J. Dhaka National Med. Coll. Hos. 2012; 18 (02): 52-57

Original article

Prediction of major adverse cardiac events of patients with acute coronary syndrome by using TIMI risk index

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Abstract:

Patient with acute coronary syndrome (ACS) has considerable variability in outcome and mortality risk. The Thrombolysis in Myocardial Infarction (TIMI) risk index (TRI) for unstable angina/non ST elevation myocardial infarction & ST elevation myocardial infarction were a convenient bedside clinical risk score for predicting 30 days mortality at presentation with ACS. This study was done to predict and validate major adverse cardiac events in patients of ACS thus it will help us to quantify risk, observe the prognostic value and to guide appropriate therapy by using TRI. This prospective study was carried out in the department of cardiology, BSMMU, Dhaka from April, 2011 to March, 2012. After considering all ethical issues, data were collected from 279 patients attending at cardiac emergency department with the presentation of ACS. History & physical examinations were done. TIMI risk index were calculated for each patient. The major adverse cardiac events (recurrent myocardial infarction, urgent revascularization, and all-cause mortality) were measured for next 30 days in hospital setting & outpatient department by follow up. After follow-up, Cox univariate and multivariate regression analysis were used to evaluate the influence of potential risk factors on duration of event-free survival, and likelihood ratio tests to assess the outcome. Major adverse events of TIMI risk index group 1, 2, 3, 4 & 5 were 0%, 0%, 3.7%, 12.9% & 19.2% respectively in UA/NSTEMI group. In STEMI group major adverse cardiac events of TIMI risk index group 1, 2, 3, 4 & 5 were 0%, 4.7%, 12.5%, 17.1% & 24.1% respectively. Increasing TRI were associated with increased risk of major adverse cardiac events. These score were a valid tool for risk assessment.

Keywords: Major adverse cardiac events, TIMI risk index.

Introduction :

Acute coronary syndrome (ACS) includes unstable angina (UA), non ST- elevation myocardial infarction (NSTEMI) and ST-elevation myocardial infarction (STEMI). All three conditions share a common pathophysiology, characterized by acute coronary insufficiency due to disruption of a vulnerable plaque with superadded thrombus formation with or without vasospasm following rupture of atheromatous plaque. By the year 2020 it is estimated that it will be the major cause of death in all regions of the world and will hold the first place in the World Health Organization's list of leading cause of disability. Coronary artery disease has been recognized as one of the leading cause of death in our country. Prevalence of IHD in urban population of Bangladesh was 100 per thousand [4]. The main complications were pump failure (53%) and ventricular fibrillation (27%). The mortality of untreated AMI

was 40% and 50% of them died with in the first two hours of the onset of AMI [4]. Mortality is high in case of cardiogenic shock in all age groups. Between these two extremes, prognosis varies widely[1]. The Thrombolysis In Myocardial Infarction (TIMI) risk index (TRI) helps to provide an assessment of a patient's prognosis. This information would be helpful for patients and their families and would also allow 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 UA/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 [8]. 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)[2] and glycoprotein (GP) IIb/IIIa inhibitors [8] and of an early invasive management strategy for ACS patients [3]. 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 [6]. 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. In our country, however no such clinical prognostic tool has been developed or evaluated as yet. This study is designed to assess and develop a clinical bedside prognostic tool for risk assessment in ACS.

Methods:

Patients with a diagnosis of ACS attending cardiac emergency of BSMMU hospital taken as sample. The purpose of the study has been explained in details to each subject. Informed written consent and age was taken. Pulse and systolic blood pressure were recorded. TIMI risk index was calculated for each patient. The main outcome of recurrent myocardial infarction, urgent revascularization, and all-cause mortality were recorded within 30 days of follow up periods.

TIMI Risk Index was $(Age/10)^2 \times HR$ divided by systolic blood pressure (Morrow et al. 2001).

- TRI less than 12.5 belongs to group 1
- TRI 12.5-17.5 belongs to group 2
- TRI 17.5-22.5 belongs to group 3
- TRI 22.5-30 belongs group 4
- TRI more than 30 belongs to group 5.

After follow-up, Cox univariate and multivariate regression analysis were used to evaluate the influence of potential risk factors. All data were analyzed by using SPSS (Statistical Package for Social Science) software version 16 for windows. Statistical significance of difference was analyzed with appropriate formula. P value of less than 0.05 was considered as significant.

Results:

This was a prospective study conducted in Bangabandhu Sheikh Mujib Medical University, Dhaka. The main objective of the study was to predict, 30 days Major Adverse Cardiac Events (MACE) by using TIMI risk index. Total 279 patients of ACS were enrolled in the study. Of them 132 were UA/NSTEMI group and 147 were in STEMI group. The findings of the study and its prediction are showed in Table I, II, III, IV, V & VI and Fig 1.

Table-I. Patients baseline characterstics. (n=279)

Variables	UA/NSTEMI (n=132) No. (%)	STEMI (n=147) No. (%)	P value
Age (years)			
<65	64 (48.5)	107 (72.8)	0.0001***
≥65	68 (51.5)	40 (27.2)	
Mean±SD	62.24±7.67	58.73±9.55	0.001**
Sex			0.029*
Male	92 (69.7)	119 (81.0)	
Female	40 (30.3)	28 (19.0)	
Weight (Kg)			0.0001***
<67	122 (92.4)	104 (70.7)	
≥67	10 (7.6)	43 (29.3)	
Mean±SD	55.83±5.73	58.84±7.99	0.0001***
Pulse(b/min)			0.0001***
<100	125 (94.7)	96 (65.3)	
>100	7 (5.3)	51 (34.7)	
Mean±SD	78.27±12.13	90.71±18.38	0.0001***
SBP(mm of Hg)			0.002**
<100	10 (7.6)	30 (20.4)	
>100	122 (92.4)	117 (79.6)	
Mean±SD	119.62±16.60	109.63±15.52	0.0001***
			0.007**
TRI Group			
1(<12.5)	5 (3.8)	10 (6.8)	
2(12.5-17.5)	16 (12.1)	12 (8.2)	
3(17.5-22.5)	22 (16.7)	34 (23.1)	
4(22.5-30)	48 (37.4)	28 (19.0)	
5(>30)	41 (31.1)	63 (42.9)	
Mean±SD	27.58±11.79	30.21±14.13	0.095 ns

Statistical analysis done by Chi- square test for categorical values and by unpaired Student's 't' test for quantitative values. ns = Not significant, * = significant at P<0.05, ** = significant at P <0.01, ***= Significant at P<0.001.

Table-II. Distribution of patients by major adverse cardiac events at 30 days. (n=279)

Variables	UA/NSTEMI (n=132) No. (%)	STEMI (n=147) No. (%)	P value
Adverse events	14 (10.6)	17 (11.6)	0.779 ns
Death	10 (7.5)	17 (11.6)	
Recurrent MI	2 (1.5)	0 (0)	
Urgent revascularization	2 (1.5)	0 (0)	

Statistical analysis done by Chi- square test. ns = Not significant.

Table-II shows, 10.6% patients had major adverse cardiac events in UA/NSTEMI group and 11.6% in STEMI group which was similar in both groups (P>0.05). In case of UA/NSTEMI death, recurrent MI and urgent revascularization were 7.5%, 1.5% & 1.5% respectively. In case of STEMI all major adverse cardiac events were death (11.6%).

Table-III. Univariate risk analysis of 30 days Major Adverse Cardiac Events of UA/NSTEMI. (n=279)

Parameters	Overall (n=14) No.	%	OR	95% CI	P value
Age ≥65 years	11	(78.5)	3.44	0.6-3.32	0.0001***
Pulse >100/min	3	(21.4)	2.49	1.81-24.86	0.022*
Systolic BP<100mm Hg	4	(28.5)	2.02	0.01-2.63	0.026*

Statistical analysis done by Cox regression.
ns = Not significant, * = significant at P<0.05, ** = significant at P <0.01, ***= Significant at P<0.001.

Table-IV. Multivariate risk analysis of 30 days Major Adverse Cardiac Events of UA/NSTEMI. (n=279)

Parameters	OR	95% CI	P value
Age ≥65 years	1.89	0.56-2.41	0.005**
Pulse >100/min	1.19	0.35-4.03	0.001**
Systolic BP<100mm Hg	1.60	0.24-3.52	0.002**

Statistical analysis done by Cox regression.
ns = Not significant, * = significant at P<0.05, ** = significant at P <0.01, ***= Significant at P<0.001.

Table-V. Univariate risk analysis of 30 days Major Adverse Cardiac Events of STEMI. (n=279)

Parameters	Overall (n=17) No.	%	OR	95% CI	P value
Age ≥75 years	2	(11.7)	1.94	0.13-2.79	0.094*
Pulse >100/min	9	(52.9)	1.91	0.22-3.74	0.004**
Systolic BP<100mm Hg	7	(41.1)	1.44	0.11-2.79	0.001**

Statistical analysis done by Cox regression.
ns = Not significant, * = significant at P<0.05, ** = significant at P <0.01, ***= Significant at P<0.001.

Table-VI. Multivariate risk analysis of 30 days Major Adverse Cardiac Events of STEMI. (n=279)

Parameters	OR	95% CI	P value
Age ≥75 years	1.83	0.32-2.17	0.001**
Pulse >100/min	1.04	0.65-1.67	0.006**
Systolic BP<100mm Hg	1.95	0.57-3.57	0.0001***

Statistical analysis done by Cox regession, ns= Not significant, * = significant at P<0.05, ** = significant at P <0.01, ***= Significant at P<0.001.

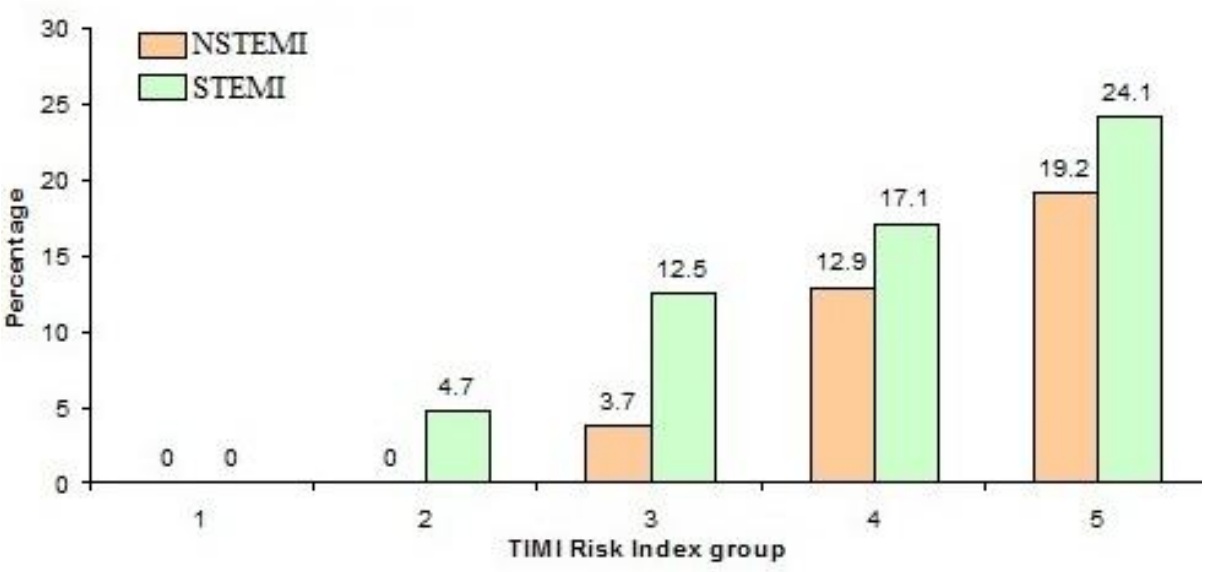

Fig-1: Risk of MACE within 30 days by TIMI risk index in UA/NSTEMI and STEMI group.

Figure 1 shows MACE of TIMI risk index group 1, 2, 3, 4 & 5 were 0%, 0%, 3.7%, 12.9% & 19.2% respectively in UA/NSTEMI group (P trend <0.01). In STEMI group MACE of TIMI risk index group 1, 2, 3, 4 & 5 were 0%, 4.7%, 12.5%, 17.1% & 24.1% respectively (P trend <0.001). MACE increased significantly as the TIMI risk index increased.

Discussion :

Morrow et al. (2000) revealed risk relations for TRI group 1, 2, 3, 4 & 5 and showed 0.8%, 1.9%, 3.3%, 7.3% & 17.4% patients respectively[5]. Quynh et al. (2009) compared TIMI risk index group-1 to Group-5, mortality in Group 5 was more than 5-fold higher (OR 5.83, p<0.0001) also increased in Group 4 (p<0.0001) and Group 3 (p=0.002)[7]. This study showed 30 days MACE were lower in TRI group 1 in both UA/NSTEMI and STEMI group. In UA/NSTEMI group,

MACE of TRI group 2 was also lower. MACE were higher in TRI group 3, 4 and 5 in case of UA/NSTEMI. MACE were higher in TRI group 2, 3, 4 and 5 in case of STEMI. This difference might be due to small sample size of study.

Conclusion:

This study tested risk stratification strategies on a group of ACS patient. The TIMI risk index may be readily applied as a prognostic tool at the bed side of hospital and may forecast the major adverse prognostic information. This risk management tool is likely to be clinically useful in the triage and management of patients eligible for fibrinolytic therapy as well as early revascularization. TIMI risk index for UA/NSTEMI & STEMI may be readily applied at the bedside at the time of hospital presentation. Patients with higher TIMI risk index at presentation needs early invasive management to reduce MACE. Although most of the results of this study have come up with the statistically significant findings, there are some facts to be considered which might affect the result. These are limited number of subjects and short follow up period.

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