

CLINICAL SIGNIFICANCE OF PRE-PROCEDURE THROMBOLYSIS IN MYOCARDIAL INFARCTION FLOW IN PATIENTS WITH ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

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ABSTRACT

Objective: To assess the clinical implications of pre-procedure Thrombolysis in Myocardial Infarction (TIMI) flow and its relationship to in-hospital outcomes in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI).

Methods: A descriptive cross-sectional study was carried out at National Institute of Cardiovascular Diseases (NICVD), Karachi, in Adult Cardiology Department. There was a total of 316 consecutive patients aged 18 to 70 years who had a presentation of STEMI and primary PCI within 24 hours of onset of symptoms. Coronary angiography was performed pre-procedure to determine TIMI flow grade and patients were divided into impaired flow (TIMI 0/I) and preserved flow (TIMI II/III). In-hospital outcomes including slow flow/no-reflow, cardiogenic shock, malignant ventricular arrhythmias, heart failure requiring medical therapy, mechanical ventilation, intra-aortic balloon pump support, in-hospital mortality, and length of hospital stay were assessed.

Results: Of 316 patients, 228 (72.2%) had impaired pre-procedure (TIMI 0/I) and preserved (TIMI II/III) flow in 88 (27.8%) patients. Patients with impaired TIMI flow had higher rates of slow flow / no reflow (20.2% vs 6.8%, $p=0.003$), malignant ventricular arrhythmias (23.2% vs 10.2%, $p=0.009$), heart failure requiring medical therapy (34.2% vs 13.6%, $p<0.001$), and longer hospital stay (37.7% vs 20.5%, $p=0.004$) than patients with preserved flow.

Conclusion: There was a correlation between impaired pre-procedure TIMI flow and in-hospital adverse outcomes in STEMI patients undergoing primary PCI. Pre-procedure TIMI flow assessment might be a valuable angiographic tool for early risk stratification and outcome prediction.

KEYWORDS: Coronary Angiography; Myocardial Infarction; ST Elevation Myocardial Infarction.

INTRODUCTION

Despite tremendous improvements in reperfusion therapy, pharmacologic treatment and interventional cardiology, ST-segment elevation myocardial infarction (STEMI) is one of the most critical cardiovascular emergencies, continuing to play a significant role in the burden of morbidity and mortality. Primary percutaneous coronary intervention (PCI) is now favored over fibrinolysis for revascularization due to quicker restoration of epicardial coronary patency and survival benefit. But reopening of the infarct related artery does not always mean myocardial reperfusion is adequate and clinical outcome is determined by multiple factors that occur before and during intervention, such as the initial coronary flow status of the artery being opened [1].

To date, the Thrombolysis in Myocardial Infarction (TIMI) flow grading system is still the reference standard for assessing coronary artery blood flow. Pre-procedure TIMI flow is a measure of spontaneous reperfusion of the infarct-related artery, and is a useful indicator of the burden of thrombus, time of coronary occlusion, and severity of myocardial ischemia. Preserved antegrade flow prior to PCI may be associated with less myocardial injury, while persistent complete occlusion (TIMI 0 flow) may signify extensive thrombotic occlusion and higher risk for adverse outcomes [2].

Pre-procedure TIMI flow is a strong predictor of the quality of myocardial reperfusion. PCI can successfully reopen epicardial vessels but poor myocardial perfusion can still occur as a result of distal embolization,

inflammation, endothelial dysfunction, and microvascular injury. This is known as 'no-reflow' and is an important determinant of infarct size, left ventricular dysfunction, heart failure and mortality after STEMI [3]. Microvascular obstruction has also been identified as a significant factor of the adverse ventricular remodeling and poor long-term outcomes even after technically successful PCI [4].

Thus, the coronary microcirculation is important in determining recovery of the myocardium after reflow. Even if the tissue flow is restored angiographically, the tissue oxygen supply may be restricted due to damage to the microvascular network. Recent studies have emphasized the need to focus on microvascular injury and microvascular reperfusion mechanisms to improve outcomes following myocardial infarction [5]. In addition, cardioprotective strategies have been aimed at minimizing ischemia-reperfusion injury and maintaining coronary microvascular function as crucial components of the management of STEMI [6].

There have been significant advances in the guidelines for the treatment of STEMI, with a focus on timely diagnosis, rapid reperfusion, and optimized PCI techniques. But pre-procedure TIMI flow assessment may offer further pre-intervention prognostic data and may help to identify patients with a higher risk of complications [7]. At present, there is evidence that the combination of angiographic markers with clinical features might be more useful in early risk stratification and provide more personalised management [8].

Although pre-procedure TIMI flow has been shown to be useful for STEMI care, there are still uncertainties about its predictive value in the modern era of PCI-treated populations. Due to differences in patient populations, ischemic time, treatment, and reperfusion success, there have been conflicting results. Hence, evaluation of pre-procedure TIMI flow is still clinically relevant to see if this angiographic parameter is useful in predicting outcomes [9,10].

This study was carried out because despite pre-procedure TIMI flow showing potential in early detection of myocardial injury, reperfusion success and prognosis in STEMI patients, its clinical implications in contemporary primary PCI populations were still not fully defined. Prior research had suggested that reduced initial coronary flow corresponded to higher thrombotic load, microvascular damage, and worse clinical outcomes. Hence, the present study was undertaken to assess the correlation between pre-procedure TIMI flow and the clinical outcomes in STEMI patients treated with PCI.

METHODS

This descriptive cross-sectional study was conducted in the Adult Cardiology Department of the National Institute of Cardiovascular Diseases (NICVD), Karachi, over a period of six months. Adult patients with acute ST-segment elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI) were included. Sample size was determined using the WHO sample size calculator version 2.0, with an expected frequency of pre-procedure TIMI III flow of 11.4%, a 95% confidence level and a 3.5% margin of error, a sample size of **316 patients** was required. A non-probability consecutive sampling method was used to recruit patients.

All patients with STEMI based on the predefined operational criteria and who underwent primary PCI within 24 hours of onset of symptoms were included regardless of gender and age (18–70 years). Patients were excluded if they had a prior history of CABG surgery, prior PCI surgery, cardiogenic shock at presentation or refused consent. Eligible subjects were recruited and demographic and clinical data was gathered after written informed consent. Baseline parameters like age, gender, total ischemic time, symptom to hospital presentation time, cardiovascular risk factors like hypertension, diabetes mellitus, smoking, dyslipidaemia, prior myocardial infarction, prior PCI, chronic kidney disease, stroke/transient ischemic attack and family history of coronary artery disease were noted. Killip classification was used for clinical status at presentation.

Coronary angiography was done in all the patients enrolled in the study and the involved vessel was scored with pre-procedural TIMI flow grade. Patients were divided into two groups, patients with reduced pre-procedure flow (TIMI 0/I) and patients with preserved flow (TIMI II/III). PCI was carried out by experienced interventional cardiologists, and procedural data such as characteristics of the culprit vessel, the number of involved vessels, the length of the lesion, and the intervention strategy were documented.

Patients with slow flow or no-reflow phenomenon were treated as per the standard institutional guidelines with pharmacological intervention such as adenosine, adrenaline and tirofiban as appropriate. Post-procedure TIMI flow was documented and patients were monitored during their hospital stays for clinical outcomes. Outcomes recorded were slow flow/no-reflow, in-hospital death, cardiogenic shock, malignant ventricular arrhythmias, medical therapy for heart failure, mechanical ventilation, intra-aortic balloon pump (IABP) support and length of hospital stay.

The collected data was kept confidential and analyzed in SPSS version 26. Normally distributed continuous variables (such as age or length of hospital stay) were expressed as mean $\pm$ standard deviation (SD) and skewed continuous variables (such as lesion length) were expressed as median (IQR). Shapiro–Wilk test was used to evaluate normality. All categorical variables such as demographic, cardiovascular risk factors, TIMI flow grades, procedural variables, and clinical outcomes were expressed as frequencies and percentages. Pre-procedure TIMI flow and clinical outcomes were compared using chi-square. Stratification was used to control for effect modifiers such as age, gender, Killip class, diabetes, hypertension, smoking, dyslipidemia, left-ventricular ejection fraction, chronic kidney disease, family history of coronary artery disease and procedural complications. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 316 patients with STEMI were included, all undergoing primary PCI. The baseline characteristics are shown in **Table 1**. The mean age was 57.9 ± 11.0 years, with male predominance (240; 75.9%). Common cardiovascular risk factors included hypertension, diabetes mellitus, and smoking and most patients were Killip class I.

Pre-procedure TIMI flow distribution and the angiographic findings are presented in **Table 2**. The pre-procedure flow (TIMI 0/I) was seen in 218 (69.0%) and preserved flow (TIMI II/III) was seen in 96 (30.4%) patients. The most common culprit vessel was the left anterior descending artery (LAD) (171; 54.1%) followed by the right coronary artery (RCA) (97; 30.7%).

Pre-procedure TIMI flow is shown in **Table 3**. Patients with reduced pre-procedure TIMI flow had a greater incidence of slow flow/no-reflow, heart failure, arrhythmias, and longer hospital stay than those with preserved flow.

The relationship between the TIMI flow category and in-hospital outcome is shown in **Table 4**. Poor pre-procedure TIMI flow was a risk factor for procedural complications and adverse clinical events, indicating that assessment of coronary flow can help in the prognosis of STEMI patients undergoing primary PCI.

Table 1. Baseline demographic and clinical characteristics of STEMI patients (n=316)

Variable	Overall population (n=316)
Age (years), mean $\pm$ SD	57.9 $\pm$ 11.0
Male gender, n (%)	240 (75.9)
Female gender, n (%)	76 (24.1)
BMI (kg/m ²), mean $\pm$ SD	26.1 $\pm$ 3.3
Hypertension, n (%)	165 (52.2)
Diabetes mellitus, n (%)	90 (28.5)
Smoking, n (%)	112 (35.4)
Dyslipidemia, n (%)	101 (32.0)
Previous myocardial infarction, n (%)	28 (8.9)
Previous PCI, n (%)	18 (5.7)
Chronic kidney disease, n (%)	21 (6.6)
Family history of CAD, n (%)	96 (30.4)
Killip classification	
Killip I, n (%)	211 (66.8)
Killip II, n (%)	29 (9.2)
Killip III, n (%)	55 (17.4)
Killip IV, n (%)	21 (6.6)

Table 2. Angiographic characteristics and pre-procedure TIMI flow distribution (n=316)

Variable	n (%)
Pre-procedure TIMI flow	
TIMI 0	180 (57.0)
TIMI I	48 (15.2)
TIMI II	52 (16.5)
TIMI III	36 (11.4)
TIMI flow category	
Impaired flow (TIMI 0/I)	228 (72.2)
Preserved flow (TIMI II/III)	88 (27.8)
Culprit vessel	
Left anterior descending artery (LAD)	171 (54.1)
Right coronary artery (RCA)	97 (30.7)
Left circumflex artery (LCX)	34 (10.8)
Other vessels	14 (4.4)
Number of vessels involved	
Single vessel disease	183 (57.9)
Two vessel disease	89 (28.2)
Three vessel disease	44 (13.9)
Drug-eluting stent implantation	295 (93.4)

Table 3. In-hospital clinical outcomes after primary PCI (n=316)

Clinical outcome	n (%)
Slow flow/no-reflow phenomenon	52 (16.5)
Cardiogenic shock	20 (6.3)
Malignant ventricular arrhythmias	62 (19.6)

Heart failure requiring medical therapy	90 (28.5)
Mechanical ventilation	17 (5.4)
IABP support	9 (2.8)
In-hospital mortality	10 (3.2)
Length of hospital stay >5 days	104 (32.9)

Table 4. Association between pre-procedure TIMI flow category and in-hospital clinical outcomes

Clinical outcome	TIMI 0/I (n=228)	TIMI II/III (n=88)	χ^2 value	p-value
Slow flow/no-reflow	46 (20.2%)	6 (6.8%)	9.04	0.003
Cardiogenic shock	18 (7.9%)	2 (2.3%)	3.74	0.053
Malignant ventricular arrhythmias	53 (23.2%)	9 (10.2%)	6.73	0.009
Heart failure requiring medical therapy	78 (34.2%)	12 (13.6%)	13.92	<0.001
Mechanical ventilation	15 (6.6%)	2 (2.3%)	2.16	0.141
IABP support	8 (3.5%)	1 (1.1%)	1.09	0.297
In-hospital mortality	9 (3.9%)	1 (1.1%)	1.48	0.224
Length of stay >5 days	86 (37.7%)	18 (20.5%)	8.34	0.004

DISCUSSION

In this study STEMI patients with impaired TIMI flow (TIMI 0/I) were more likely to have slow flow/no-reflow, malignant ventricular arrhythmias, heart failure (that required medical therapy), and longer hospital stay. These findings also emphasized the need to assess the flow in the infarct-related artery before PCI, since the initial coronary patency may be a reflection of the amount of thrombotic occlusion, length of time of ischemia, and extent of the myocardial injury.

The correlation between decreased pre-procedure TIMI flow and adverse outcomes was biologically plausible. Patients with complete or near-complete occlusion may be at risk of more thrombus burden and longer ischemic exposure which can cause more myocardial damage despite restoration of epicardial flow. The coronary microcirculation is very important in deciding myocardial recovery after successful PCI and post PCI ongoing microvascular injury may limit the benefits of successful PCI [11]. Microvascular obstruction post STEMI has been shown to be associated with poor ventricular remodeling, left ventricular function recovery and cardiovascular event risk [12].

The greater incidence of slow flow/no reflow seen in patients with poor initial TIMI flow correlated well with the past work showing that poor myocardial perfusion could remain despite a successful reopening of the culprit artery. The no-reflow phenomenon is a complicated phenomenon with several contributing factors such as distal embolization, endothelial damage, inflammation, vasoedema, and ischemia-reperfusion injury [13]. These mechanisms account for the increased risk for post procedural complications in patients with poor initial coronary flow.

It is, therefore, important to preserve the coronary microvascular function, which has become a target in the management of STMI. As mentioned in previous studies, the focus on cardio protection to minimize reperfusion injury and ensure microvascular blood flow may lead to greater myocardial salvage after PCI [14]. The contemporary management guidelines have also emphasized the need for rapid reperfusion, optimized PCI techniques, and identification of patients with increased risk of complications, to improve outcomes from STEMI [15].

The results of this study also confirmed the notion that pre- interventional angiographic parameters could offer further information of prognosis than conventional clinical assessment. Although pharmacoinvasive and reperfusion strategies are continually evolving, patients who present late, have a high thrombus burden and poor baseline coronary flow continue to have a high risk of inadequate myocardial reperfusion [16]. In addition, microvascular obstruction and inadequate tissue level perfusion have been shown to be important determinants of prognosis even if epicardial TIMI flow is restored [17].

Multiple investigations have highlighted the association of inadequate myocardial reperfusion, inflammatory response and poor clinical outcomes after STEMI. Early identification of high-risk patients is warranted as the presence of microvascular obstruction has been linked to larger infarct size, worse ventricular function and higher mortality [18]. Likewise, markers of reperfusion failure could help to better predict the complications following primary PCI [19]. Pre-procedure TIMI flow has also been the focus of recent studies to assess its value as an important angiographic predictor of the outcome in STEMI patients treated with modern antiplatelet and interventional strategies [20].

The strengths of this study were: assessment of a clinically relevant angiographic marker, inclusion of consecutive STEMI patients treated with primary PCI, and assessment of several clinically important in-hospital outcomes. The research offered regional data on the prognostic value of pre-procedure TIMI flow in an area where there is limited data.

There were some limitations in this study. The cross-sectional design limited the evaluation of long-term results and causal associations. The study was performed in a single centre, which limited the generalizability of the results to other healthcare settings. Further, the advanced assessment techniques (namely cardiac magnetic resonance imaging for microvascular obstruction and infarct size estimation) were not available. Larger

multicentre prospective studies with longer follow-up are encouraged to further investigate the role of pre-procedure TIMI flow in prognosis. Combining angiographic parameters with clinical and imaging-based risk markers could be useful in creating more effective prediction models for STEMI outcome.

CONCLUSION

Preprocedural TIMI flow was linked to in-hospital outcomes in patients with STEMI who underwent primary PCI. Patients with impaired TIMI 0/I flow were more likely to experience adverse events such as slow flow/no-reflow, heart failure, arrhythmias, and longer hospital stay. Pre-procedure TIMI flow may be used as a simple angiographic tool to risk-stratify and predict outcome in STEMI patients.

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