Predictability of adverse clinical events following ST-elevation myocardial infarction by risk assessment tools

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Abstract

Background: Killip classes, TIMI and GRACE scores are simple validated clinical risk scores used in risk stratification in acute coronary syndrome including ST-elevation myocardial infarction (STEMI).

Objectives: Our study aimed to determine the predictive ability of post-myocardial adverse events by commonly used clinical risk scores.

Materials and Methods: Data were analysed from 120 male patients with acute STEMI, admitted to Teaching Hospital, Karapitiya. The risk scores were calculated during the acute phase. Patients were followed up for 365 days for the occurrence of clinically significant adverse cardiovascular events.

Results: Adverse clinical events related to STEMI developed in 50(41.7%) patients during the hospital stay. Later, during the follow up of 365 days, 39 (32.5%) patients developed major complications. Killip class II-IV was significantly ($p = 0.001$) associated with adverse clinical events during the hospital stay, but not later. TIMI score was a significant predictor of the occurrence of the clinically significant STEMI related adverse events, while in the ward ($p = 0.004$, OR = 1.51) and during the first 30 days ($p = 0.008$, OR = 1.42), but not beyond this period. GRACE score was unable to predict the adverse cardiovascular events in this patient cohort. Negative predictive values for both TIMI and GRACE scores were close to 100 at each time interval.

Conclusions: The development of major complications or adverse clinical events following STEMI was less common in the cohort. The TIMI score could predict the adverse events until 30 days, but not later. GRACE score was unable to predict adverse events. Killip class grading was strongly associated with the major complications occurred during the hospital stay.

Keywords: *Myocardial infarction, adverse clinical events, clinical risk scores, predictability*

Introduction

The age-standardized death rates for coronary heart disease are declining in many developed countries but are increasing in developing countries including Sri Lanka and demographic changes, urbanization, and lifestyle changes seen in these countries probably contribute to this trend (1,2). Coronary artery disease (CAD) is one of the leading causes of mortality in men. Cardiovascular disease accounts for the highest rate of hospital deaths in Sri Lanka (2). Traditional cardiovascular risk factors (CVRFs) such as advancing age, diabetes mellitus, hypertension, dyslipidaemia, smoking, obesity and family history of CAD are well recognized for their association with acute coronary syndromes (3).

Risk stratification is important in acute coronary syndromes (ACS). It provides information to both patients and clinicians on the possible prognosis and

serves as a guide to appropriately strategizing therapy (4-5). ST-segment elevation myocardial infarction (STEMI) forms the most severe spectrum of ACS. Killip classes, TIMI (Thrombolysis in Myocardial Infarction) and GRACE (Global Registry of Acute Cardiac Events) risk scores are popular and powerful tools for risk stratification in the acute phase of myocardial infarction (6). In most cases, these have been developed from selected populations of patients, very often subjected to fibrinolytic therapy (7,8).

Materials and Methods

Patients were diagnosed as STEMIs according to the Universal Definition for myocardial infarction (9). One hundred and twenty male patients with STEMI admitted consecutively to Teaching Hospital, Karapitiya were interviewed using an interviewer-administered questionnaire. Further details were extracted from the hospital and personal records. They were followed up over a period of one year (365 days) for the occurrence of clinically significant major adverse cardiovascular events (MACE) at specific time intervals of 30 days (short-term), 31 - 90 days, 91 - 180 days and >180 days to 365 days (medium-term) from the first ACS event (8,10). Development of heart failure, unstable angina, myocardial infarction, cardiac arrhythmias, cardiogenic shock, intracardiac clots and death were considered as adverse cardiovascular events.

Weight and height were measured. Killip classes were assigned and the two clinical risk scores; TIMI and GRACE were calculated from the initial clinical history, electrocardiogram and laboratory values collected on admission (11-13). Heart failure (HF) with cardiogenic shock was defined as Killip class IV and HF without shock, requiring diuretic treatment classified as Killip class IIIII, absence of HF as Killip class I. TIMI score ranged from 0 to 10 while GRACE score ranged from 85 to 244. Two-dimensional echocardiography was done in all patients during the hospital stay and ejection fraction was estimated.

Numerical data were examined for normality and presented as mean ± SD. Categorical data are displayed as percentages or frequencies. Categorical data were analysed using the Fisher's exact test or Chi-square test. Statistical significance was defined when p values was <0.05. Binary logistic regression was used in analysing the predictive ability of the risk score on the occurrence of adverse effects, where complications were used as responses and the scores were applied as factors in the model. Sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) were calculated.

Ethical clearance was obtained from the Ethical Review Committee of Faculty of Medicine, University of Ruhuna. Informed written consent was obtained from all participants.

Results

One hundred and twenty (n=120) male patients admitted with STEMI were in the mean (SD) age of 54 (8) years. Mean (SD) body mass index (BMI) was 21 (4) kgm^{-2}. The baseline characteristics of the patients are illustrated in table 1. The prevalence of CAD risk factors was high and among them smoking had the highest prevalence of 96 (80 %).

Table 1: Baseline characteristics of male patients with ST-elevation myocardial infarction

Characteristics	STEMI patients (n = 120)
Age (years)	54 ± 8
History of hypertension	23 (19.2 %)
Diabetes mellitus	19 (15.8 %)
Previous ACS events	12 (10 %)
Family history premature CAD	3 (2.5 %)
Smoking	96 (80 %)
Overweight and obesity	14 (11.7 %)
Location of MI	
Anterior MI	64 (53.3 %)
Inferior MI	53 (44.2 %)
Other types of MI	3 (2.5 %)
Acute complications while in hospital	
LBBB	3 (2.5 %)
Cardiogenic shock	4 (3.3 %)
Heart failure	40 (33.3 %)
Cardiac arrest	3 (2.5%)
Intraventricular clots	10 (8.3 %)
In-hospital reinfarction	1 (0.83 %)
Ejection fraction (%) on admission	48.6 ± 11
Thrombolysis therapy	106 (88.3%)

ACS = Acute Coronary Syndrome, MI = Myocardial Infarction, CAD = Coronary artery disease, STEMI = ST-elevation myocardial infarction, LBB = Left Bundle Branch Block, 2DEho = Two-dimensional echocardiography. Data presented as Mean ± SD and frequencies or %.

Adverse clinical events related to STEMI developed in 50 (41.7%) patients during the hospital stay. Following discharge from the hospital adverse events were observed during the first 30 days, 31 - 90 days, 91 - 180 days and 181 days to 365 days in 8 (6.7%), 7 (5.8%), 2 (1.7%) and 5 (4.2%) patients respectively. There were 2 (1.7%) deaths, 7 (5.8%) recurrent myocardial infarctions and 30 (25%) patients with unstable angina. Only 7 (5.8%) needed interventional treatment, while the rest of the patients were managed medically.

Killip class I, II, III, IV categories included 80 (66.7%), 34 (28.3%), 2 (1.6%) and 4 (3.3%) patients respectively. The severity assessed by KIllip classes as the presence of HF in the acute stage of the disease (Killip class II-IV) or absence of HF (Killip class I) was associated strongly with the development of major complications related to STEMI during the hospital stay (p = 0.001), but not for the periods thereafter (first 30 days, p = 0.266; 31-90 days, p = 0.422; 91-180 days, p = 1; 181-365 days, p = 0.663).

TIMI score was a significant predictor of the clinically significant STEMI related adverse events while in the ward and during the first 30 days following the first STEMI, but not beyond this period (Table 2). However, GRACE score was not significantly associated with post-myocardial events (Table 2).

Table 2: Predictive ability of risk scores on the development of STEMI related complications

Predictors	*p* value	Odds ratio	95% CI
Complications during hospital stay			
TIMI score	0.004	1.51	1.14 - 1.99
GRACE score	0.065	1.02	1.00 - 1.04
Complications during first 30 days			
TIMI score	0.008	1.42	0.22 - 1.79
GRACE score	0.094	1.03	1.00 - 1.07
Complications during 31 - 90 days			
TIMI score	0.572	1.15	0.70 - 1.89
GRACE score	0.745	0.99	0.96 - 1.03
Complications during 91 - 180 days			
TIMI score	0.699	1.19	0.49 - 2.90
GRACE score	0.978	1.00	0.95 - 1.06
Complications during 181 - 365 days			
TIMI score	0.541	1.20	0.67 - 2.13
GRACE score	0.802	1.00	0.96 - 1.03

TIMI = Thrombolysis in Myocardial Infarction, GRACE = Global Registry of Acute Cardiac Events, Binary logistic regression was used; presence of complication was used as the response and the scores were applied in the model predictors.

Table 3 shows the performances of the TIMI score with the cut off values of ≥ 4. The sensitivity, specificity, positive predictive value (PPV) and the negative predictive value (NPV) are varying at different time intervals. However, it seemed that NPV remained close to 100%, while PPV was low. Specificity and the sensitivity were close to 50%.

Table 3: Performance of TIMI risk score

TIMI score	Cutoff utilized	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV
During hospital stay	≥ 4	56.7%	55.4%	36.2%	74.6%
During first 30 days	≥ 4	50.0%	49.1%	20.0%	87.3%
During 31 - 90 days	≥ 4	51.7%	53.0%	7.0%	95.2%
During 91 - 180 days	≥ 4	50.0%	52.5%	1.7%	98.4%
During 181 - 365 days	≥ 4	60.0%	53.0%	5.3%	96.8%

PPV = Positive predictive value, NPV = Negative predictive value, TIMI = Thrombolysis in Myocardial Infarction, CI = Confidence interval

Table 4 demonstrates the performance characteristics of GRACE score cut off of =113 value. Sensitivity was high, while specificity was low. The NPV remained close to 100%, whilst PPV stayed low as in TIMI score.

Table 4: Performance of GRACE risk score

GRACE score	Cutoff utilized	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV
During hospital stay	≥ 113	81.0%	22.9%	31.9%	73.0%
During first 30 days	≥ 113	62.5%	20.5%	5.3%	88.4%
During 31 - 90 days	≥ 113	71.4%	21.2%	5.3%	92.3%
During 91 - 180 days	≥ 113	97.8%	22.0%	2.1%	98.3%
During 181 - 365 days	≥ 113	80.0%	21.7%	4.2%	96.1%

PPV = Positive predictive value, NPV = Negative predictive value, GRACE = Global Registry of Acute Cardiac Events, CI = Confidence interval

Discussion

In our study, TIMI score in the acute phase of the myocardial infarction significantly associated with clinically important short-term (during the hospital and during first 30 days) adverse events, but not with medium term outcomes. The NPV of TIMI score at different time intervals remained close to 100%, while PPV was low. Specificity and the sensitivity were close to 50% for TIMI score at the specified cut off values according to our study. In the present study, GRACE score was unable to predict the outcome following acute STEMI. It showed high sensitivity but low specificity with low PPV and high NPV at the 113 cut off values. The NPV remained close to 100%, whilst PPV stayed low in both scores at the used cut offs. It is reassuring that the patient is less likely to have the major adverse cardiovascular events if TIMI score is <4 and GRACE is <113.

Several risk scores have been developed for predicting survival after myocardial infarction from patient cohorts treated with thrombolysis (14-16). The risk stratification tools such as Killip classes, TIMI and GRACE risk scores were shown to have strong association with future events in patients with

unstable angina, non ST-elevation myocardial infarction and ST-elevation myocardial infarction and are used to guide treatment options (12-17). However, these studies included heterogeneous groups of populations with STEMI and non-STEMI patients, but the present study included 120 STEMI patients. There is a previous study done on closely similar number of study subjects (18).

Current AHA/ACC and ESC guidelines promote the use of the TIMI and GRACE risk scores to evaluate the in-hospital and post-discharge risk of ACS patients (19-21). Both of these scoring systems have been shown to predict the response of ACS patients to various treatment modalities and therefore significantly influence therapeutic management (22-24). The GRACE risk score developed from a large multinational prospective patient registry and has been validated and shown to be a strong predictor of in-hospital mortality of ACS patients (25-26). It has been validated in patient population in Canada (27), Potugal (28) and United Kingdom (25).

TIMI risk score is the most validated and the most extensively used in patients with non-ST-elevation ACS. TIMI risk score for STEMI has been derived from databases of clinical trials and has been validated in non-selected Western patient populations (12, 17, 29-31). The TIMI risk score has shown to provide the ability of predicting mortality at 30 days. However, it is not known how the TIMI risk score performs in a population with many characteristic differences from the population the risk score was derived from. A multi-ethnic study conducted in Malaysia has shown that TIMI risk score was strongly associated with 30-day mortality (32).

Killip class grading was strongly associated with the major complications occurred during the hospital stay, but not thereafter according to the present study. Killip class has been one of the most important variable in predicting death, survival and complications after myocardial infarction (33-34).

In developing countries where there is a wide variation of provision of healthcare facilities, it is often challenging to provide the best treatment strategies recommended in international guidelines. Hence, using simple bedside risk stratification tools to do prompt risk stratification of patients with STEMI is of great importance to achieve the clinical benefits. These types of risk scores which are low cost risk estimation tools may be suitable to use in developing countries like ours. It needs to be validated further in real life patient cohorts and also in different treatment settings with the availability of novel management options, such as early revascularization. Our study included all consecutive patients admitted to the hospital with acute STEMI and 106 (88.3%) received thrombolytic therapy and standard medical therapy in line with current clinical practice guidelines. Lesser number of patients developed complications after the 30 days from STEMI among our study subjects. It is possible that these risk scores therefore failed to show strong associations with clinical events in the medium term. In addition, parameters reflecting final infarct size (left ventricular ejection fraction and peak cardiac enzymes) are lacking in the traditional risk scores as TIMI and GRACE investigators (12-16). The present study being restricted to male is a limitation.

Conclusions

The development of major complications following an episode of STEMI was less common in the cohort. TIMI score appear to predict the short-term, but not medium term adverse events. GRACE score was unable to predict the adverse events following acute STEMI. Both TIMI and GRACE scores had NPPV close to 100. Killip classes showed significant association with in-hospital adverse events. The risk stratification is important in special focus on cardiovascular mortality and morbidity. The results of the present evaluation need to be confirmed and validated by conducting prospective studies including a large series of STEMI patients treated with current strategies.

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