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Original Article

A prospective risk stratification and validation of HEART, GRACE and TIMI scores for chest pain patients presenting to the emergency department

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Abstract

Objective: Chest pain is amongst the most frequently occurring symptoms in patients presenting to the emergency department (ED). Accurate and fast risk stratification is paramount for identification of patients with immediate risk of acute coronary syndrome (ACS). The present study has compared different scoring systems like HEART (History, ECG, Age, Risk factors, Troponin), Thrombolysis in Myocardial Infarction (TIMI), and Global Registry of Acute Coronary Events (GRACE) scores and their efficacy in predicting incidence of major adverse cardiac events (MACE).

Methods: The present prospective observational study was conducted on 199 patients who presented in the ED with complaint of chest pain. HEART, GRACE and TIMI scores were calculated with collected patient data which was further evaluated for efficacy by calculating area under ROC curves (AUCs). Data were analyzed by using R statistical software version 4.0.3 and Microsoft Excel. *P* value less than or equal to 0.05 indicates statistical significance.

Results: In the current study, 76 (38%) patients reported MACE. The HEART score identified the largest number of patients as high risk 74 (37%) and among them 69 patients developed a MACE. The AUC of HEART score was the highest with 0.96 (95% CI: 0.93-0.98), followed by TIMI score with 0.815 (95% CI: 0.75-0.873) and the GRACE score with 0.814 (95% CI: 0.75-0.813). The sensitivity of HEART score of ≥7 for MACE was found to be 90.78%, specificity was 95.96%, positive predictive value (PPV) was 93.24% and negative predictive value (NPV) was 94.4%. The sensitivity of GRACE score was 39.4%, specificity was 95.16%, PPV was 83.3% and NPV was 71.95%. The sensitivity of TIMI score was 30.2%, specificity was 95.96%, PPV was 82.14% and NPV was 69.18%.

Conclusion: The HEART score showed higher efficacy in predicting risk levels in patients and incidence of MACE in comparison with GRACE and TIMI scores in the included study cohort.

Keywords: Acute coronary syndrome, Cardiovascular diseases, Chest pain, Emergency service, Risk assessment

Introduction

Chest pain is amongst the most common complaints reported by the patients in the emergency department (ED) accounting for 9-10% of yearly visits to the hospitals (1,2). The reasons for chest pain are extremely varied with a plethora of diagnoses starting from a dangerous condition like coronary artery disease (CAD) up to smaller issues like minor intercostal neuralgia (3). CAD can lead to acute coronary syndrome (ACS), which describes any condition characterized by signs and symptoms of sudden myocardial ischemia—a sudden reduction in blood flow to the heart. According to the data by the World Health Organization, CAD is one of the most frequently occurring reasons for death throughout the world which contributed to around 7.2 million deaths in the year 2005 (4). Even though developed countries have shown a remarkable decrease in CAD-affected population and related deaths, an alarming increase has been observed in India and other Asian countries. India reported 1.13 million confirmed deaths due to CAD in 2010 (5,6).

As the proportion of ACS patients is less than 25% amongst those presenting with chest pain, distinction between ACS and non-ACS patients is very important (7). ACS patients should not be discharged, and non-

ACS patients should not be unnecessarily hospitalized exhausting the hospital resources. To ensure this, there is immense requirement for patient stratification in the ED for individuals presenting with chest pain. Risk stratification aids in deciding the mode of assessment for patients to identify those at low risk as well as avoiding major adverse cardiac events (MACE) (8-10). Hence, there is a need for different prediction tools to accurately identify patients with intermediate to high risk for hospitalization as well as low risk patients for quick discharge. There are more than twelve established risk stratification scoring systems based on chest pain to predict CAD in patients (11,12).

Several studies have individually assessed different scoring systems like Thrombolysis in Myocardial Infarction (TIMI) score, Global Registry of Acute Coronary Events (GRACE) score, Asia-Pacific evaluation of chest pain trial (ASPECT), Platelet glycoprotein IIb/IIIa in Unstable angina: Receptor Suppression Using Integrilin (eptifibatide) Therapy (PURSUIT) score, Fast Revascularization in Instability in Coronary disease (FRISC) score, Accelerated Diagnostic Protocol to Assess Patients With Chest Pain Symptoms Using Contemporary Troponins (ADAPT), North American Chest Pain Rule (NACPR) and History, ECG, Age, Risk factors, Troponin (HEART) score for clinical parameters, changes in electrocardiogram (ECG) and relative outcomes which makes comparative analysis difficult for estimation of relative performances (13-20).

In this study, comparative analysis of GRACE, TIMI and HEART scores have been used for the identification of high-risk ACS patients who present with chest pain in the ED followed by correlation of these scores with MACE prediction amongst high risk patients.

Methods

The present prospective observational study was conducted on 200 patients who visited the ED of a hospital in Bengaluru with a complaint of chest pain during the period from October 2015 to August 2017. They were assessed for risk stratification and validation scores like GRACE, TIMI and HEART upon admission to the ED. Written informed consent was obtained from the patients prior to access to their medical records. Ethical approval was received by the Institutional Ethics Committee (EC/PG-75/2018).

All the patients presenting to the ED with the age of 15 years and above were included in this study. However, patients with chest pain due to trauma and those with remarkable ST elevation in the ECG were excluded. A minimum sample size of 60 patients needed to be included in each group with power of 80% and α-error of 5%. Thus, a minimum of 200 patients collectively were included in the study where each patient was scored using GRACE, HEART and TIMI scores based on the patient's clinical condition.

All the patients included in this study were evaluated by the emergency physician for the patient details, clinical information and investigation reports to be used in risk scores calculation during admission to ED. GRACE, HEART and TIMI scores were calculated for every patient (21-23). The primary endpoint was MACE within 6 weeks after the initial ED presentation (including the index event). MACE consisted of unstable angina (UA), non-ST elevation myocardial infarction (NSTEMI), STEMI, percutaneous coronary intervention (PCI), coronary arterial bypass grafting (CABG), stenosis managed conservatively, cardiovascular death, non-cardiovascular death and death with unknown cause. The patients were followed up to 6 weeks or till the primary end point was reached. GRACE, HEART and TIMI scores were evaluated for sensitivity, specificity, positive and NPVs of high-risk score for predicting MACE occurrence.

Data were analyzed by using R statistical software version 4.0.3 and Microsoft Excel. Continuous variables are represented by mean ± SD form and categorical variables by a frequency table. Chi square test was used to observe the association between two categorical variables. The discrimination of the three scores was compared by examining their ROC curves and calculating the areas under the ROC curve (AUCs). $P \leq 0.05$ indicates statistical significance.

Results

A total of 199 patients participated in this study with the mean age 51.61 ± 16.47 years with the age group in the range of 19 years to 87 years. Out of these patients, there were 138 males (69.35%) and 61 females (30.65%). In the present study, 76 (38%) of the patients developed MACE, and 70 (35%) underwent PCI. Out of these 70 patients who underwent PCI, 10 patients were managed by conservative treatment whereas the remaining 60 patients were managed by percutaneous transluminal coronary angioplasty. Due to cardiovascular cause, 3 (1.5%) patients died and 3 (1.5%) patients underwent coronary artery bypass grafting (CABG). Out of the total patients, 29 (14.5%) were obese, 53 (26.5%) were smokers, 38 (19.0%) had hypercholesterolemia, 112 (56.0%) had hypertension, 47 (23.5%) had a history of ischemic heart disease and 107 (53.5%) had diabetes mellitus as represented in Table 1.

Chi square was performed to test the association between the presence of risk factors and the occurrence of MACE Out of the total patients studied, presence of risk factors like obesity ($P = 0.005$), hypertension ($P < 0.001$) and diabetes mellitus ($P < 0.001$) showed a significant correlation with the development of MACE.

GRACE, HEART and TIMI scores were used for risk stratification for MACE as represented in Figure 1. For HEART score, 74 (37%) patients with the score of 7-10 belonged to the high-risk category. For GRACE score, 35

Table 1. Descriptive analysis between major adverse cardiac events and risk factors

Variables		No	Yes	*P* value
Gender	Female	41 (33.33)	20 (26.32)	0.38
	Male	82 (66.67)	56 (73.68)	
Obesity	No	112 (90.24)	58 (77.64)	0.005*
	Yes	12 (9.76)	17 (22.37)	
Smoking	No	96 (78.05)	50 (65.79)	0.08
	Yes	27 (21.95)	26 (34.21)	
Hypercholesterolemia	No	102 (82.93)	59 (77.63)	0.46
	Yes	21 (17.07)	17 (22.37)	
Hypertension	No	69 (56.1)	19 (25)	<0.001*
	Yes	54 (43.9)	57 (75)	
History of IHD	No	96 (78.05)	56 (73.68)	0.59
	Yes	27 (21.95)	20 (26.32)	
Diabetes mellitus	No	70 (56.91)	22 (28.95)	<0.001*
	Yes	53 (43.09)	54 (71.05)	
Age group	15-29	19 (15.45)	3 (3.95)	0.01
	30-39	23 (18.70)	10 (13.16)	
	40-49	27 (21.95)	10 (13.16)	
	50-59	19 (15.45)	19 (25)	
	60-69	19 (15.45)	14 (18.42)	
	70-79	13 (10.57)	15 (19.74)	
	>80	3 (2.44)	5 (6.58)	

IHD: Ischemic heart disease.
*Statistical significance. *Pearson's and Chi-Squared test

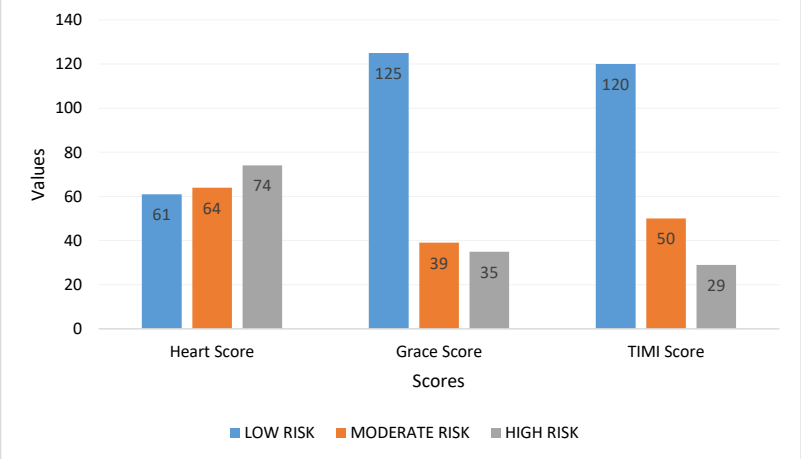

Figure 1. Risk stratification according to HEART, GRACE and TIMI scores. GRACE: Global registry of acute coronary events; HEART: History, 12-lead electrocardiogram, age, risk factors and troponin; TIMI: Thrombolysis in myocardial infarction.

(18%) patients had a score higher than 119 and belonged to the high-risk category. For TIMI scores, 29 (14%) patients had a score of 5-7 and belonged to the high-risk category.

Efficiency of HEART, GRACE and TIMI scores in evaluating MACE is shown in Table 2. In the present study, 74 patients were identified to be at high risk based on high HEART scores, out of which 69 patients were true positives for MACE whereas 5 patients were false positives. Amongst 125 patients with moderate and low risk groups, 7 patients were false negatives and 118 patients were true negatives. A total of 35 patients were identified to be at high risk based on high GRACE scores, out of which 29 patients were true positives and 6 patients were false positives. Amongst the 164 patients in low and moderate risk groups, 47 patients were false negatives and 117 patients were true negatives. Out of 197 patients who were identified to have high risk based on high TIMI

scores, 76 patients were true positives for MACE and 121 patients were false positives. Amongst the 2 patients in low and moderate risk groups, there were no false negatives whereas 2 patients were true negatives.

Table 2. Prediction of MACE with the help of HEART, GRACE and TIMI scores

Scoring system	Score	MACE		Total
		Present	Absent	
HEART	Present	69	5	74
	Absent	7	118	125
	Total	76	123	199
GRACE	Present	29	6	35
	Absent	47	117	164
	Total	76	123	199
TIMI	Present	76	121	197
	Absent	0	2	2
	Total	76	123	199

GRACE: Global registry of acute coronary events; HEART: History, 12-lead electrocardiogram, age, risk factors and troponin; MACE: Major adverse cardiac events; TIMI: Thrombolysis in myocardial infarction.

Table 3. Efficiency of HEART, GRACE and TIMI scores in predicting MACE.

Scoring System	Parameter	Value (%)
HEART	Sensitivity	90.78
	Specificity	95.96
	PPV	93.24
	NPV	94.4
GRACE	Sensitivity	39.4
	Specificity	95.16
	PPV	83.3
	Negative predictive value	71.95
TIMI	Sensitivity	30.2
	Specificity	95.96
	PPV	82.14
	NPV	69.18

GRACE: Global registry of acute coronary events; HEART: History, 12-lead electrocardiogram, age, risk factors and troponin; MACE: Major adverse cardiac events; TIMI: Thrombolysis in myocardial infarction; PPV, Positive predictive value; NPV, Negative predictive value.

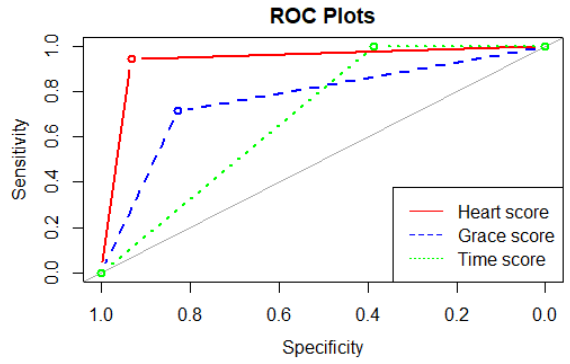

Figure 2. ROC curve of the HEART score, GRACE score and the TIMI score. GRACE: Global registry of acute coronary events; HEART: History, 12-lead electrocardiogram, age, risk factors and troponin; ROC, Receiver operating characteristic; TIMI: Thrombolysis in myocardial infarction.

The efficiency of HEART, GRACE and TIMI scores in predicting MACE is presented in Table 3. The sensitivities observed by HEART, GRACE and TIMI scores were 90.78%, 39.4%, and 30.2%, respectively for the prediction of MACE.

The ROC curves were used for efficacy of the HEART score, GRACE score and TIMI score in predicting MACE within 6 weeks as shown in Figure 2. The area under the curve (AUC) of HEART score was the highest with 0.96 (95% CI: 0.93-0.98), followed by the AUC of the TIMI score with 0.815 (95% CI: 0.75-0.873) and the GRACE score with an AUC of 0.814 (95% CI: 0.75-0.813).

Discussion

Diagnostic processes focus upon identification for ACS patients based on risk levels in case of chest pain patients at the ED. Risk scores have been used to evaluate patients with ACS as a reliable predictor outcome very soon after the arrival of patient which will in turn help the clinician in deciding the course of treatment (24). However, identification of ACS patients with low and high risk is still challenging as a normal ECG and negative biomarkers in initial stages do not exclude ACS. Risk scores can aid in the prediction of low, intermediate and high-risk ACS patients which would further help the physicians in deciding the course of treatment (25).

The current study is the first prospective observational analysis on the Indian sub-population evaluating efficacy of three different risk stratification scoring systems, namely, HEART score, GRACE score and TIMI score to identify patients presented with a complaint of chest pain to the ED with high risk of developing ACS and further on having a MACE.

In this study, 137 (68.5%) males and 63 (31.5%) females were reported to have chest pain. This finding is similar to a study reported by Sakamoto et al which showed 418 (69.2%) males out of among the 609 patients (26). Patients from age groups ranging from 19 years to 87 years with the mean age of 51.50 years were reported in this study. This finding is consistent with the results of the study conducted by Backus et al showing patients with the mean age of 60.6 years (27).

Poldervaart et al reported the incidence of six-week MACEs of 1.3%, 7.9% and 90.8% respectively for patients identified as low, moderate and high risk. (28). Leite et al showed the incidence of six-week MACE to be 2% and 15.6% in low and medium risk patients, respectively (29). Similarly, in the current study, 38% of patients were observed to meet the incidence of six-week MACE. Hence, it was observed that high acuity patients had higher HEART score and more MACE.

HEART score of high-risk patients for the prediction of MACE showed 90.78% sensitivity, 95.96% specificity,

93.24% positive predictive value (PPV) and 94.4% negative predictive value (NPV). GRACE score of high-risk patients for the prediction of MACE showed 39.4% sensitivity, 95.16% specificity, 83.3% PPV and 71.95% NPV. TIMI score of high-risk patients for the prediction of MACE showed 30.2% sensitivity, 95.96% specificity, 82.14% PPV and 69.18% NPV. According to the study conducted by Bodapati et al, HEART score for predicting MACE reported 99% (95–100) sensitivity, 43% (39–48), specificity, 99% (97–100) NPV and 32% (27-36) PPV (30). Another study reported GRACE scores with 70.9% sensitivity, 77.2% specificity, 70.3% PPV and 77.8% NPV. TIMI scores showed 90% sensitivity, 63% specificity, 65.2% PPV and 89.9% NPV value was 97.87% (31). Thus, the current study had a lower sensitivity but better specificity and PPV in all three scores.

In this study, HEART score was found to significantly outperforms GRACE score and TIMI score for the prediction of 6- week MACE in high acuity chest pain patients in the ED as depicted by c-statistics for HEART being 0.96 (95% CI: 0.93-0.98), TIMI score with 0.815 (95% CI: 0.75-0.873), and GRACE score of 0.814 (95% CI: 0.75-0.813). Similar results have been observed in studies reported by Backus et al and Six et al thereby comparing the HEART, GRACE and TIMI scores in a general population (27,32). Comparative analysis of GRACE and TIMI risk scores have shown marginal differences between the TIMI score 0.79 (95% CI: 0.74–0.83) and GRACE score 0.83 (95% CI: 0.79–0.87), which is similar to the current study (33).

However, the current study does have its share of limitations. As the data have been generated from a single medical center, a chance of statistical bias cannot be denied. A multi-center analysis needs to be done with a large sample size to validate these preliminary results. Also, the efficacy of other scoring systems needs to be considered along with the currently studied GRACE, HEART and TIMI scores. The exact variables considered by physicians while treating chest pain patients need to be considered for improving this accuracy of these scoring systems. Higher consideration of objective variables for predicting GRACE and TIMI scores as compared to HEART scores might generate a bias to some extent.

Conclusion

In a comparative analysis of HEART, GRACE and TIMI scores performed on a prospective cohort of chest pain patients presenting to the ED, prediction of MACE using HEART scores was higher in comparison with GRACE and TIMI scores. Efficacy of HEART, GRACE and TIMI scores in identifying patients at the highest risk of an ACS and predicting the occurrence of MACE showed that HEART score performed the best in risk stratification in patients with a higher sensitivity, specificity, PPV and NPV. Thus, HEART score serves as an efficient prediction tool to identify high-risk patients as early as hospital admission and hence it is highly recommended for hospital use, especially in the ED.

Author's contributions

MVD participated in literature search, clinical studies, data acquisition, data analysis, statistical analysis and manuscript preparation. ACR framed the concepts, design, definition of intellectual content, performed literature search, participated in clinical studies, analyzed the data and reviewed the manuscript. KMMR and HKV framed the concepts, design, definition of intellectual content and edited the manuscript. All authors read and approved the manuscript.

Ethical issues

Written informed consent was obtained from the patients prior to access to their medical records. Ethical approval was received by the Institutional Ethics Committee (EC/PG-75/2018).

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