

## Prediction of Thirty (30) Days Mortality in Acute STEMI by Triscore (TIMI Risk Index, TRI)

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### I. Introduction

Effective risk stratification is integral to the management of patients with acute ST elevation myocardial infarction (STEMI) and has an impact on early therapeutic decision making. In addition, increasing economic pressures have intensified the need for appropriate triage and clinical resource utilization. Tools that enhance the clinician's ability to rapidly and accurately assess risk are thus of substantial interest.

Multiple classification schemes have been developed and validated for the prediction of mortality among patients with STEMI.<sup>[1]</sup> Although, such sophisticated multivariable models identify independent clinical predictors and quantify their relative contribution to mortality risk<sup>[2]</sup> but are too cumbersome to be applied in routine clinical practice.

A simple, generalizable and practical risk index for the rapid evaluation of patients with MI could therefore prove valuable.

Available models includes up to 45 variables but it has been consistently shown that out of the total 45 variables, the 3 strongest predictors are:<sup>[3]</sup>

- Advanced age
- Increased heart rate
- Decreased blood pressure

Using these 3 variables from the 'TIMI risk score for STEMI', a simplified 'TIMI risk index (TRI)' was developed for predicting mortality over 30 days by using TRISCORE equation:<sup>[3]</sup>

**Triscore equation = heart rate x (age/10)<sup>2</sup> ÷ systolic blood pressure**

TIMI risk index was derived on the basis of observed risk relation among 13253 patients of STEMI enrolled in the intravenous nPA for treatment of infarcting myocardium early (InTIME II) trial<sup>[3,4]</sup> and subsequently validated in the Thrombolysis in Myocardial Infarction (TIMI) 9A and 9B trial samples.<sup>[5,6]</sup> The risk index offered strong discrimination of mortality risk at 24 h, hospital discharge, and 30 days. The TIMI risk index has the advantage that it retains much of the predictive capacity of more complex systems but can also be applied by any paramedical personnel outside the hospital on first contact with the patient or rapidly applied at the bedside by clinical personnel with minimal clinical information.

There are practically no Indian studies on this TRISCORE equation (TIMI risk index, TRI). Therefore, we decided to conduct this simple study aimed to validation of thrombolysis in myocardial infarction (TIMI) risk index (Triscore) in predicting mortality and various morbid events (upto 30 days) in fibrinolytic eligible patients of acute STEMI.

### II. Material and Methods

This was a prospective study conducted in Intensive Cardiac Care Unit (ICCU) at University of Health Sciences and Research, PGIMS, Rohtak. Approval from the ethical committee of the institute was taken.

#### 2.1 Patient Selection

The study subjects included 100 consecutive patients of acute STEMI, aged >18 years who presented within 24 hours of onset of typical ischemic symptomatology admitted to ICCU. New criteria of diagnosing acute MI were applied and diagnosis of acute STEMI was made as per modified definition of acute myocardial infarction.<sup>[7]</sup> Patients who fulfilled the criteria for thrombolysis were included.

Excluded patients were those who had at the time of presentation any history of cerebrovascular disease; Heart rate of <50 or >150; severe uncontrolled hypertension with systolic blood pressure > 180mmHg or diastolic blood pressure >110mmHg; cardiogenic shock; CRF; increased risk of severe bleeding.

#### 2.2 Method

Immediately on ICCU arrival, patients were sedated and total 3 readings each of systolic BP and heart rate were measured and the average of these readings was applied in the triscore equation to calculate Triscore.

Bed side TRISCORE was calculated before administration of thrombolytics and other agents by applying the equation mentioned below:

**Triscore (TIMI Risk index, TRI) = Heart rate x (Age/10)<sup>2</sup> ÷ Systolic blood pressure**

After ICCU admission serial 12 lead ECG's were recorded. Blood samples were taken for all the routine investigations including serial cardiac enzyme levels. Contraindications for thrombolysis were ruled out. Written informed consent was taken from the patient and patient was thrombolysed with streptokinase or tenecteplase accordingly.

**End points** - Clinical end points were death or major adverse coronary events (MACE) (cardiogenic shock, arrhythmias including tachy/bradyarrhythmias; heart failure; cardiac arrest, electromechanical complications; recurrent myocardial ischemia; myocardial reinfarction; myocardial rupture; cardiac tamponade; pericarditis, pericardial effusion; mitral regurgitation and LV thrombus, pulmonary embolism). After discharge patients were followed up in cardiovascular clinic on 30<sup>th</sup> day of post MI. They were examined thoroughly to find out any clinical or ECG evidence of any post MI event. Patients were encouraged to report if during anytime end point event develops.

**Triscore categorization (Table I & Fig. 1)**

Mean triscore was categorized into 3 grades and patients were categorized into three different groups depending on their mean triscore values.

Group A - Mean triscore value <25 - low risk group

Group B - Mean triscore value 25-45 - moderate risk group

Group C - Mean triscore value >45 - high risk group

Distribution of patients according to their mean triscore was as per table I.

In each group, we analysed the frequency of death and MACE during hospital stay (0-5 days) and post discharge upto 30 days (5-30 days).

**2.3 Statistical analysis:** Statistical software used was SPSS v. 17.0.

**III. Results**

The patients included in the study were in the age range of 24-90 years. The mean age was 55.65±14.30 years. Total number of males and females were 77 and 23 respectively. Mean systolic blood pressure was 120±26.29 mmHg, mean diastolic blood pressure was 75.3±20.93 mmHg and mean heart rate was 86.42±19.86 bpm.

The range of Triscore value was from 5.63 to 74.11. The mean triscore was 24.56±14.93. Total number of MACE recorded during hospital stay (0-5) were 67. Out of the total 100 patients, 9 patients died, 20 developed arrhythmias, 16 developed acute pulmonary edema, 11 developed cardiogenic shock, 7 developed post-MI angina, 2 had major bleeding episodes, 1 developed CHF and 1 patient had extension of infarct. Total number of MACE after hospital discharge upto thirty days were 26. 3 patients died, 10 developed post-MI angina, 6 developed arrhythmias, 5 developed CHF and 2 had reinfarct (Table 1).

**Clinical Events as stratified by TIMI Risk Index (Triscore) (Table I)**

**Table I**

Groups	Triscore category	Total number of patients	Total number of death during hospital stay (0-5 days)	Total number of major events (MACE) during hospital stay (0-5 days) including death	Total number of death after discharge upto 30 days (5-30 days)	Total number of major events (MACE) after discharge upto 30 days (5-30 days) including death	Total cumulative death (0-30 days)	Total cumulative major events (MACE) (0-30 days) (including death)	Number (%age) of patients (out of total number of patients in a particular group) who developed events (MACE)
(A)	<25 (low risk group)	65 (65%)	01 (1.54%)	20	0	11	01 (1.54%)	31*	20 (30.76%)
(B)	25-45 (moderate risk group)	22 (22%)	02 (9.09%)	20	0	09	02 (9.09%)	29**	15 (68.18%)
(C)	>45 (high risk group)	13 (13%)	06 (46.15%)	27	03 (23.07%)	06	09 (69.23%)	33***	12 (92.30%)

\*A versus B <0.001 VHS; \*\*A versus C <0.01 HS; \*\*\*B versus C NS

**3.1 Number of Deaths (Table I)**

**During hospital stay (0-5 days) – 9**

In hospital mortality rate was 1.54% in group A; 9.09% in group B and 46.15% in group C. Difference in the mortality rates between low risk group vs. high risk group was statistically highly significant with p value of <0.001. However, the difference between low risk vs. moderate risk and moderate risk vs. high risk group was not significant (p>0.05).

**After discharge upto 30 days (5-30 days) – 3**

There was no mortality in group A and B, 3 patients expired in group C. Thus post discharge mortality rate was nil in group A and B and 23.07% in group C. Difference in the mortality rates between low risk group and high risk group was statistically highly significant (p <0.001) and between moderate risk vs. high risk group was significant (p <0.05).

**Total number of cumulative deaths (0-30 days) - 12**

Composite mortality from the day of admission in ICCU till 30 days was 12 in our study. 1 patient expired in group A, 2 in group B and 9 in group C. Thus 30 days mortality rate was 1.54% in group A; 9.09% in group B and 69.23% in group C. Difference in composite mortality rates between low risk group vs. high risk group as well as between moderate risk vs. high risk group was highly significant (p <0.01). However, difference between low risk vs. moderate risk group was not significant (p>0.05).

**3.2 Number of Major Adverse Coronary Events (MACE) including Death (Table I)**

**Total number of Cumulative Major Events including Deaths (0-30 days) - 93**

31 major events including death occurred in group A (21 during hospital stay and 11 post discharge), 29 in group B (20 during hospital stay and 9 post discharge) and 33 in group C (27 during hospital stay and 6 post discharge). Statistically the difference between low risk group vs. moderate risk group as well as between low risk vs. high risk group was highly significant (p <0.01). However difference between moderate risk vs high risk group was not significant (p >0.05).

**3.3 Predictive Value of Triscore on Composite Major Events including Death upto 30 Days (0-30 Days) (Table I and II)**

It was observed in the present study that total number of composite major events from the day of ICCU admission upto 30 days were 93. Total 31 major events (including death) occurred in 20 patients out of 65 patients in group A and rest of the 45 patients in this group had no event. Total 29 major events (including death) occurred in 15 out of 22 patients of group B while rest of the 7 patients in this group had no event. Total 33 major events (including death) occurred in 12 patients out of 13 patients of group C and 1 patient had no event in this group. Thus, rate of occurrence of a major event (including death) from the day of ICCU admission upto 30 days was 30.76% in group A, 68.18% in group B and 92.30% in group C.

**Table II: Triscore categorisation**

Group	Triscore category	Total number of patients	Number of patients [out of total patients in a particular risk group] who developed these events	Total number of events including death (0-30 days)
(A)	<25 (low risk group)	65	20 (30.76%)	31
(B)	25-45 (moderate risk group)	22	15 (68.18%)	29
(C)	>45 (high risk group)	13	12 (92.30%)	33
	p value		<0.001*; <0.01 **; NS***	

\* A versus B; \*\*A versus C; \*\*\*B versus C

**IV. Discussion**

Mean age of the patients was 55.65±14.30 years. Patients less than 40 years of age were 16 while patients with age more than 70 were 12. Majority of the patients were in the age group of 41-70 years. This shows that more than 40 years of age in an Indian person puts him into the age group, where they are susceptible to coronary artery disease. This is in correspondence with findings that Indian patients get coronary artery disease one decade earlier as compared to western counterparts.<sup>[8]</sup> In a study of usefulness of the TIMI risk index by Ilkhanoff L et al,<sup>[9]</sup> mean age of the patients was 68±13 years. In a study by Wiviott SD et al,<sup>[1]</sup> to evaluate the TIMI risk index for routine practice, mean age of the patients was 67.6±14.7. Hence the patients in our study were comparatively younger than the previous studies on TIMI risk index.

The range of triscore value was from 5.63 to 74.11. The mean triscore was  $24.56 \pm 14.93$ . In a study on TIMI risk index by Ilkhanoff L et al,<sup>[9]</sup> the mean triscore was  $27.3 \pm 15.0$  (median 24.1, range 3.4 to 135.3). In an intravenous nPA for treatment of infarcting myocardium early (InTIME II) substudy on risk index by Morrow DA,<sup>[3]</sup> the risk index values at presentation for the population ranged from 1.6 to 110 with a median of 20 (20-75<sup>th</sup> percentiles 14-27).

#### 4.1 Correlation of Mortality and Morbidity with Triscore

##### Mortality

Our study revealed highly significant mortality rate difference between low risk and moderate / high risk group patients. Risk index maintained a strong graded association with in hospital mortality (mortality rate 1.54% to 46.15%) across the risk index categories. Similar association was observed in post discharge mortality upto 30 days (mortality rate Nil to 23.07%) across the risk index categories.

Cumulative mortality from ICCU admission upto 30 days (1.54%-69.23%) also revealed substantially increased mortality rate in a stepwise fashion with the increasing TIMI risk index across the 3 groups and the proportion of deaths occurring by 30 days increased with ascending triscore values across the risk groups.

In a study by Wiviott SD et al,<sup>[11]</sup> the risk index maintained a significant graded association with in-hospital mortality across risk index groups (0.9-53.2%) with p value of  $<0.001$ . In a study by Ilkhanoff L et al<sup>[9]</sup> mortality rates for patients with each ACS subtypes increased significantly with increased TIMI risk index quintile at all time points. Triscore therefore provides valuable prognostic information in patients presenting with acute STEMI. These high risk patients therefore can benefit from initial triage or early coronary evaluation / intervention.

##### Morbid events

It was found that during hospital stay a large number of patients had one or the other MACE (excluding death) if they belong to the moderate or high risk group. On the other hand if the patient belonged to low risk triscore group then they were less likely to suffer from morbid events during hospital stay.

Classification of patients into risk groups based on triscore values revealed a significant graded relationship with mortality and morbid events. Proportions of death and major morbid events occurring during hospital stay and after discharge upto 30 days increased with increasing triscore value, across the 3 risk groups. It was observed in our study that in group A 30.76%, in group B 68.18% and in group C 92.30% of the patients were at risk of developing a major event from ICCU admission upto 30 days. Triscore gave insight into extent of coronary disease as its impact on outcome in the present study. The events were higher in the high risk group suggesting larger area of necrosis.

Traditionally risk stratification of acute MI patients has been carried out based on Killip class, serious tachyarrhythmias, extent of infarction and other comorbid events. Many of these risk factors occur well after Acute MI has developed and timely interventions are usually not carried out. TIMI risk index (TRISCORE) can identify patients of STEMI at high risk of mortality and even morbid events right at the initial presentation in hospital. This could impact the ultimate outcome of these patients. However, exact relationships of TIMI risk index (Triscore) with the extent of coronary disease and myocardial damage needs evaluation in large study cohorts. Our study depicted that triscore calculation in patients of acute MI on admission in ICCU is very simple and useful tool which can be practiced in any hospital. Based on the various categorization mentioned above, it is possible to identify high risk patients who then can be subjected to further evaluation and investigation. These patients then can be subjected to various coronary interventions which can result in modification of the outcome of acute MI. This can also prevent unnecessary coronary evaluation/intervention being practiced in these acutely ill patients without determining the risk profile of these patients.

The TIMI risk index was designed to provide a preliminary risk assessment during the first patient encounter. It does not integrate the effects of treatment, care settings, co-morbid illnesses (including those potentially involved in reperfusion eligibility), or baseline medications on the outcome. Such information may be added to the initial risk assessment later on to update the initial evaluation.

The risk index was not developed with the objective of deriving the best fitting model, but rather, to construct a measure that is simple to calculate and provides reasonable prognostic discrimination for a rapid risk assessment at first medical contact, establishing, a more than 20 fold gradient of risk for early events with high discriminatory capacity. The risk index meets that objective, and is thus a good initial rapid assessment tool. None of the previous studies and trials on TIMI risk index (triscore) was designed to assess the mechanism by which the TIMI risk index (TRI) predicts mortality in these distinct patient populations.<sup>[11]</sup> The risk index likely integrates baseline risk (age) with the hemodynamic effects of MI (HR and SBP).<sup>[11]</sup> Additional evaluation in data sets in which more detailed information is available regarding ventricular function, the extent of coronary artery disease, and the cause of death may help to elucidate the mechanism by which the TIMI risk index (TRI) predicts mortality.<sup>[11]</sup>

### V. Conclusion

TIMI risk index grouped into different risk categories based on triscore value is capable of discriminating between patients at low and high risk for death and morbid events during hospital stay and after discharge upto 30 days, in the fibrinolytic eligible patients of acute STEMI.

### References

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