

## SHORT TERM CLINICAL OUTCOMES IN NON ST SEGMENT ELEVATION MYOCARDIAL INFARCTION PATIENTS WITH HIGH THROMBOLYSIS IN MYOCARDIAL INFARCTION (TIMI) RISK SCORE

Fazal E Akbar<sup>1</sup>, Sher Bahadar Khan<sup>2</sup>, Umair Ali<sup>3</sup>

<sup>1</sup>Interventional Cardiology National Institute of Cardiovascular Disease, Karachi, Pakistan.

<sup>2</sup>Department of Cardiology, Lady Reading Hospital, Peshawar, Pakistan.

<sup>3</sup>Department of Cardiology, Khyber Teaching Hospital, Peshawar, Pakistan.

Address for Correspondence:

**Sher Bahadar Khan**

Department of Cardiology, Lady Reading Hospital, Peshawar, Pakistan.

Emails: sbk.cardiology@gmail.com

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### Contribution

FEA conceived the idea, did data collection and designed the study. SBK did final review. Both authors contributed equally to the submitted manuscript.

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### ABSTRACT

**Objective:** To determine short-term clinical outcomes and factors related to them in non ST segment elevation myocardial infarction (NSTEMI) patients with high Thrombolysis in Myocardial Infarction (TIMI) risk score.

**Methodology:** This cross-sectional study was conducted in the Department of cardiology, Lady Reading hospital, Peshawar from 1st January 2016 to 30th June, 2016. Patients of Non STEMI elevation acute myocardial infarction (MI) having high TIMI score were included in the study in a consecutive manner and followed to determine the short-term clinical outcome. Socio-demographic factors were correlated with the outcome among the study participants.

**Results:** In this study 167 patients were included, with 65.3% males. Mean age of the patients was 52.8 ± 7.6 years. About 56.3% patients had hypertension, 41.3% had diabetes mellitus and smoking was recorded in 52.7% of patients. Ventricular tachycardia was recorded in 10.2%, VF in 17.4%, AF in 9.6%, cardiopulmonary edema in 65.3%, cardiogenic shock in 49.7%, CHB in 32.3% and in hospital death was recorded in 48.5% of patients. Presence of DM and smoking were significantly correlated with presence of various complications among the study participants.

**Conclusion:** Adverse clinical outcome were highly prevalent in our patients presenting with NSTEMI and high TIMI score. Patients who have been cigarette smokers and suffering from diabetes mellitus should be cautiously followed up and screened for the complications after the NSTEMI.

**Key Words:** TIMI score, NSTEMI, Risk factors

## INTRODUCTION

Coronary Artery disease (CAD) is an international health problem in both men and women and is the leading cause of death in the developed countries. The association between socioeconomic position and outcome of myocardial infarction (MI) is generally well documented in Western countries indicating that those with lower socioeconomic status experience the most burden of the condition.<sup>1</sup> Given the attendant risks of mortality and morbidity, acute MI remains a principal focus of cardiovascular therapeutics. Moreover, 30-day mortality and re-hospitalization rates of acute MI are publicly reported in an effort to promote optimal acute MI care, and all aspects of MI care delivery are the focus of local, regional, and national quality initiatives.<sup>2</sup> The prevalence of CAD is equally high in south Asia including Pakistan.<sup>3</sup> According to the most careful estimates based on sound scientific studies nearly 100, 000 suffered an acute MI in Pakistan in the calendar year 2002.<sup>4</sup>

Risk stratification and identification of individuals at high risk of death remains a significant issue in the management of ST elevation MI (STEMI) and effective risk stratification is integral to management.<sup>5</sup> When a patient is identified to be at high risk, he or she becomes a candidate for aggressive therapy.<sup>6</sup>

In terms of multivariate analyses, the thrombolysis in myocardial infarction (TIMI) risk score has proven to be an effective risk assessment tool for predicting the risk of death and ischemic events among patients with MI.<sup>7</sup> The scheme of risk stratification in TIMI risk score is based on seven independent clinical indicators that are evaluated on patient's presentation.<sup>8</sup> It has the advantage of being easy to calculate and has broad applicability in the early assessment of patients.<sup>8</sup> The most frequently used risk stratification system is Thrombolysis in Myocardial Infarction (TIMI) Risk Score for STEMI patients.<sup>9</sup> Post MI complications occurred on the average across different risk group with high TIMI score was 63.2% (which included ventricular arrhythmias, CHB, Hemodynamic & mechanical complications) and in hospital death in 42.7%.<sup>10</sup>

In another study by Masood A et al, post MI arrhythmias were noted in 50%; It was recorded in another study VT occurred in (7.6%) and (4.3%) required defibrillation, CHB in 32% 11Atrial fibrillation in 7.7% cardiogenic shock in 60%; pulmonary edema in 80%; mechanical complications of MI in 30%; death in 8% of patients having high TIMI scores at presentation with MI.<sup>11-13</sup>

The rationale of this study is to determine the frequency of short term clinical outcomes in NSTEMI patients with high TIMI risk score. MI is very common in our population and a lot of severity and predictive risk scores are available in the literature and utilized by cardiologists. TIMI risk score is based on seven independent clinical indicators that are evaluated on patient's presentation. Once short term clinical outcomes (ventricular tachycardia, ventricular fibrillation, cardiogenic shock and in hospital mortality) are frequently identified in patient with high TIMI risk score. The TIMI risk score can then be used as an effective risk assessment tool for predicting the risk of death and arrhythmia among patients with NSTEMI. Besides it has the advantage of being easy to calculate and has broad applicability in the early assessment of patients. Patients with high TIMI risk score can then be subjected to early invasive strategy and thus these

adverse cardiovascular outcomes can be prevented. It is found through literature search that high TIMI risk score patients are at risk for adverse short term and in hospital complications.

This study will provide us with local statistics of the usefulness of TIMI risk score and observe the short term complications of NSTEMI and factors related to presence of the complications.

## METHODOLOGY

This cross-sectional study was conducted at Cardiology Unit, Lady Reading Hospital, Peshawar between 1st January 2016 to 30th June, 2016. The duration of study was six months after approval from hospital ethical committee. Non-probability consecutive sampling technique was used to gather the sample. Patients of both genders between 30 to 80 years of age presenting with NSTEMI having high TIM risk score were included in the study. Patients with previous history of stroke, history of previous myocardial infarction and presence of chronic renal Failure were excluded from the study. The TIMI risk score for non ST-segment elevation myocardial infarction (NSTEMI) is a simple score based on seven high-risk parameters and 1 score for each parameter. High TIMI risk score will be defined as a score of > 4.

Short term clinical outcomes were defined as major cardiovascular events which occurred during hospital stay and included the followings:

Ventricular tachycardia, defined by the occurrence of a series of three or more consecutive abnormally shaped premature ventricular complexes on surface ECG whose duration exceeds 120 ms with the ST-T vector pointing opposite the major QRS deflection.

Ventricular fibrillation, defined by the presence of irregular undulations of varying contour and amplitude, without possible distinction of QRS complexes, ST segment or T waves on surface ECG in the presence of recordable carotid pulse and blood pressure taken at arm.

Irregularly irregular pulse by palpating radial pulse with irregular interval between QRS Complexes with absent P waves on rhythm strip of ECG defined as lead II was defined as atrial fibrillation.

Complete heart block was defined as pulse rate less than 60/minute with complete dissociation between P wave and QRS complex on ECG.

Cardiac pulmonary edema was defined as when the respiratory rate is more than 20, bilateral rales on chest auscultation, S3 gallop detected on cardiac auscultation and heart rate of >120 bpm on palpating radial/brachial pulse.

Cardiogenic shock, defined as systolic blood pressure <90 mm Hg measured on mercury sphygmomanometer (Riester) for 1 hour that is not responsive to normal saline of 1litre alone and associated with signs of hypoperfusion i.e. central cyanosis (blue discoloration of lips and tongue), cold clammy extremities (by palpation), persistent oliguria <30ml/hr, or congestive heart failure.

Acute myocardial infarction was defined as the presence of the two of the following: prolonged chest pain of more than 30 minutes, cardiac enzymes (CKMB) elevation > 2 times upper normal limit measured 4 hours after onset of chest pain, ECG

changes as ST elevation or depression of more than 1mm in two or more contiguous leads or new onset left bundle branch block (LBBB).

Non ST elevation myocardial infarction was defined as Myocardial infarction without the ECG changes of ST segment elevation.

All patients presenting with acute MI were included in the study through OPD and ER department and was admitted in the ward for further evaluation.

All patients were subjected to detailed history. A detailed clinical examination with TIMI scores was calculated. All the patients was followed up to 7 days after admission to determine the clinical outcome in terms of ventricular tachycardia, ventricular fibrillation, atrial fibrillation, complete heart block, cardiopulmonary edema, cardiogenic shock & in hospital death.

Data collected was analyzed using SPSS version-23. Frequencies and percentage for categorical variables like gender and common clinical outcome (ventricular tachycardia, ventricular fibrillation, atrial fibrillation, cardiopulmonary edema, cardiogenic shock & in

hospital death) while Means + SD was calculated for numerical variable like age and TIMI score were calculated. Common clinical outcome was stratified among age, gender and other modifiable risk factors like hypertension, diabetes, current smokers to see the effect modifications. Post stratification Chi-square test was applied keeping  $p \leq 0.05$  as significant.

## RESULTS

The mean age of our sample was 52.8 +7.6 years. Out of 167 patients, there were 65.3% males and 34.7% females. Mean TIMI risk score was 5.89 + 0.7. On follow up and doing relevant investigations, we observed that VT was recorded in 10.2%, VF in 17.4%, AF in 9.6%, cardiopulmonary edema in 65.3%, cardiogenic shock in 49.7%, CHB in 32.3% and in hospital death was recorded in 48.5% of patients with MI having high TIMI risk score (Table 1). 56.3% patients had HTN, 41.3% had DM and smoking was recorded in 52.7%. Pearson chi-square revealed that presence of diabetes mellitus and smoking were significantly correlated with presence of various complications among the study participants (Table 2).

**Table 1: Demographic Variables of Study Populations (n=167)**

Variables	Frequency and Percentage
<b>Age (years)</b>	
Mean (SD)	52.82 (7.6)
Range (min-max)	40 years - 64 years
<b>Gender</b>	
Male	109 (65.3%)
Female	58 (34.7%)
<b>Complications after NSTEMI</b>	
Ventricular tachycardia	17
Ventricular fibrillation	29
Atrial fibrillation	16
Cardiopulmonary edema	109
Cardiogenic shock	83
Complete heart block	54
Hospital death	81

**Table 2: Pearson chi-square Test for Stratification of Various Factors with the Presence of Complications (n=167)**

Variables	No Complication n (%)	Presence of any complication n (%)	P-value
	57(34.1)	110 (65.8)	
<b>Age</b>			
<55 years	2543.8	3733.6	0.195
>55 years	3256.2	7366.4	
<b>Gender</b>			
Male	3442.1	7568.2	0.272
Female	2357.9	3531.8	
<b>Smoking</b>			
No	3764.9	4238.2	0.001
Yes	2035.1	6861.8	
<b>Diabetes</b>			
No	4171.9	5751.8	0.011
Yes	1628.1	5348.2	
<b>Hypertension</b>			
No	2645.6	4742.7	0.721
Yes	3154.4	6357.3	

## DISCUSSION

The most important decision for patients with NSTEMI is to restore the blood flow. The method is effective in balancing the demand and supply of blood. To select a method for restoring the blood flow (either medical or emergency angioplasty), several criteria including the time of disease onset, the risk of brain hemorrhage, the time required to transfer the patient to a center with angioplasty facilities and the risk of MI, must be considered.<sup>14-17</sup> Several diagnostic and therapeutic scoring systems have been proposed for NSTEMI and can be helpful in decision making.<sup>18</sup> The ideal scoring system should possess high predictive capacity, availability, and ease of performance at patient's bedside.<sup>19</sup> Thrombolysis in MI (TIMI) is one of the suggested scoring systems. It is designed on the basis of 8 clinical indicators by which patients can be divided into two categories of low risk (scores of 0-4) and high risk (scores of more than 5).

In terms of multivariate analyses, the TIMI risk score has proven to be an effective risk assessment tool for predicting the risk of death and ischemic events among patients with ACS. The scheme of risk stratification in TIMI risk score is based on seven independent clinical indicators that are evaluated on patient's presentation.<sup>20</sup> It has the advantage of being easy to calculate and has broad applicability in the early assessment of patients.

The TIMI risk index (TRI) helps to provide an assessment of a patient's prognosis. This information is helpful for patients and their families and allows for more effective triaging and clinical allocation. So management of patients with an acute coronary syndrome requires accurate risk stratification to guide appropriate therapy. TIMI risk index for NSTEMI and STEMI is an easy approach that used baseline variables of patients that are part of the routine medical evaluation in clinical setting to identify

patients at high risk for death and other major cardiac ischemic events.<sup>21</sup> Previous study showed that death rate, recurrent MI or urgent revascularization significantly increased when TIMI risk index increased. Trials have demonstrated the efficacy of new pharmacologic agents, such as low-molecular-weight heparins (LMWH) and glycoprotein (GP) IIb/IIIa inhibitors<sup>19</sup> and of an early invasive management strategy for ACS patients.<sup>22</sup> However, these treatment options are expensive and with risk of complications. Risk stratification can be used to identify patients who would derive particular benefit from these therapies.<sup>23</sup> TIMI risk index is likely to be clinically useful to predict the short term prognosis and help in planning in early management of patients and may also serve as a valuable aid in designing clinical research. To be practical clinically, a risk stratification tool should be simple & easily applied at the bedside and should make use of clinical data that are routinely available at hospital presentation.

To be practical clinically, a risk stratification tool should be simple and easily applied at the bedside and should make use of clinical data that are routinely available at hospital presentation. However, to perform accurately, the tool should use data that offer independent prognostic information and must take into account the complex profile of patients with multiple risk factors.<sup>135</sup> A risk model satisfying these objectives could also be useful in adjusting for baseline risk in epidemiological studies, such as those examining variation in practice patterns, provider types, or specific therapies.<sup>24-26</sup> Though many studies have attempted to define the prognosis of patients with MI and/or provide risk algorithms, they were performed before the widespread use of thrombolytic agents.<sup>22,27</sup>

Clinical data provide clear evidence that patients with inferior MI are at substantially increased risk of major complications, including death, cardiogenic shock, and ventricular arrhythmias.<sup>28-32</sup>

In our study, in-hospital mortality was similar to the findings of Mehta and Gumina et al. In our study, similar to some other reports, in hospital complications were significantly more common in the high TIMI group in patients with NSTEMI and these include ventricular arrhythmias, atrio-ventricular block, VT and VF.<sup>33-36</sup> The development of the TIMI risk score has created a useful tool with which to risk-stratify patients with acute MI.<sup>37</sup> It has been validated in a large, non-selected registry of AMI patients.<sup>38</sup> Our observations extend previous work by demonstrating the utility of the TIMI risk score to patients with MI. The score accurately predicted incremental short-term mortality risks in patients with MI.

It has been reported in literature that in-hospital mortality increased step-wise from 0 in TIMI risk score 0-1 to 70.5% in those with TIMI risk score  $\geq 6$ . There was no further increase in mortality with risk scores beyond 4-5 in the Gumina study.<sup>39</sup> In this study, the number of patients within each score group was not reported, so we could not find a definite explanation for this finding. One possible cause may be related to a higher rate of reperfusion therapy in the Gumina study (61.8%), which has led to decreased mortality of high score patients.

Berger et al. identified 58 patients with right ventricular dysfunction out of 1110 patients undergoing pre-discharge radionuclide ventriculography in the TIMI-2 trial. Right ventricular function had returned to normal by 6 weeks in over 80% of patients, and the initial right ventricular dysfunction was not associated with increased mortality at 1 year.<sup>40</sup> Also, using echocardiography, Keitkoglou et al. showed significant improvement in RV systolic and diastolic function 3 months after acute MI.<sup>30</sup> However, other studies have shown that right ventricular dysfunction may persist and if it does, it predicts an adverse long-term outcome.<sup>32,40</sup>

Our study demonstrates that among patients presenting with NSTEMI who are high TIMI scores, the risk of adverse short term clinical outcome was quite high. This may be due to the fact that patients with high TIMI risk scores were more likely to have severe multi-vessel CAD compared with those who have low scores. A routine invasive strategy in high TIMI risk score patients should be considered as the preferred strategy.

## CONCLUSION

Adverse clinical outcome are highly prevalent in our patients who are presenting with NSTEMI and high TIMI score. Patients who have been cigarette smokers and suffering from diabetes mellitus should be cautiously followed up and screened for the complications after the NSTEMI.

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