflow group had significantly longer (>20) Stent compared to

Transient no reflow and control groups. Transient no reflow group had significantly longer (>20) Stent compared to control group. Post-procedural TIMI flow score was significantly different between Persistent no reflow (most patients had TIMI grades 0 and I) and transient no reflow groups (TIMI grades II, III were the most common). Post-procedural TIMI flow score was significantly different between Persistent no reflow (most patients had TIMI grades 0 and I) and control groups in which all patients had TIMI III. Post-procedural TIMI flow score was significantly different between transient no reflow groups (TIMI grades II, III were the most common) and control groups in which all patients had TIMI III. Table 2

**Table 2: Comparison between the three studied groups according to age, sex, risk factors and An-giographic and procedural characteristics**

		Persistent no reflow (n= 163)	Transient no reflow (n= 211)	Control (n= 374)	p
		No (%)	No (%)	No (%)	
<b>Age (years)</b>	<60	12 (7.4 %)	16 (7.6 %)	284 (75.9 %)	<0.001* p <sub>1</sub> =0.936 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
	>60	151 (92.6 %)	195 (92.4 %)	90 (24.1 %)	
<b>Age (years)</b>		65.79 ± 4.43	65.80 ± 4.59	54.02 ± 8.65	<0.001* p <sub>1</sub> =1.000 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
<b>Sex</b>	Male	142 (87.1 %)	179 (84.8 %)	233 (62.3 %)	<0.001* p <sub>1</sub> =0.541 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
	Female	21 (12.9 %)	32 (15.2 %)	141 (37.7 %)	
<b>DM</b>		125 (76.7 %)	156 (73.9 %)	215 (57.5 %)	<0.001* p <sub>1</sub> =0.541 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
<b>HTN</b>		128 (78.5 %)	157 (74.4 %)	223 (59.6 %)	<0.001* p <sub>1</sub> =0.354 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
<b>Smoker</b>		84 (51.5 %)	97 (46 %)	235 (62.8 %)	<0.001* p <sub>1</sub> =0.286 p <sub>2</sub> =0.014* p <sub>3</sub> <0.001*

<b>Dyslipidemia</b>		82 (50.3 %)	103 (48.8 %)	184 (49.2 %)	0.957
<b>Family History</b>		54 (33.1 %)	69 (32.7 %)	89 (23.8 %)	0.051
<b>SBP</b>	>90	56 (34.4 %)	79 (37.4 %)	273 (73 %)	<0.001* p <sub>1</sub> =0.538 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
	<90	107 (65.6 %)	132 (62.6 %)	101 (27 %)	
<b>HR</b>	<75	39 (23.9 %)	51 (24.2 %)	61 (16.3 %)	0.098
	>75	124 (76.1 %)	60 (75.8 %)	313 (83.7 %)	
<b>Killip Class</b>	< III	56 (34.4 %)	81 (38.4 %)	301 (80.5 %)	<0.001* p <sub>1</sub> =0.422 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
	≥ III	107 (65.6 %)	130 (61.6 %)	73 (19.5 %)	
<b>Location of infarction</b>	Ant	112 (68.7 %)	138 (65.4 %)	158 (42.2 %)	<0.001* p <sub>1</sub> =0.885 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
	Inferior	42 (25.8 %)	58 (27.5 %)	61 (16.3 %)	
	Lat	6 (3.7 %)	11 (5.2 %)	126 (33.7 %)	
	Other	3 (1.8 %)	4 (1.9 %)	29 (7.8 %)	
<b>Total Ischaemia Time</b>	<6 hrs	26 (16 %)	42 (19.9 %)	251 (67.1 %)	<0.001* p <sub>1</sub> =0.326 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
	>6 hrs	137 (84 %)	169 (80.1 %)	123 (32.9 %)	
<b>Lesion length</b>	< 20	37 (22.7 %)	57 (27 %)	192 (51.3 %)	<0.001* p <sub>1</sub> =0.340 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
	≥ 20	126 (77.3 %)	154 (73 %)	182 (48.7 %)	
<b>MVD</b>		76 (46.6 %)	91 (43.1 %)	101 (27 %)	<0.001* p <sub>1</sub> =0.500 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
<b>Lesion Localization Proximal</b>	Proximal	114 (69.9 %)	142 (67.3 %)	159 (42.5 %)	<0.001* p <sub>1</sub> =0.645 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
	Midsegment	43 (26.4 %)	57 (27 %)	127 (34 %)	
	Distal	6 (3.7 %)	12 (5.7 %)	88 (23.5 %)	
<b>IRA</b>	LAD	124 (76.1 %)	155 (73.5 %)	224 (59.9 %)	<0.001*

	LCX	11 (6.7 %)	117 (8.1 %)	84 (22.5 %)	p <sub>1</sub> =0.826 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
	RCA	28 (17.2 %)	39 (18.5 %)	66 (17.6 %)	
<b>TIMI pre</b>	>1	15 (9.2 %)	41 (19.4 %)	58 (15.5 %)	0.024* p <sub>1</sub> =0.006* p <sub>2</sub> =0.049* p <sub>3</sub> <0.001*
	≤1	148 (90.8 %)	170 (80.6 %)	316 (84.5 %)	
<b>Thrombus grade</b>	<4	39 (23.9 %)	71 (33.6 %)	215 (57.5 %)	<0.001* p <sub>1</sub> =0.034* p <sub>2</sub> <0.001* p <sub>3</sub> =0.224
	≥4	124 (76.1 %)	140 (66.4 %)	159 (42.5 %)	
<b>Predilatation</b>		128 (78.5 %)	145 (68.7 %)	215 (57.5 %)	<0.001* p <sub>1</sub> =0.340 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
<b>Stent length</b>	<20	35 (21.5 %)	70 (33.2 %)	244 (65.2 %)	<0.001* p <sub>1</sub> =0.013* p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
	>20	128 (78.5 %)	141 (66.8 %)	130 (34.8 %)	
<b>Postdilatation</b>		69 (42.3 %)	69 (32.7 %)	78 (20.9 %)	<0.001* p <sub>1</sub> =0.056 p <sub>2</sub> <0.001* p <sub>3</sub> =0.002*
<b>TIMI Post</b>	TIMI 0	135 (82.8 %)	0 (0 %)	0 (0 %)	<0.001* p <sub>1</sub> <0.001* p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
	TIMI 1	28 (17.2 %)	0 (0 %)	0 (0 %)	
	TIMI 2	0 (0 %)	184 (87.2 %)	0 (0 %)	
	TIMI 3	0 (0 %)	27 (12.8 %)	374 (100 %)	

Data are presented as mean ± SD and frequency (%), \* significant as P value ≤ 0.05, p<sub>1</sub>: p value for comparing between persistent no reflow and transient no reflow, p<sub>2</sub>: p value for comparing between persistent no reflow and control, p<sub>3</sub>: p value for comparing between transient no reflow and control. DM: Diabetes mellitus, HTN: Hypertension, SBP: Systolic blood pressure, HR: Heart rate, MVD: Coronary microvascular disease, IRA: Infarct-related artery, LAD: Left anterior descending artery, LCX: Left circumflex artery, RCA: Right coronary artery, TIMI: Thrombolysis in myocardial infarction.

Persistent no reflow and Transient no reflow groups had significantly higher WBCs number, elevated S. Creatinine and CRP (mg/L) levels compared to control group. Persistent no reflow and Transient no reflow groups had significantly lower EF (<40) compared to control group. No significant difference was found between Persistent no reflow and Transient no reflow groups regarding WBCs, S.

Creatinine, CRP (mg/L) and EF. Persistent no reflow group had significantly more Malignant arrhythmia compared to Transient no reflow group. No significant variation was found between Persistent no reflow and control groups and between Transient no reflow and control groups. Persistent no reflow and Transient no reflow groups had significantly more cardiogenic shock and in hospital mortality compared to control group. Hb had no significant difference between the studied groups.

Table 3

**Table 3: Laboratory findings and common in hospital complications in no reflow and control groups**

		Persistent no reflow (n= 163)	Transient no reflow (n= 211)	Control (n= 374)	p
<b>Hb</b>		12.53 ± 0.53	12.53 ± 0.54	12.45 ± 0.73	0.184
<b>WBCs</b>		13.34 ± 1.13	13.20 ± 1.16	11.70 ± 1.28	<0.001* p <sub>1</sub> =0.537 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
<b>S. Creatinine level</b>		1.44 ± 0.25	1.42 ± 0.26	1.16 ± 0.23	<0.001* p <sub>1</sub> =0.731 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
<b>CRP (mg/L)</b>		63.98 ± 32.17	59.94 ± 33.46	26.50 ± 21.59	<0.001* p <sub>1</sub> =0.236 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
EF	>40	39 (23.9 %)	68 (32.2 %)	260 (69.5 %)	<0.001* p <sub>1</sub> =0.078 p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
	<40	124 (76.1 %)	143 (67.8%)	114 (30.5 %)	
<b>Malignant arrhythmia</b>		20 (12.3 %)	10 (4.7 %)	28 (7.5 %)	0.025* p <sub>1</sub> =0.008* p <sub>2</sub> =0.074 p <sub>3</sub> =0.195
<b>Cardiogenic shock</b>		107 (65.6 %)	52 (24.6 %)	48 (12.8 %)	<0.001* p <sub>1</sub> <0.001* p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*

<b>In hospital mortality</b>	111 (68.1 %)	68 (32.2 %)	36 (9.6 %)	<0.001* p <sub>1</sub> <0.001* p <sub>2</sub> <0.001* p <sub>3</sub> <0.001*
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Data are presented as mean ± SD and frequency (%), \* significant as P value < 0.05, p1: p value for comparing between persistent no reflow and transient no reflow, p2: p value for comparing between persistent no reflow and control, p3: p value for comparing between transient no reflow and control. Hb: haemoglobin, WBCs: White blood cells, CRP: C-reactive protein, EF: Ejection fraction.

Multivariate analyses identified that age (OR=1.417, 95%CI 1.319–1.521, P=0.001), DM (OR=10.110, 95%CI 3.950–25.880, P=0.001), HTN (OR=0.326, 95%CI 0.142–0.752, P=0.001), total ischemia time ≥6 hours (OR=60.511, 95%CI 24.973–146.618, P=0.001), SBP<90 mmHg (OR=0.238, 95%CI 0.091–0.621, P=0.003), lesion length ≥20 mm (OR=16.182, 95%CI 5.008–52.287, P=0.001), high thrombus burden (thrombus grade ≥4) (OR=2.914, 95%CI 1.018–8.338, P=0.046), balloon pre dilatation (OR=0.272, 95%CI 0.093–0.791, P=0.017), stent length ≥20 mm (OR=7.709, 95%CI 3.346–17.758, P=0.001), balloon post dilatation (OR=5.885, 95%CI 2.571–13.474, P=0.001), CRP (OR=1.016, 95%CI 1.002–1.030, P=0.027) were the independent predictors of the no-flow phenomenon. Table 4

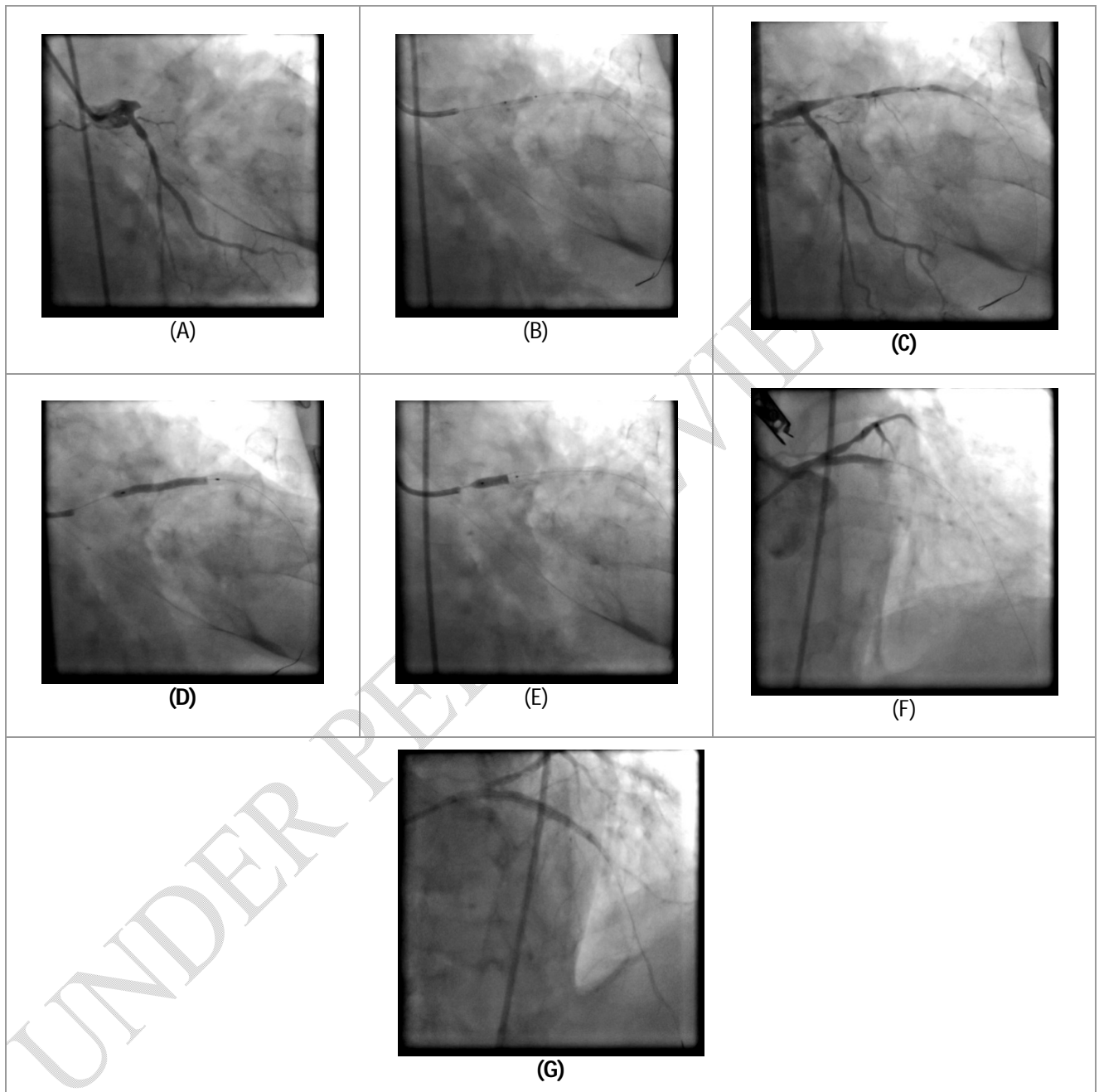
**Table 4: Univariate and multivariate regression analysis of independent predictors of No-Reflow in study population (n = 374 vs 374)**

	Univariate		#Multivariate	
	p	OR (95% C.I)	p	OR (95% C.I)
<b>Age</b>	<0.001*	1.286 (1.241 – 1.332)	<0.001*	1.417 (1.319–1.521)
<b>DM</b>	<0.001*	2.235 (1.637 – 3.051)	<0.001*	10.110 (3.950–25.880)
<b>HTN</b>	<0.001*	2.168 (1.582 – 2.972)	<0.001*	0.326 (0.142–0.752)
<b>Killip Class (≥III)</b>	<0.001*	7.133 (5.122 – 9.933)	0.266	1.782 (0.644–4.929)
<b>Total Ischaemia Time (&gt;6)</b>	<0.001*	9.183 (6.536 – 12.901)	<0.001*	60.511 (24.973–146.618)
<b>SBP (&lt;90)</b>	<0.001*	0.209 (0.153 – 0.285)	0.003*	0.238 (0.091–0.621)

<b>IRA (LAD)</b>	<0.001*	1.995 (1.460 – 2.725)	0.061	0.465 (0.208–1.037)
<b>Lesion Localization Proximal</b>	<0.001*	2.934 (2.175 – 3.957)	0.472	1.333 (0.610–2.914)
<b>Thrombus grade (≥4)</b>	<0.001*	3.245 (2.398 – 4.392)	0.046*	2.914 (1.018–8.338)
<b>Pre dilatation</b>	<0.001*	1.999 (1.471 – 2.717)	0.017*	0.272 (0.093–0.791)
<b>Stent length</b>	<0.001*	4.808 (3.526 – 6.557)	<0.001*	7.709 (3.346–17.758)
<b>Lesion Length (≥20)</b>	<0.001*	3.142 (2.306 – 4.282)	<0.001*	16.182 (5.008–52.287)
<b>Post dilatation</b>	<0.001*	2.219 (1.602 – 3.075)	<0.001*	5.885 (2.571–13.474)
<b>CRP (mg/L)</b>	<0.001*	1.043 (1.036 – 1.050)	0.027*	1.016 (1.002–1.030)

DM: Diabetes mellitus, HTN: Hypertension, SBP: Systolic blood pressure, #: All variables with  $p < 0.05$  was included in the multivariate, IRA: Infarct-related artery, CRP: C-reactive protein.

Figure 1

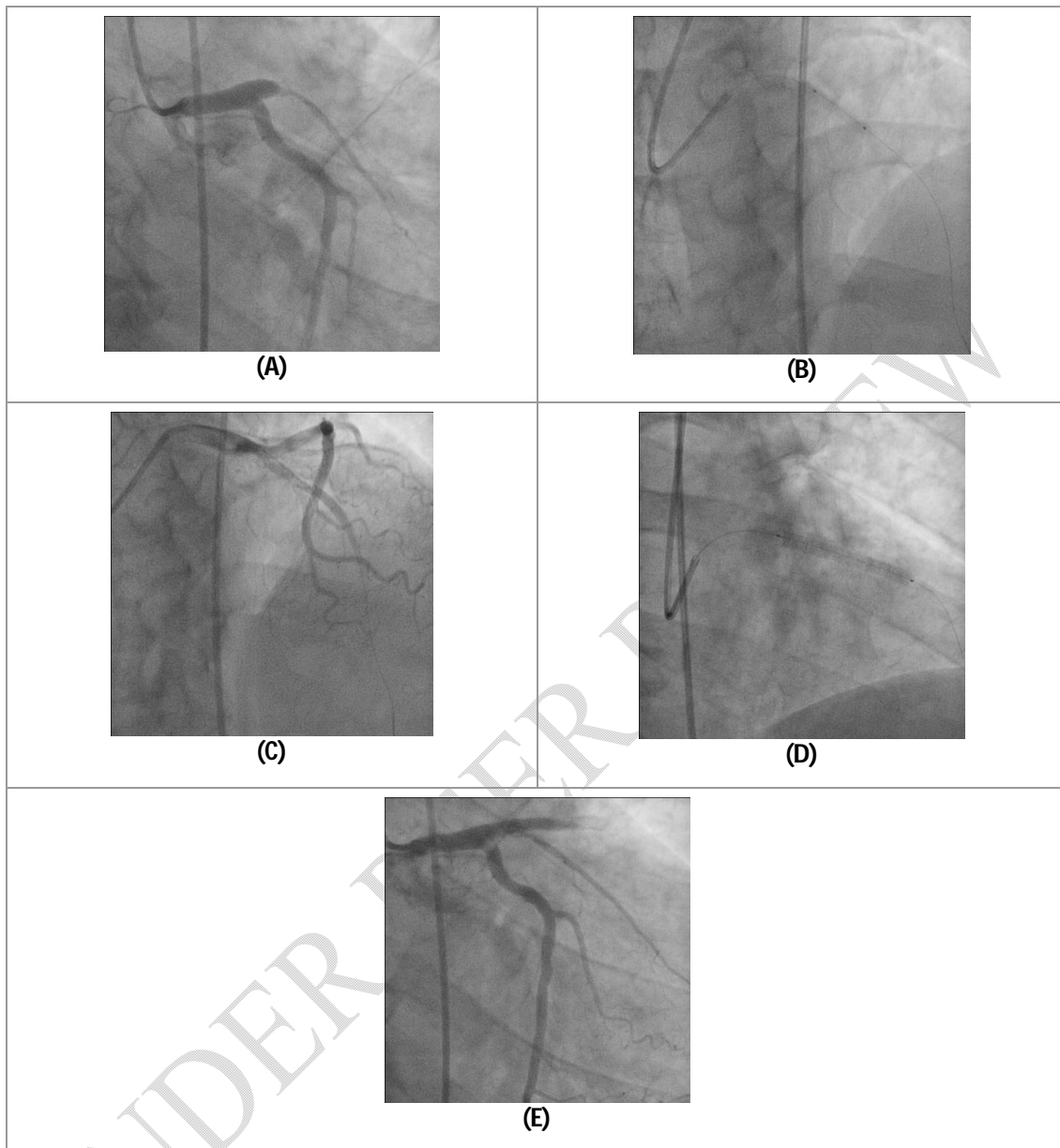


**Figure 1 :Female patient aged 74 years, known to be a diabetic and hypertensive patient. she wasn't smoker and had no history of dyslipidemia nor family history of previous coronary artery diseases and not known to be a cardiac patient before. The LAD was the IRA .(A) Injection of left coronaries in Right Anterior Oblique (RAO )caudal view showing proximal total thrombotic occlusion of the LAD (IRA) and proximal 50 % occlusion of LCX, (B) Balloon pre dilatation of proximal LAD using 2 \*12 mm semicompliant balloon, (C) Injection of left coronaries**

in RAO caudal view after balloon pre dilatation showing TIMI I flow of the LAD, (D) Stenting of proximal LAD in RAO caudal view using 3 \*33 mm DES stent, (E) Stenting of osteo proximal LAD in RAO caudal view using 3.5\*12 mm stent, (F) Injection of left coronaries in Postero Anterior (PA) cranial view after LAD stenting showing TIMI 0 flow in the LAD, (G) Injection of left coronaries in PA cranial view showing TIMI I flow in the LAD after injection of tirofiban and calcium channel blockers .The patient returned to the CCU where she started Glycoprotein IIb/IIIa IV infusion. The patient was still hemodynamically unstable and died within 4 hours after PCI.

UNDER PEER REVIEW

Figure 2



**Figure 2: Male patient aged 53 years, known to be a diabetic patient, smoker and had history of dyslipidemia, no family history of previous coronary artery diseases and not known to be a cardiac patient before. The LAD was the IRA. (A) Injection of left coronary artery in RAO caudal view showing proximal total thrombotic occlusion of the LAD TIMI 0, (B) Pre dilatation of the LAD in PA cranial view using 2.5\*10 mm balloon, (C) Injection of left coronary in PA cranial view after balloon pre dilatation showing TIMI I flow, (D) Stenting of proximal LAD in RAO cranial view using stent 4\*38 mm stent, (E) Injection of left coronary artery in RAO caudal view after LAD stenting showing TIMI 0 flow in the LAD and thrombus dislodgement in distal of the left main artery and ostial LCX artery. Trials of intracoronary injection of nitrates, Glycoprotein IIb/IIIa, calcium channel blockers and epinephrine failed to get reflow. The pa-**

**tient transferred to the CCU, he was hemodynamically unstable so, he received I.V. vaso-pressors, positive inotropic drugs, Glycoprotein IIb/IIIa, anticoagulant and assistive respiratory support. He improved and discharged 5 days later.**

## **Discussion**

Although primary PCI is the most beneficial and rewarding reperfusion technique in patients with acute ST-segment– elevation myocardial infarction (STEMI), it fails to restore optimal myocardial reperfusion in a considerable number of cases mostly due to NRP. <sup>[19]</sup>

In our trial, 22.9 % of cases developed no-reflow. Patients with persistent no reflow was 10 % and patients with transient no reflow was 12.9%. Measured by TIMI grade, the incidence of no-reflow following routine PCI is 1% to 5%, and the incidence of no-reflow in AMI cases is 2.3% to 41% in some studies. <sup>[6]</sup>

In Papapostolou et al. <sup>[1]</sup> trial, the occurrence of transient no-reflow was 3.2 % (590 patients) and the occurrence of persistent no-reflow was 0.8% (144 patients). In Kim et al. <sup>[20]</sup> the occurrence of transient no reflow was 4.9 % (213 patients) and the occurrence of persistent no reflow was 1 % (45 patients). In Aggarwal et al. <sup>[21]</sup>, the occurrence of no reflow was 18.9 % (182 patients) by myocardial blush grade (MBG)<2. In Ghazanfer Ali Shah et al. <sup>[22]</sup> angiographical slow/no flow during the operation occurred in 53 (9.5%) cases, while normal flow was achieved in 506(90.5%). In Pantea-Roşan et al. <sup>[23]</sup> the incidence of no reflow was 14.6%.

In Yang et al. <sup>[6]</sup> the incidence of no-reflow was 29.5% (331 patients). In Jomaa et al. <sup>[24]</sup> no-reflow occurred in 44 (12.5%) cases. The incidence of noreflow was 6.2 % in a study conducted by Ipek et al. <sup>[25]</sup>. In Aefin et al. <sup>[26]</sup> the occurrence of NRP was 63 (15.9%). In Zhou et al. <sup>[27]</sup> the incidence of no reflow was 17.3% (54 patients). In Tasar et al. <sup>[28]</sup> the no reflow was reported in 10% of the patients (324 patients). In a trial by Li Dong-bao et al. <sup>[29]</sup> the no reflow was reported in 19.5 % of the cases with acute STEMI (41 cases). In a trial conducted by Harrison et al. <sup>[30]</sup> the no reflow was reported in 2.3% of the STEMI cases (6,553 cases). In Al Azzoni et al. <sup>[31]</sup> the incidence was 2.6%. It is also known that higher rates have been noted with other modalities that can assess microvascular flow: 34 to 39 percent using myocardial contrast echocardiography. <sup>[32]</sup>

In our study, multivariate analyses identified that age (OR=1.417, 95% CI 1.319–1.521) , DM (OR=10.110, 95% CI 3.950–25.880) ,HTN (OR=0.326, 95% CI 0.142–0.752), total ischemia time  $\geq$ 6 hours (OR=60.511, 95% CI 24.973–146.618) , SBP<90 mmHg (OR=0.238, 95% CI 0.091–0.621) , lesion length  $\geq$ 20 mm(OR=16.182, 95% CI 5.008–52.287) , high thrombus burden (thrombus grade  $\geq$ 4 )(OR=2.914, 95% CI 1.018–8.338), balloon pre dilatation (OR=0.272, 95% CI 0.093–0.791), stent length  $\geq$ 20 mm (OR=7.709, 95% CI 33.346–17.758), balloon post dilatation (OR=5.885, 95%CI 2.571–13.474) ,CRP (OR=1.016, 95% CI 1.002–1.030) were the independent predictors of the no-flow phenomenon.

In the trial by Sabin Padmajan et al. <sup>[33]</sup> Univariate analyses identified that age >60 years, reperfusion time >6 h, low initial TIMI flow ( $\leq$ 1), low initial TMPG flow ( $\leq$ 1), a high thrombus burden, a long target lesion, Killip Class III/IV and overlap stenting were the independent predictors of no-reflow. CPK MB was not included as a predictor as it was a result of no-reflow and not a predictor (it took place following the no-reflow).

In Zhou et al. <sup>[27]</sup> Univariate analysis showed that age, time from onset to reperfusion, systolic blood pressure (SBP) on admission, Killip class of myocardial infarction, intra-aortic balloon pump (IABP) uses prior to primary PCI, TIMI flow grade prior to primary PCI, occlusion type, thrombus burden on baseline angiography, length of target lesion, reference luminal diameter and method of reperfusion were related to no-reflow ( $p<0.05$  for all).

Multiple logistic regression analysis identified that age >65 years, reperfusion time>6 hours, SBP on admission  $\leq$ 100 mmHg, IABP use before PCI, a low initial TIMI flow ( $\leq$ 1), a high thrombus burden, and a long target lesion were the independent predictors of the NRP. <sup>[27]</sup>

**Limitations:** This is a single-center experience and small number of cases mainly due to the world-wide decrease in STEMI related admissions during COVID-19 period. Also, our definition of no-reflow depended on TIMI flow post-PCI. The MBG score was not included in our definition. This could have resulted in choosing only the worst no-reflow cases. IVUS hasn't been used to quantitatively assess plaque content and thrombus burden. non-invasive measures as MCE and contrast-enhanced cardi-

ovascular magnetic resonance which can detect no-reflow and also define the extent of myocardium affected wasn't used. Lastly, the low use of thrombus-aspirating device, which may improve myocardial reperfusion.

**Conclusions:**

As regards clinical and laboratory predictors age, DM, HTN, total ischemia time  $\geq 6$  hours, SBP $<90$  mmHg, and CRP levels on admission were associated with higher percentage of NRP. Whereas the angiographic predictors; lesion length  $\geq 20$  mm, high thrombus burden (thrombus grade  $\geq 4$ ), balloon pre dilatation, stent length  $\geq 20$  mm and balloon post dilatation could independently predicts no-reflow after Primary PCI. The persistent no reflow phenomenon was associated with a poor in-hospital outcome and increased incidence of malignant arrhythmia, cardiogenic shock and in hospital mortality compared to the transient no reflow phenomenon or normal reflow.

**Conflict of Interest:** Nil

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