

Thrombolysis in Myocardial Infarction (TIMI) Risk Index as a Predictor of successful Primary Percutaneous Coronary Intervention

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Abstract: Objective: The thrombolysis in myocardial infarction (TIMI) risk score, global registry of acute coronary events (GRACE) risk score (GRS) and the TIMI risk index (TRI) have been reported in acute coronary artery disease patients. We investigated whether admission TRI is associated with no-reflow (NRF), in-hospital major cardiac events (MACE) and in-hospital mortality in patients underwent primary percutaneous coronary intervention (P-PCI). **Methods:** The study population consisted of 100 consecutive patients presented with STEMI and treated with PPCI during the period from March 2017 to November 2017 in Al-Azhar Main University Hospital, and the national heart institute (NHI), Giza, Egypt. All patients were subjected to informed consent, detailed history taking, clinical evaluation, ECG analysis and coronary risk factor assessment. Additionally, Killip class examinations of all patients were recorded. GRS, TRS and TRI were calculated. **Results:** GRS, TRS and TRI for STEMI patient who underwent P-PCI showed that the increase in these scores was associated with increased NRF, MACE, and increase in hospital mortality, so TRI is a simple score with fewer parameters which can predict a successful P-PCI. **Conclusion:** TRI significantly related to in-hospital MACE and in-hospital mortality. TRI uses simple and inexpensive methods for evaluating patients with STEMI. In addition, high TRI may be helpful in identifying high-risk patients and determining appropriate treatment strategies.

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1. Introduction:

Rapid restoration of coronary blood flow to the jeopardized myocardium is the crux of therapy after AMI. The invention and usage of stents have made percutaneous coronary intervention (PCI) a safe, effective, and preferred treatment of ST-segment elevation myocardial infarction (STEMI)¹.

The success of a PCI procedure is best defined by 3 interrelated components: angiographic findings, procedural events, and clinical outcomes. Angiographic Success was defined in ACCF/AHA/SCAI 2011 As a minimum diameter stenosis of < 10% (with an optimal goal of as close to 0% as possible) With final TIMI flow grade 3, without occlusion of a significant side branch, flow-limiting dissection, distal embolization, or angiographic thrombus, the procedural success of PCI was defined as achievement angiographic success without associated in-hospital major clinical complications (e.g. death, MI, stroke, emergency CABG), while the clinically successful PCI requires both anatomic and procedural success along with relief of signs and/or symptoms of myocardial ischemia².

However, even after patency of an infarcted artery was achieved via stent implantation, sufficient

myocardial reperfusion was not observed in 2.3% to 29% of patients in the setting of AMI, often called the no-reflow (NRF) phenomenon³.

Factors associated with increased primary PCI complication rates include advanced age, diabetes, CKD, congestive heart failure, and multivessel CAD. A large number of scoring systems and laboratory parameters have been used in clinical practice to predict mortality with PCI. Nevertheless, those interested in cardiovascular medicine still need an easily accessible, cost effective, and noninvasive predictor of primary PCI success. In order to identify high-risk patients with STEMI, various risks classification systems and scoring systems are used frequently. Prediction of early and late mortality in hundreds of thousands of patients has been shown by the in-hospital death global registry of acute coronary events (GRACE) risk score (GRS) and the thrombolysis in myocardial infarction (TIMI) risk score (TRS)⁴.

Recently, the TIMI risk index (TRI) which can predict mortality, may be easier to assess and can be scored with fewer parameters in patients with STEMI who was improved.

2. Patients and Methods

This study is a prospective study, comprised 100 patients with STEMI presenting to Al-Azhar Main University Hospital and National heart institute (NHI) from March 2017 to November 2017. Patients with STEMI eligible for PPCI according to European Society of Cardiology (ESC) guidelines were included. while the following were excluded Patients who were not treated with PPCI, patients who were treated by thrombolytic therapy, patients who presented more than 12 hours after symptoms onset and patients with chronic kidney disease on medical treatment or in dialysis.

Every patient's record included: Informed consent taken from patients. In case of incompetent patients, the informed consent were taken from the guardians. Thorough history taking with special emphasis on: Risk factors (Age, gender, diabetes, hypertension, smoking, dyslipidemia, family history). History of acute coronary syndromes (ACS) and revascularization, complete clinical examination, with demonstration of admission blood pressure, pulse, and killip class. Creatinine level and CKMB level were measured on admission.

Standard 12 lead electrocardiogram (ECG) was performed and transthoracic two dimensional echocardiography was performed upon admission to CCU. Conventional coronary angiography indicating initial TIMI flow in the infarcted related artery (IRA). TRS was assessed for all patients according to age, diabetes mellitus (DM), hypertension (HTN), angina, heart rate of <100 bpm, systolic blood pressure (SBP) of <100 mmHg, Killip class II-IV, weight of <67 kg, anterior MI or LBBB presentation, and latency of >4 h were recorded⁵.

GRS also was determined for all patients including age, creatinine, heart rate, SBP, Killip class, cardiac arrest on admission, elevated cardiac markers, and ST-segment deviation were recorded⁶.

TRI of patients was calculated for all patients by the formula

$$\{\text{Heart rate} \times (\text{age} \mp 10)^2\} / \text{SBP}^7.$$

During the in-hospital follow-up period patients were monitored for MACE.

Statistical analysis:

Data were fed to the computer and analyzed using IBM SPSS software package version 24.0. Qualitative data were described using number and percent. Quantitative data were described using Range (minimum and maximum), mean standard deviation and median. Comparison between different groups regarding categorical variables was tested using Chi-square test. When more than 20% of the cells have expected count less than 5, correction for chi-square was conducted using Fisher's exact test or Monte Carlo correction. The distributions of quantitative

variables were tested for normality using Kolmogorov-Smirnov test, Shapiro-Wilk test and D'Agostino test, also Histogram and QQ plot were used for vision test. If it reveals normal data distribution, parametric tests were applied.

If the data were abnormally distributed, non-parametric tests were used. For normally distributed data, comparison between two independent population were done using independent t-test, while abnormally distributed data was assessed using Mann Whitney test. Significance test results are quoted as two-tailed probabilities. Significance of the obtained results was judged at the 5% level.

3. Results

The study was a two-center, prospective, observational study consisted of 100 consecutive patients admitted at Al-Hussein University Hospital and the National Heart Institute for primary PCI from March 2017 to November 2017. The patients are divided into two groups according to the final TIMI flow after the primary PCI as follows:

- **The re-reflow group (Group A):**

This group included 82 patients, 64 patients were male (78%) while the remaining 18 patients were female (22%).

- **The no-reflow group (Group B):**

This group included 18 patients, 11 patients were male (61.1%), while only 7 patients were female (38.9%).

The two groups were then compared with respect to various clinical and laboratory variables (age, gender, absence of pre-infarction angina) and cardiac risk scores on admission.

Baseline clinical characteristics: table (1,2)

- **Age:** no-reflow patients were older than reflow with statistically significant p value (0.014*), the mean age was 52.44± 10.792 years for group A, and 60.66± 12.17 years for group B.

- **Sex:** no significant differences regarding gender in both groups, in group A 64 (78%) patients were males and 18(22%) were females, while in group B 11 (61.1%) patients were males and 7(38.9%) were females.

- **Diabetes Mellitus:** In group A, 22 (26.8%) patients are diabetic. In group B, 9 (50%) patients are diabetic. There was no statistically significant difference between the two groups with the P value > 0.05.

- **Hypertension:** Hypertension was present in 32(39.0%) patients of group A, and in 7(38.9%) patients of group B. There was no statistically significant difference between the two groups with the P value > 0.05.

- **Dyslipidemia:** Dyslipidemia is present in 45(54.8%) patients of group A, and in 13(72.2%)

patients of group B. There was no statistically significant difference between the two groups with the P value > 0.05.

- **Smoking:** In group A, 45(54.9%) patients were smokers. In group B, 10(55.6%) patients are smokers. There was no statistically significant difference between the two groups with the P value > 0.05.

- **History of IHD:** In group A 7 (8.5%) patients had history of IHD, while in group B there was 1 (5.6%) patient had history of IHD. There was no

statistically significant difference between the two groups with the P value > 0.05.

- **Family history of IHD:** In 17(20.7%) patients of group A, and in 2(11.1%) patients of group B. There was no statistically significant difference between the two groups with the P value > 0.05.

- **Previous PCI:** In 3(3.7%) patients of group A, and 1(5.6%) patients of group B. There was no statistically significant difference between the two groups with the P value > 0.05.

Table (1): Comparison between the two studied groups according to demographic data

	Group A (n = 82)		Group B (n = 18)		Test of sig.	p
	No	%	No	%		
Sex						
Male	64	78	11	61.1	$\chi^2=2.25$	0.133
Female	18	22.0	7	38.9		
Age						
Min. – Max.	29.0 – 81.0		44.0 – 78.0		t=2.647	0.014*
Mean ± SD	52.44± 10.792		60.66± 12.17			
Median	58.0		62.0			

χ^2 : Chi square test, t: Student t-test, *: Statistically significant at $p \leq 0.05$.

Table (2): Comparison between the two studied groups according to diabetes, hypertension, smoking, and other risk factors.

	Group A (n = 82)		Group B (n = 18)		χ^2	p
	No	%	No	%		
Diabetes						
Non-diabetic	60	73.2	9	50.0	2.803	0.094
Diabetic	22	26.8	9	50.0	2.083	
Hypertension	32	39.0	7	38.9	1.602	0.206
Smoking						
Non-smoker	37	45.1	8	44.4	0.560	0.454
Smoker	45	54.9	10	55.6	0.648	0.421
Dyslipidemia	45	54.8	13	72.2	2.021	0.155
Family History	17	20.7	2	11.1	0.760	^{FE} p=0.521
Previous IHD	7	8.5	1	5.6	0.279	^{FE} p=0.762
previous PCI	3	3.7	1	5.6	1.584	0.208

χ^2 : Chi square test, FE: Fisher Exact test.

Admission characteristics: (Table 3,4)

The admission systolic blood pressure (SBP):

In group A was 123.17 mmHg, and in group B was 97.77± 15.55 mmHg. The average mean pulse rate was 84.56 ± 16.33 bpm for group A, and 84.29 ± 15.69 bpm for group B. There was no statistically significant difference between the two groups

regarding the systolic BP and pulse rate with the P value > 0.05.

Killip class:

The number of patients with Killip I class, Killip II class was 76 (92.7%) in group A, and 13(72.2%) in group B. The number of patients with Killip III class Killip VI class was 6(7.3%) in group A, and 5(27.8%) in group B. There was statistically significant

difference between the two groups with the P value < 0.05.

ECG diagnosis:

As regard ECG diagnosis; 52(63.4%) patients presented with anterior STEMI in group A, and 12 (66.7%) patients in group B. 30 (36.6%) patients presented with non-anterior MI in group A, and 6 (33.3%) patients in group B. There was no statistically

significant difference between the two groups with the P value > 0.05.

Duration of chest pain:

The mean time from onset of symptoms to presentation was 6±3.8 hours in group A, versus 15.9±7.8 hours in group B. There was no statistically significant difference between the two groups with the P value > 0.05.

Table (3): Comparison between the two studied groups according to SBP, pulse, and killip class.

	Group A (n = 82)		Group B (n = 18)		T	P
SBP						
Min. – Max.	50.0 – 200.0		70.0 – 160.0			
Mean ± SD	123.17± 14.7		97.77± 15.55		1.971	0.051
Median	130.0		120.0			
Pulse						
Min. – Max.	41.0 – 120.0		60.0 – 130.0			
Mean ± SD	84.56 ± 16.33		84.29 ± 15.69		0.069	0.945
Median	80.0		88.0			
	Group A (n = 82)		Group B (n = 18)		Z	P
	No	%	No	%		
Killip class						
Killip class I & II	76	92.7	13	72.2	-2.50	0.012*
Killip class III & IV	6	7.3	5	27.8		

t: Student t-test, *: Statistically significant at p ≤ 0.05, Z: Z for Mann Whitney test,

Table (4): Comparison between the two studied groups according to ECG.

	Group A (n = 82)		Group B (n = 18)		χ^2	p
	No	%	No	%		
ECG						
Anterior MI	52	63.4	12	66.7	0.313	0.576
Non anterior MI	30	36.6	6	33.3	0.150	^{FE} p=0.656

χ^2 : Chi square test, FE: Fisher Exact test.

Table (5): Comparison between the two studied groups according to Duration of chest pain.

	Group A (n = 82)	Group B (n = 18)	Z	p
Duration of chest pain (h)				
Min. – Max.	<4 – 10.5	<4 – 9		
Mean ± SD	4.40 ± 2.70	5.33 ± 2.12	-1.483	0.173
Median	3.5	5.75		

Z: Z for Mann Whitney test, *: Statistically significant at p ≤ 0.05.

Table (6): Comparison between the two studied groups according to Cardiac risk scores on admission.

	Group A (n = 82)	Group B (n = 18)	Test of sig.	p
TIMI risk score				
Min. – Max.	0.0 – 10.0	2.0 – 10.0	t = -8.334	0.001*
Mean ± SD	2.37 ± 1.83	6.50 ± 2.20		
Median	2.0	6.50		
GRACE score				
Min. – Max.	72 – 240	31.0 – 211.0	t = -2.934	0.0014*
Mean ± SD	134.32 ± 23.97	157.44 ± 50.48		
Median	130.0	178.5		
TIMI risk index				
Min. – Max.	5.0 – 53.0	16.0 – 223.0	t = -5.168	<0.001*
Mean ± SD	20.48 ± 9.71	54.16 ± 56.27		
Median	18.50	35.0		

t: Student t-test, *: Statistically significant at $p \leq 0.05$.

Cardiac risk scores on admission: Table (6)

The mean results of TIMI risk score, GRACE score, and TIMI risk index are higher in group B (6.50 ± 2.20, 157.44 ± 50.48, 54.16 ± 56.27 respectively) than in group A (2.37 ± 1.83, 134.32 ± 23.97, 20.48 ± 9.71 respectively). There was statistically significant difference between the two groups with the P value < 0.05. High level of TIMI risk index was an independent predictor of no reflow.

Echocardiographic parameters:

The mean Ejection fraction values was higher in group A 53.22 ± 10.522 more than group B 48.67 ± 11.712, but statistically no significant difference p value >0.05. As regard LVEDD, LVESD, LA diameter there was no significant difference between both groups as p value >0.

Table (7): Comparison between the two studied groups according to Echocardiographic parameters.

	Group A (n = 99)	Group B (n = 21)	Test of sig.	p
Ejection fraction EF %				
Min. – Max.	23.0 – 71.0	30 – 70	t = 1.628	0.348
Mean ± SD	53.22 ± 10.522	48.67 ± 11.712		
Median	55.00	48.50		
LVEDD cm				
Min. – Max.	3.80 – 7.70	2.10– 6.00	t = 0.318	0.543
Mean ± SD	5.06 ± 0.73	4.99 ± 0.90		
Median	5.00	3.65		
LVESD cm				
Min. – Max.	2.50 – 6.70	2.70 – 5.10	t = -0.396	0.415
Mean ± SD	3.65 ± 0.82	3.73 ± 0.65		
Median	3.40	12.20		
LA diameter cm				
Min. – Max.	2.30– 5.20	2.90 – 4.40	t = -0.777	0.821
Mean ± SD	3.51 ± 0.47	3.61 ± 0.44		
Median	3.50	3.60		

t: Student t-test

Initial laboratory results: Cardiac enzymes:

In group A the mean CKMB value was 75.64±49.05 mg/dl. While in group B it was

85.50±45.55. There was no statistically significant difference between the two groups with the P value > 0.05.

Serum creatinine:

In group A the mean creatinine value was 0.908±0.206 mg/dl, while in group B it was 1.012±0.267. There was statistically significant difference between the two groups with the P value = 0.035*.

Table (8) comparison between two groups according Serum creatinine level.

	Group A (n = 82)		Group B (n = 18)		Z	P value
	Mean	SD	Mean	SD		
CKMB	75.64	49.05	85.50	45.55	-781	0.907

Z: Z for Mann Whitney test.

Table (9) comparison between two groups according CKMB level.

	Group A (n = 82)		Group B (n = 18)		Z	P value
	Mean	SD	Mean	SD		
Creatinine	0.908	0.206	1.012	0.267	-1.836	0.035*

Z: Z for Mann Whitney test, *: Statistically significant at $p \leq 0.05$.

Angiographic findings and procedural aspects:

Number of vessels:

In group A 50(61%) patients had one vessel disease and 32(39%) had more than one vessel, while

in group B 7(38.9%) patients had one vessel disease and 11(61.1%) had more than one vessel occlusion. There was no statistically significant difference between the two groups with the P value > 0.05.

Table (10): Number of vessels.

	Group A (n = 82)		Group B (n = 18)		χ^2	P
	No	%	No	%		
Number of vessels						
One vessel	50	61	7	38.9	2.937	0.0865
More than one	32	39	11	61.1		

χ^2 : Chi square test, *: Statistically significant at $p \leq 0.05$.

Infarct related artery (IRA):

In group A, IRA was LAD in 49 (59.7%) patients, LCX in 9 (11%) patients, RCA in 24 (29.3%) patients. In group B, IRA was LAD in 10(55.6%)

patients, LCX in 1(5.6%) patients, and RCA in 7 (38.8%) patients. There was no statistically significant difference between the two groups with the P value > 0.05.

Table (11): Comparison between the two studied groups according to infarct related artery.

	Group A (n = 82)		Group B (n = 18)		χ^2	P
	No	%	No	%		
Infarct related artery						
LAD	49	59.7	10	55.6	0.054	0.817
LCX	9	11	1	5.6	2.71	^{FE} p = 0.143
RCA	24	29.3	7	38.8	0.64	^{FE} p = 0.424

χ^2 : Chi square test, FE: Fisher Exact test.

Site of lesion:

In group A, proximal lesions was 47 (57.3%), mid lesions 32 (39%), and distal lesions 3(3.7%). In group B, proximal lesions was 10 (55.6%), mid lesions

8 (44.4%), and no patients had distal lesions 3(3.7%). There was no statistically significant difference between the two groups with the P value > 0.05.

Table (12): Comparison between the two studied groups according to site of lesion.

	Group A (n = 82)		Group B (n = 18)		χ^2	P
	No	%	No	%		
Site of lesion						
Proximal	47	57.3	10	55.6	0.019	0.891
Mid	32	39	8	44.4	0.180	^{FE} p = 0.670
Distal	3	3.7	0	0.0	0.679	^{FE} p = 0.409

χ^2 : Chi square test, FE: Fisher Exact test.

TIMI flow:

In group A, 82(100%) patients had initial TIMI 3 flow, in group B, 1(5.6%) patients had initial TIMI 0 flow, 9(50%) patient had initial TIMI 2 flow, and 3

(44.4%) patient had initial TIMI 3 flow. Significantly more patients with TIMI flow grade 2 in the no reflow group = 0.042

Table (13): Comparison between the two studied groups according to initial TIMI flow.

	Group A (n = 82)		Group B (n = 18)		Test of sig.	P
	No	%	No	%		
Initial TIMI flow						
0	0	0.0	1	5.6	0.113	^{FE} p = 1.000
1	0	0.0	0	0.0	0.0	0.0
2	0	0.0	9	50	4.286*	^{FE} p = 0.042*
3	82	100	8	44.4	0.113	^{FE} p = 1.000

FE: Fisher Exact test, *: Statistically significant at $p \leq 0.05$.

Hospitalization duration:

In group A the mean duration for hospital stay was 3.40± 1.023 hrs. Compared to 4.33± 2.223 hrs in

group B, There was statistically significant difference between the two groups with the P value < 0.05.

Table (14): Comparison between the two studied groups according to hospitalization duration.

	Group A (n = 82)		Group B (n = 18)		Test of sig.	P
	No	%	No	%		
Hospitalization duration (hrs)						
Min. – Max.	2.50 – 7.0		0.0 – 10.0			
Mean ± SD	3.40± 1.023		4.33± 2.223		t=-2.725	0.0008*
Median	3.0		4.0			

t: Student t-test, *: Statistically significant at $p \leq 0.05$.

In hospital course follow up:

In-hospital mortality, cardiogenic shock, severe ventricular arrhythmia, and cardiopulmonary

resuscitations were more common in the no reflow group.

Table (15): Comparison between the two studied groups according to in hospital course follow up.

	Group A (n = 82)		Group B (n = 18)		χ^2	p
	No	%	No	%		
Advanced HF	5	6	2	11.1	1.084	^{FE} p=0.297
Pulmonary edema	4	4.9	4	22.2	6.033	^{FE} p=0.014*
Cardiogenic shock	3	3.7	4	22.2	7.813	^{FE} p= 0.019*
Complete AV block	3	3.7	2	11.1	0.279	^{FE} p=0.762
Ventricular arrhythmia	2	2.4	3	16.7	6.290	^{FE} p= 0.039*
In- hospital mortality	2	2.4	5	27.8	7.709	^{FE} p= 0.002*
Cardiopulmonary resuscitation	4	4.9	5	27.8	23.977	^{FE} p= 0.002*

χ^2 : Chi square test, FE: Fisher Exact test, *: Statistically significant at $p \leq 0.05$.

4. Discussion

Baseline clinical characteristics:

In our study, mean age of **group A** at presentation was 52.44 ± 10.792 years, 78% were male, 26.8% had diabetes, 39% were hypertensive, 54.9% were smokers, 54.8% were dyslipidemia, 8.5% had a prior ACS, 20.7% had family history of IHD, and previous PCI was in 3.7%. In **group B**, mean age at presentation was significantly higher (60.66 ± 12.17 years, $p=0.014$), with insignificant difference as regards sex, hypertension, diabetes, smoking status, dyslipidemia, history of prior ACS, family history of IHD, and previous PCI where 61.1% were male, 50% had diabetes, 38.9% were hypertensive, 55.6% were smokers, 72.2% were dyslipidemia, 5.6% had a prior IHD, 11.1% had family history of IHD, and previous PCI was 5.6%.

Ndrepepa G et al.,⁸ studied the clinical factors related to the development of no-reflow phenomenon after successful coronary reperfusion in patients with AMI. Between January 1998 and December 2007, 1518 patients with STEMI presenting within 24 hours from the symptom onset were treated with PPCI in the Deutsches Herz zentrum Munich. Mean age of the no reflow group patients was significantly higher than the reflow group (65.8 vs. 61.4 years, $p=0.001$), and history of previous MI was significantly higher in no reflow group than reflow group (18.5% vs. 11.7% respectively, $p=0.041$), with non-significant difference in sex (71.3% vs. 75% respectively), presence of DM (14.8% vs. 20.3%, respectively), hypertension (66.7% vs. 67.3% respectively), current smoking (30.6% vs. 40.5% respectively) & dyslipidemia (57.4% vs. 58.1% respectively).

Admission characteristics:

In this study, no significant difference between group A and group B regarding SBP (123.17 ± 14.7 mmHg vs.. 97.77 ± 15.55 mmHg respectively), pulse rate (84.56 ± 16.33 Bpm vs.. 84.29 ± 15.69 Bpm respectively), and Killip class (class I & II 92.7% vs..

72.2% respectively, class III & IV 7.3% vs.. 27.8% respectively). As regards the ECG, there was no significant difference between group A and B in the location of MI (anterior 63.4% vs.. 66.7%, non-anterior 36.6% vs.. 33.3% respectively).

In our study, we find the significant difference between group A and B (the normal flow and no reflow groups respectively) regarding Killip class Killip class (class I & II 92.7% vs.. 72.2% respectively, class III & IV 7.3% vs.. 27.8% respectively). More patients with Killip class \geq II were found in the no reflow group in some studies in the literature, pulse rate (pulse rate was significantly higher in no reflow group in some studies in the literature), location of MI (anterior MI was significantly higher in the no reflow group in some studies in the literature).

Ndrepepa G et al.,⁸ reported that there was significant difference between the no reflow and reflow groups as regards killip class (class I 63% vs. 70.9%, class \geq II 34% vs. 29.1%, $p=0.019$), with no significant difference between the study groups with respect to median SBP (125 vs. 130 mmHg), median DBP (70 mmHg in both groups), median of pulse rate (78 bpm in both groups), and location of MI (anterior 41.7% vs. 43%, inferior 41.7% vs. 38.1%, lateral 16.6% vs. 18.9%).

Ito M et al.,⁹ there was significant difference between the no reflow and reflow groups as regards killip class (class I % 83.3% vs. 72.1%, class \geq II 16.7% vs. 27.9%, $p=0.03$).

Duration of chest pain:

In present study, the time from onset of symptoms to presentation was significantly longer in group B than in group A (mean 4.40 ± 2.7 hours vs.. 5.33 ± 2.12 hours, median 3.5 hours vs.. 5.75 hours, $p < 0.001$).

In our study the time from onset of symptoms to presentation in the normal flow group was near to that published in the literature, but the time from onset of

symptoms to presentation in the no reflow group was much longer than that published in the literature.

Longer the time from onset of symptoms to presentation is associated with more ischemic injury to tissues, hence the occurrence of no reflow and in hospital MACE.

Ndrepepa et al.,⁸ reported that door to balloon time was significantly longer in the no reflow group than reflow group (the median was 10.7 vs.. 6.5 hours, $p=0.001$).

Ito et al.,⁹ reported that door to balloon time was **not** significantly different between the no reflow group and the reflow group (the mean was 5.8 ± 4.1 hours vs.. 6.3 ± 4.5 hours, $p=0.41$).

Iwakura et al.,¹⁰ reported that mean door to balloon time was **not** significantly different in the no reflow group and the reflow group (the mean was 5.2 ± 4.1 hours vs.. 6.1 ± 4 hours, $p=0.40$).

Akpek et al.,¹¹ reported that door to balloon time was significantly longer in the no reflow group than reflow group (the mean was 4.8 ± 1.3 hours vs.. 4.2 ± 1.4 hours, $p < 0.001$).

Cardiac risk scores:

In the present study we showed that increased TRI, TRS and GRS on admission were significantly associated with the development of angiographic no reflow phenomenon in patients with acute STEMI who underwent p-PCI. Moreover, TRI was a significant and independent predictor of no reflow.

The mean results of TIMI risk score, GRACE score, and TIMI risk index are higher in group B ($6.50 \pm 2.20, 157.44 \pm 50.48, 54.16 \pm 56.27$ respectively) than in group A ($2.37 \pm 1.83, 134.32 \pm 23.97, 20.48 \pm 9.71$ respectively). There was statistically significant difference between the two groups with the P value < 0.05 .

Halit et al.,¹² showed that the mean values of risk scores TIMI risk index (TRI), TIMI risk score (TRS), and GRACE score (GRS) on admission are higher in group of no reflow ($32.1 \pm 15.8, 4.8 \pm 2.9, 177.0 \pm 51.4$ respectively) than in reflow group ($25.6 \pm 12.5, 3.8 \pm 2.2, 151.7 \pm 35.4$). There was statistically significant difference between the two groups with the P value < 0.05 . They concluded that admission TRI may predict the development of NRF phenomenon after p-PCI in patients with acute STEMI.

Initial laboratory results:

• Cardiac enzymes:

In our study in group A the mean CKMB value was 75.64 ± 49.05 mg/dl. While in group B it was 85.50 ± 45.55 . There was no statistically significant difference between the two groups with the P value > 0.05 . In **Halit et al.,¹²** study also there was no significant difference between the two groups.

Serum creatinine:

In our study the admission serum creatinine was high in no reflow group with statistically significant p value 0.035. But other studies did not report that serum creatinine were a predictor of no reflow.

Angiographic findings

In this study, there was no significant difference between groups A and B regarding IRA LAD 59.7% vs.. 55.6%, LCX 11% vs.. 5.6%, and RCA 29.3% vs.. 38.8% respectively). No significant difference was present between the two groups regarding the number of vessels occluded. TIMI flow grade significantly more patients with TIMI flow grade 2 in the no reflow group (TIMI 0 in 0 % vs.. 5.6 %, TIMI 2 in 0 % vs.. 50 %, TIMI 3 in 100% vs.. 44.4%, respectively). No significant difference between the two groups regarding the site of the lesion (proximal in 57.3% vs.. 55.6%, mid 39% vs.. 44.4%, and distal in 3.7% vs.. 0.0%, respectively).

Halit et al.,¹² found no significant difference between the reflow and no reflow groups regarding IRA (LAD 46% vs.. 57%, LCX 17% vs.. 4 %, RCA 37% vs.. 39%), the number of vessels occluded (1 vessel in 44% vs.. 37%, >1 vessel in 56% vs.. 63%).

Ndrepepa et al.,⁸ found no significant difference between the reflow and no reflow groups regarding IRA (LAD 43.3% vs.. 42.6%, LCX 20.7% vs.. 15.7%, RCA 33.6% vs.. 37.1%).

Akpek et al.,¹¹ reported that there was no significant difference between no reflow and reflow groups regarding IRA (LAD 53% vs.. 48%, LCX 18% vs.. 22%, RCA 29% vs.. 30%).

Huczek et al.,¹³ reported that there was no significant difference between the low MPV and high MPV groups regarding IRA (LAD 46.1% vs.. 41.7%, LCX 14.5% vs.. 9.8%, RCA 39.5% vs.. 48.5%, respectively), initial TIMI flow (grade 0/1 in 80.9% vs.. 83.3%, respectively).

Iwakura et al.,¹⁰ found that significantly more patients having LAD as IRA (83.7% vs.. 53.6%, $p=0.0002$), and more patients with initial TIMI 0 flow (89.8% vs.. 70. %, $p=0.005$) in the no reflow group than in the reflow group.

Halit et al.,¹² TRI is significantly related to SS and Gensini score in predicting the extent and severity of CAD in patients with STEMI.

In-hospital course:

In this study in-hospital MACE, In-hospital mortality, cardiogenic shock, severe ventricular arrhythmia, and cardiopulmonary resuscitations were more common in the no reflow group; cardiac mortality occurred in 2.4% in reflow group vs.. 27.8% in no reflow group, in reflow group 4.9% patients developed pulmonary edema vs... 22.2% in no reflow group. 3.7% of patients developed cardiogenic shock in group A (reflow group), vs... 22.2% of patients in

group B (no reflow group). 3.7% of patients developed complete AV block in group A (reflow group), vs. 11.1% of patients in group B (no reflow group), in group A 2.4% patients had Ventricular arrhythmia vs. 16.7% in group B, In group A 4.9% patients had CPR at hospital stay, while in group B 27.8% of patients had cardiopulmonary resuscitation.

Halit et al.,¹² reported that in-hospital MACE significantly higher in the no reflow group (17% vs. 44%, $P < 0.001$); cardiac death (7% vs. 26%, $P < 0.001$), Advanced pulmonary edema (4% vs. 9%, $P = 0.043$), Cardiogenic shock (6% vs. 20%, $P < 0.001$), Serious ventricular arrhythmia (7% vs. 19%, $P < 0.001$), and Cardiopulmonary resuscitation (8% vs. 29%, $P < 0.001$).

Morrow et al.,¹⁴ TRI was a strong and independent predictor of mortality at 24 hours. It was validated in external data set of STEMI patients from the TIMI-9 trials that showed both a high discriminatory capacity and concordance between the observed 30-day mortality and the predictions based on the In TIME-II data.

PJ Bradshaw et al.,¹⁵ The TIMI risk index was strongly associated with 30-day mortality for both STEMI and non-STEMI patients. The C statistic was 0.82 for STEMI and 0.80 for non-STEMI patients, with overlapping 95% CI. The discriminatory capacity was somewhat lower for patients older than 65 years of age (0.74). The model was well calibrated.

Pier Woudstra et al.,¹⁶ TIMI-RI predicts not only short but also long-term mortality in STEMI patients treated with PPCI.

TRI, calculated using the formula, $\text{heart rate} \times (\text{age}/10)^2 / \text{SBP}$, was derived from observed risk relations among 13,253 patients enrolled in the In TIME-II randomized trial of lanoteplase versus alteplase as reperfusion therapy for STEMI [**In TIME-II Investigators, 2000**].¹⁷

TRI significantly related to in-hospital MACEs and in-hospital mortality. TRI uses simple and inexpensive methods for evaluating patients with STEMI. In addition, high TRI may be helpful in identifying high-risk patients and determining appropriate treatment strategies. TRI can be readily calculated at point of care, thereby facilitating short- and long-term risk prediction for STEMI patients, even prior to revascularization.

Study Limitations:

1. The sample size is relatively small compared to large studies published in the literature, and larger studies are needed to validate these results.

2. They do not represent all-comers who were presented with acute STEMI because there are still many patients in our country treated with fibrinolysis only without further PCI because of financial aspect. That is to say that the presumed lower mortality rate of

affluent patients and the higher mortality rate of the sicker patients may balance each other out.

3. There is a delay from first medical contact to primary PCI and comprises the time taken by patients to decide whether they can proceed with the procedure, based on financial constraints.

4. Our data represent a two-centre experience where the operators are experienced and the hospital has good medical and paramedical team and good ambulance system. Whether these results can be generalized to other hospitals in our country is unclear.

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