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PREVALENCE AND ASSOCIATION OF NO-REFLOW WITH THE TOTAL ISCHEMIC TIME IN PATIENTS UNDERGOING PRIMARY ANGIOPLASTY

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ABSTRACT:

INTRODUCTION: *The no-reflow phenomenon is harmful; hence, early diagnosis of its prevalence and predictors is crucial. Few said the time between the first symptom and PCI was a risk factor. After 6 hours of STEMI, myocardial necrosis causes capillary bed edema, cell enlargement, neutrophil clogging, and microvascular dysfunction, causing no-reflow.*

AIMS & OBJECTIVE: *To determine the prevalence of the no-reflow phenomenon & its association with total ischemia time among patients of ST-elevation myocardial infarction undergoing primary PCI.*

MATERIAL & METHODS: *After the approval of IERB, a cross-sectional study was conducted at the cardiology department of CEPIC, Multan, using data from 1 September 2023 to 31 March 2024. 300 patients presenting with STEMI or new LBBB <24 hours were enrolled using a non-probability consecutive sampling technique. TIMI flow grade before and after primary PCI, along with the total ischemic time, was calculated (time from chest pain onset to balloon dilatation). The association was calculated using a student t-test through SPSS v26.*

RESULTS: *The mean age of the study population was 55.06±11.7 years. The incidence of No-reflow in our study population was 46 (15.3%). Regarding the association of no-reflow with TIT, the mean TIT was higher than in the normal TIMI flow showing a significant association ((489.35±387.83 vs 271.437±190.69; p<0.01). Similarly, No reflow as significantly affects the LV ejection fraction. When data was stratified, the association of no-reflow with TIT and LVEF was significant in older age groups, males, diabetics, hypertensives, and smokers.*

CONCLUSION: *No-reflow is significantly affected by total ischemic time, which in turn affects the left ventricular ejection fraction.*

KEY WORDS: *No Reflow; Total ischemic Time; Ischemic Time; TIMI; Thrombolysis; Myocardial Infarction; STEMI*

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INTRODUCTION:

One of the major causes of death worldwide is ST-elevation myocardial infarction (STEMI), which occurs due to complete thrombotic blockage from an atherosclerotic plaque in an epicardial coronary artery.[1] The main goal of acute STEMI treatment is to recanalize the occluded vessel for better results early through primary percutaneous coronary intervention (PCI) all over the world.[2] Despite recent breakthroughs in Primary PCI, over 25% of patients still experience no-reflow, which challenges interventionists.[3,4,5] Historically, thrombolysis in myocardial infarction (TIMI) scores of less than 3 during post-PCI are used to identify no-reflow objectively.[6] Studies have linked ischemia-reperfusion damage, inflammation, cellular edema, vasospasm, and distal micro-embolization to slow or no coronary flow.[7] No-reflow phenomenon affects the patient outcome with larger infarct size, lower left ventricular ejection fraction (LVEF), heart failure, malignant arrhythmias, re-infarction, cardiac rupture, and death, affecting both short-term and long-term prognoses.[8] Recognition of incidence & predictors of no-reflow phenomenon for early detection is essential due to the detrimental effects. Previous studies have not clearly identified all of its risk factors and predictors. However, a few indicated that the time from the onset of the first symptom to PCI was a significant risk factor.[9] Because after about 6 hrs. of STEMI, myocardial necrosis starts leading to capillary bed edema, cell swelling, neutrophil plugging and microvascular dysfunction, all of which add to the no-reflow phenomenon.

Mohamed Khalfallah et al. studied 545 patients of STEMI undergoing primary PCI at Tanta University.[10]

We aim to study the total cases of no-reflow & to see the effect of total ischemia time on it as an independent risk factor through its correlation with TIMI flow during primary PCI in our hospital. Many studies have been done on door-to-balloon time as a risk factor, but not much on total ischemia time. As Ischemia time is a modifiable risk factor, preventing this by public awareness & improved hospital settings would lessen in-hospital complications. It would enhance the long-term survival of STEMI patients.

MATERIAL & METHODS:

After the approval of IERB (# 45, dated 10-08-2023), a cross-sectional study was done at the cardiology department of CEPIC, Multan, using the data from 1st September 2023 to 31st March 2024. The required minimum sample size was 184, keeping in view the anticipated population proportion with NR phenomenon as 0.139 10 at an absolute precision of 0.05%. So, 300 patients aged 18–75 years, of either gender, presenting with STEMI or new LBBB for $<$24 hours were enrolled using a non-probability consecutive sampling technique. Patients with NSTEMI/UA, a history of thrombolytic therapy of $<$24 hours or having a history of coronary artery bypass graft or patients with contraindication of PCI, i.e., contrast allergy, serum creatinine $>$ 2 mg/dl, active bleeding from any site etc. were excluded. Total Ischemia Time was defined as the time interval (hours) from the onset of symptoms to balloon dilatation during Primary PCI. At the same time, No-Reflow was defined as a TIMI flow grade of $\leq$2 during the procedure without evidence of dissection, residual stenosis, distal embolism, or vasospasm.

After informed consent, a total of 300 patients fulfilling the inclusion criteria were enrolled. Baseline characteristics like age, gender, diabetes, hypertension, smoking, dyslipidemia, family history, & total time from chest pain onset to hospital door will be noted. A full complete examination,12 lead ECG, Transthoracic echocardiography & sample for routine labs were sent. After receiving the standard institutional ACS protocol, primary PCI was performed via a trans-radial or trans-femoral artery

route under standard conditions. Two experienced interventionists assessed the parameters, including the culprit vessel and TIMI flow grade before and after primary PCI, along with the time from hospital door to balloon dilatation. Total Ischemic time was calculated (time from chest pain onset to hospital door + time from hospital door to balloon dilatation). After primary PCI, the patients were admitted to the CCU for post-PCI care and left ventricular ejection fraction. All the data was recorded on Performa.

The data analysis was done through SPSS version 26.0. Quantitative data like age, TIT, TIMI flow and LVEF were presented as mean and standard deviation. Qualitative data like gender, hypertension, hyperlipidemia, diabetes, smoking, and No-reflow were given as frequency and percentages. The association between no-reflow and TIT was examined using an independent t-test. A p-value <0.05 was considered statistically significant. Confounders and effect modifiers were controlled using stratification.

RESULTS:

The mean age of the study population was 55.06±11.7 years. The major risk factor in our study population was smoking, and the major culprit vessel was LAD. Descriptive statistics of qualitative variables in terms of risk factors and the culprit's vessel are shown in Table 1. The incidence of No-reflow in our study population was 46 (15.3%), as shown in Figure 1. The mean total ischemic time was 304.8±244.12 min, ranging from 27 min to 1485 min. When data was divided based on no-reflow to find out its association with TIT, the mean TIT was higher than in the normal TIMI flow showing a significant association ($p<0.01$). Similarly, No reflow as significantly affects the LV ejection fraction. Table 2. When data was stratified, the association of no-reflow with TIT and LVEF was significant in older age groups, males, diabetics, hypertensives, and smokers. Still, the association was also significant in non-smokers for TIT, and for non-diabetics, it was significant for LVEF.

Table 1: Descriptive statistics of the study population (N=300)

Variables	Frequency (%)
Diabetes	109 (36.3%)
Hypertension	121 (40.3%)
Smoking	125 (41.7%)
Hyperlipidemia	17 (5.7%)
Family History	34 (11.3%)
LAD	144 (48%)
RCA	126 (42%)
LCX	34 (10%)

Table 2: Association of No-Reflow with TIT & LVEF (n=300)

Variable	No-Reflow (N=46)	TIMI -III Flow (N=254)	Mean Diff.	p-value
Total Ischemic Time (min)	489.35±387.83	271.437±190.69	217.92	**<0.001**
LV Ejection Fraction (%)	40.11±8.27%	43.73±6.17%	-3.62	**0.001***

Table 3: Post-Stratification analysis of No-Reflow association with TIT & LVEF (n=300)				
Stratification Group (N)	**Variables**	**No-Reflow (N)**	**TIMI -III Flow(N)**	**p-value**
Age 18-50 years (116)	**TIT (min)**	550.70±423.63 (20)	271.44±190.69 (96)	0.07
	LVEF (%)	41.25±8.41(20)	44.50±5.57(96)	0.112
Age >50 years (184)	**TIT (min)**	442.15±359.20 (26)	279.10±187.6 (158)	**0.032**
	LVEF (%)	39.24±8.21(26)	43.26±6.48(158)	**0.024**
Males (225)	**TIT (min)**	486.80±408.57 (34)	265.64±182.1 (191)	**0.04**
	LVEF (%)	40.29±8.43(34)	43.83±6.19(191)	**0.025**
Females (75)	**TIT (min)**	496.59±338.32 (12)	289.01±215.35 (63)	0.062
	LVEF (%)	39.59±8.11(12)	43.41±6.16(63)	0.143
Diabetics (109)	**TIT (min)**	610.94±322.73 (17)	266.80±189.10 (92)	**<0.01**
	LVEF (%)	38.53±8.62(17)	43.15±5.92(92)	**0.047**
Non-Diabetics (191)	**TIT (min)**	418.07±409.86 (29)	274.07±192.1 (162)	0.073
	LVEF (%)	41.03±8.06(29)	44.06±6.31(162)	**0.024**
Hypertensives (121)	**TIT (min)**	638.83±415.82 (23)	261.02±162.62 (98)	**<0.01**
	LVEF (%)	38.70±7.57(23)	42.65±6.02(98)	**0.008**
Non-Hypertensives (179)	**TIT (min)**	339.87±296.72 (23)	277.98±206.6 (156)	0.343
	LVEF (%)	41.52±8.85(23)	44.40±6.19(156)	0.144
Smokers (125)	**TIT (min)**	581.80±485.24 (15)	278.59±213.01 (110)	**0.031**
	LVEF (%)	41.00±8.87(15)	43.38±6.01(110)	0.159
Non-Smokers (175)	**TIT (min)**	444.61±330.75 (31)	265.97±172.29 (158)	**0.006**
	LVEF (%)	39.67±8.94(31)	43.99±6.30(158)	**0.015**

(Table 3)

DISCUSSION:

Since the TIMI trial in 1987 and onward TIMI trials,[11] the TIMI flow rate has been a prime indicator for successful revascularization. Although other indicators for microvascular perfusion have also been developed, like myocardial blush grade, the TIMI flow rate is of foremost importance.[12] Apart from many other factors leading to suboptimal epicardial flow after PCI like presentation blood pressure, heart rate,[13] thrombus burden,[14] stent length, post-dilatation,[15] total ischemic time is one of the

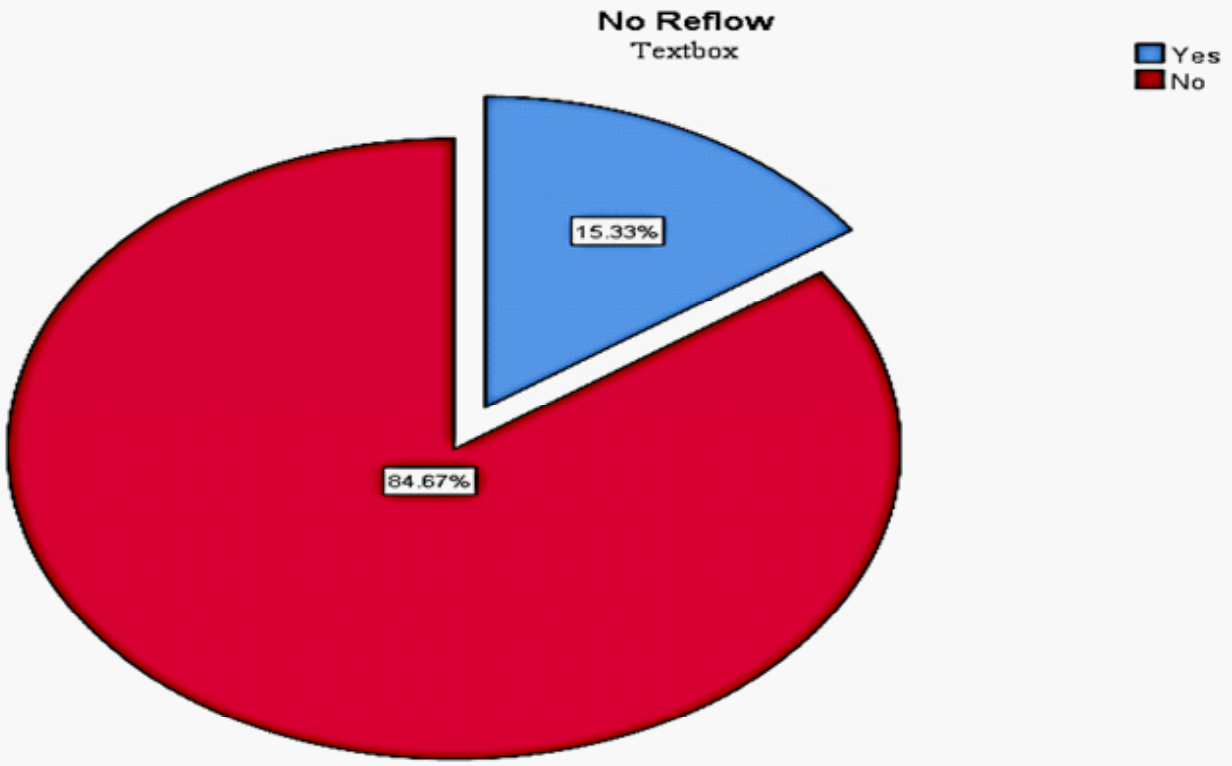

Fig -1: Prevalence of No-Reflow (n=300).

major determinants which have immediate and long-term prognostic significant as an old narrative "Time is myocardium and time is the outcome."[16]

The prevalence of no-reflow, which shows the efficiency of a cardiac center, is about 15% in our study. Previous literature shows a similar frequency, such as in one study by Dong-bao et al. [17], which had a no-reflow incidence of 19% in a population of 210 AMI patients. Another study by Zhou et al.[18] had a no-reflow of 17.3%. Our study has a slightly lower incidence of no-reflow due to advancements in technique, as it is the latest one, and other studies are somewhat older. One pooled analysis of more than 17000 patients showed a prevalence of 17%, which is also consistent with our research.[19]

The total ischemic time in our study was 304.8±244.12 min (approx. 5 hours). The TIT in the no-reflow group was higher than in the normal reflow group (489.35±387.83 vs 271.437±190.69 $p<0.05$). Previous literature has depicted similar results as in one study; it was 8.17 ± 4.02 in no-reflow compared to 4.54 ± 3.24 h in another group, respectively, $p<.001$.[20] A study in Karachi reported no flow in 31.4% of patients. Patients having TIT >6 hours comprised 97.8% of the no-reflow group and 32.5% of the reflow group, with a p-value of <0.05.[21] The latest study in Pakistan regarding comparative effects of two groups based on TIT showed the prevalence of TIT of >120 min in 66% patients. It is also associated with MACEs.[22] Like the previous literature, no-reflow was associated with older age groups, males, having major risk factors like diabetes, hypertension, and smoking in our study.[15,20,21,23]

Our study has a few limitations. Considering the burden of disease, it is still an insufficient sample, and the study is descriptive. More studies are warranted for comparison groups and long-term follow-up involving more tools measuring microvascular perfusion.

CONCLUSION:

No-reflow is a prevalent condition in patients of STEMI undergoing primary

PCI, which is significantly affected by total ischemic time, which in turn affects the left ventricular ejection fraction.

CONFLICT OF INTEREST:
Authors have no conflict of interest.
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