

Comparison of Global Registry of Acute Coronary Events and Thrombolysis in Myocardial Infarction Risk Scores in non-ST-Elevation Acute Coronary Syndrome

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INTRODUCTION

Cardiovascular diseases are currently the leading cause of mortality and morbidity in industrialized countries. Among these, coronary artery disease (CAD) is the most common and is associated with high rate of mortality and morbidity.^[1] Ischemic heart disease contributed to 17.8% of total deaths and 8.7% of total disability-adjusted life years in India.^[2]

Unstable angina/non-ST-elevation myocardial infarction (UA/NSTEMI) constitutes a clinical syndrome subset of the acute coronary syndrome (ACS) that is usually, but not always, caused by atherosclerotic CAD and is associated with an increased risk of cardiac death and subsequent myocardial infarction. NSTEMI is defined by Electrocardiography (ECG) ST-segment depression or prominent T-wave inversion with positive biomarkers of necrosis in the absence of

persistent (<20 min) ST-segment elevation. Patients without typical symptoms and serial negative biomarkers of necrosis are diagnosed as UA.^[3]

The number of patients with non ST elevation acute coronary syndrome (NSTEMI ACS) as compared to ST elevation myocardial infarction is increasing. This may be due to change in the demography of population, growing number of aging population, and increase incidence of obesity and diabetes mellitus.^[4] NSTEMI-ACS causes 2–2.5 million annual worldwide

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ABSTRACT

Context: The Global Registry of Acute Coronary Events (GRACE) and Thrombolysis in Myocardial Infarction (TIMI) scores in predicting coronary disease severity in patients with non-ST-elevation acute coronary syndromes (NSTEMI-ACS) have not been proved. **Aims:** We aimed to compare the GRACE score with TIMI risk score for prediction of the angiographic severity of coronary artery disease (CAD) in patients with NSTEMI-ACS. **Settings and Design:** This was an observational cross-sectional study. **Subjects and Methods:** Total 202 NSTEMI-ACS (NSTEMI myocardial infarction and unstable angina) patients were included. The GRACE and TIMI scores were estimated. Coronary angiogram was done and the Gensini score and vessel score were used to assess the severity of CAD. **Statistical Analysis Used:** SPSS software version 27.0 was used for statistical analysis. For comparison of two means, independent sample *t*-test/Mann–Whitney *U*-test was used, while for more than two means, one-way ANOVA/Kruskal–Wallis test was used. The receiver operating characteristic (ROC) curve was applied for the predictability of GRACE and TIMI scores for severity of disease. **Results:** A positive association between the Gensini score and vessel score was observed with both the GRACE ($P = 0.001$) and TIMI ($P = 0.001$) scores. The area under the ROC curve for the GRACE score was 0.765 (95% confidence interval [CI] = 0.676–0.854), significantly superior to the area under the ROC curve of the TIMI score (0.715; 95% CI = 0.618–0.812). Risk factors such as higher age, hypertension, smoking history, dyslipidemia, ECG changes such as ST deviation and T inversion, and Killip classification showed a statistically significant association with severity of disease. **Conclusions:** Both the GRACE and TIMI risk scores were a good predictor of angiographic severity of CAD in patients with NSTEMI-ACS, and the GRACE score was found to be superior to the TIMI risk score.

KEYWORDS: Coronary angiography, coronary artery disease, non-ST-elevation acute coronary syndrome

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hospitalizations.^[5] According to Kerala and Himachal Pradesh ACS registries, NSTEMI-ACS accounts for 63% and 54.5% of ACS, respectively.^[6,7]

Several risk scores are used to assess the prognosis in patients with NSTEMI-ACS that integrate clinical variables, findings on ECG, and from serum biomarkers have been developed. The Global Registry of Acute Coronary Events (GRACE) and Thrombolysis in Myocardial Infarction (TIMI) scores are most commonly used for risk stratification, and the prognostic value of each score has been established by several studies.^[8,9] Vessel score and Gensini score are widely used in the assessment of the severity of CAD.^[10]

Though both the scores correlate directly with mortality and recurrent ischemia, however are not meant to identify the angiographic severity of CAD. A positive correlation of GRACE and TIMI risk scores with the severity of CAD has been reported by several studies, but which score is higher in predicting the severity of CAD has not yet been established.^[11] Patients with high GRACE and TIMI risk scores before performing coronary angiography may change the therapeutic decisions and the timing or intensity of treatment.^[12] In this study, we aimed to predict the angiographic severity of CAD in patients with NSTEMI-ACS by GRACE and TIMI risk scores and to compare the GRACE score with TIMI risk score in patients with NSTEMI-ACS for their accuracy in predicting the angiographic severity of coronary disease.

SUBJECTS AND METHODS

Study design

This observational cross-sectional study was carried out after the study protocol was approved by the Institutional Ethics Committee. A total of 202 patients with NSTEMI-ACS who gave consent for undergoing coronary angiography were included in the study. Patients with a history of prior myocardial infarction, valvular heart diseases, congenital heart diseases, cardiomyopathy, suspected myocarditis, or pericarditis and who underwent prior percutaneous coronary intervention or coronary artery bypass grafting were not included in the study.

Procedure

After enrollment, all patients were evaluated clinically at the first presentation. Risk factors including diabetes, smoking, hypertension, dyslipidemia, and family history of premature CAD were noted. A 12-lead resting ECG was done on admission and looked for any ST segment depression, T wave inversion. Cardiac troponin T, serum creatinine, fasting, postprandial blood sugar, and lipid profile were measured.

The GRACE and TIMI scores were calculated during hospital admission. GRACE score has eight parameters (age, heart rate, systolic blood pressure (SBP), Killip class of heart failure, cardiac arrest at admission, serum creatinine, ST-segment deviation on ECG, and elevated cardiac biomarker) with the score from 1 to 372. Each variable has different points. The patients were divided into low-risk (≤ 108), intermediate-risk (109–140), and high-risk (> 140) groups in accordance with the GRACE score.

TIMI score has seven criteria (age > 65 , prior CAD stenosis $> 50\%$, risk factors [hypertension, diabetes, smoking, hyperlipidemia, and family history], history of angina episodes in 24 h, history of aspirin intake in the last 7 days, ST-segment deviation on ECG, and elevated cardiac biomarker) with the score from 1 to 7. Each criterion consists of score 1. After calculation of TIMI score, the patients were also divided into low-risk (0–2), intermediate-risk (3–4), and high-risk (5–7) groups.

In a fasting state, coronary angiography was performed through the femoral or radial artery approach. The Gensini score and vessel score were used to assess the severity of CAD. Modified Gensini score was calculated by taking three factors of coronary lesion, severity coefficient, multiplying factor for region, and collateral adjustment factor. Severity coefficients were 1, 2, 4, 8, 16, and 32 for obstruction 1%–25%, 26%–50%, 51%–75%, 76%–90%, 91%–99%, and 100%, respectively. Multiplying factor for each lesion depends on its location in coronary anatomy and functional significance of the area; it supplies and ranges from 0.5 to 5. When there was 99% or 100% obstruction and receiving collaterals, an adjustment factor for collateral was used. Gensini score of each segment was calculated by multiplying severity coefficient and multiplying factor. The points of all segments were added to get the total Gensini score of the patient. Patients were divided into absent or mild CAD and moderate-to-severe CAD. Absent or mild CAD is defined as a Gensini score of ≤ 20 and moderate-to-severe CAD is defined as a Gensini score of > 20 .^[13]

Vessel score defines $\geq 70\%$ stenosis in any major epicardial coronary arteries or $\geq 50\%$ stenosis in the left main coronary artery as significant CAD.^[14]

Statistical analysis

All the data were entered in Microsoft Excel software version 2007 and analyzed in the SPSS software version 27.0 (IBM corporation, Armonk, New York, USA). All the categorical variables were expressed in terms of numbers and percentages. All the continuous variables were expressed in terms of mean and standard deviation. A comparison of two categorical variables was carried out using Chi-square/Fisher's exact test. For comparison of two means, independent sample *t*-test/Mann–Whitney *U*-test was used, while for more than two means, one-way ANOVA/Kruskal–Wallis test was used. The receiver operating characteristic (ROC) curve was applied to find out the predictability of GRACE and TIMI scores for severity of disease in terms of area under the curve. A *P* value of < 0.05 was considered statistically significant.

RESULTS

A total of 202 patients were enrolled, out of which 26 (13%) were UA and 176 (87%) were NSTEMI. The mean age of the study participants was 59.28 ± 9.19 years, and the age ranged from a minimum of 39 years to a maximum of 78 years. The majority of the patients were male 144 (71.5%) compared to females 58 (28.5%). One hundred and twenty-three (60.8%) patients were hypertensive while only seventy (34.6%) were diabetic. Smoking history was found in 47 (23.3%)

In our study, angiographic severity was determined by vessel score and Gensini score. Mean GRACE score and TIMI score steadily increased from a patient without any vessel involvement to triple-vessel disease and were statistically significant. Similar results were found in a study done by Roy *et al.* and Mahmood *et al.*^[11,19]

Mean Gensini score steadily increased from low-risk GRACE and TIMI score to high-risk GRACE and TIMI score with $P < 0.001$. These findings suggest the tendency toward severe

Table 5: Mean Global Registry of Acute Coronary Events and Thrombolysis in Myocardial Infarction score according to severity category of Gensini score (n=202)

Gensini score	GRACE score	P	TIMI score	P
None/mild CAD severity score	106.22±34.95	<0.001	2.11±1.56	<0.001
Moderate-to-severe CAD score	142.76±37.94		3.18±1.42	

TIMI=Thrombolysis in Myocardial Infarction, CAD=Coronary artery disease, GRACE=Global Registry of Acute Coronary Events

CAD according to mean GRACE and mean TIMI scores, similar to the results of Roy *et al.* and Barbosa *et al.* study.^[11,15]

This study showed the superiority of the GRACE score to the TIMI score in assessing the angiographic extension of CAD in NSTEMI-ACS. In our study, both GRACE and TIMI scores showed a high predictive capacity for severity of CAD with an area under the ROC curve of 0.765 (95% confidence interval [CI] = 0.676–0.854) and 0.715 (95% CI = 0.618–0.812), respectively, at a significance level of $P < 0.001$. The area under the curve difference was 0.05 between the two scores, which was statistically significant to establish that the GRACE score was better than TIMI score in assessing the severity of CAD in patients with NSTEMI-ACS, similar to the results of Roy *et al.*^[11]

Barbosa *et al.*^[15] suggested that the TIMI and GRACE scores were not accurate in predicting the CAD extension in patients with NSTEMI ACS Figure 1 and 2, but the results of our study showed that these two scores had a high predictive capacity for severity of CAD with the GRACE score as a better predictor.

Table 6: Association of different risk factors with the severity (n=202)

	None/mild CAD severity score, n (%)	Moderate-to-severe CAD score, n (%)	P
Age (years)			
<50	11 (30.6)	24 (14.6)	0.036
50-60	14 (38.9)	61 (36.7)	
>60	11 (30.6)	81 (48.7)	
Gender			
Male	24 (66.7)	120 (72.2)	0.499
Female	12 (33.3)	46 (27.8)	
Hypertension			
Present	16 (44.4)	107 (64.5)	0.025
Absent	20 (55.6)	59 (35.5)	
Diabetes			
Present	13 (36)	57 (34.3)	0.839
Absent	23 (64)	109 (65.6)	
Smoking history			
Present	2 (5.6)	47 (28.3)	0.004
Absent	34 (94.4)	119 (71.7)	
Family history			
Present	4 (11.1)	39 (23.4)	0.099
Absent	32 (88.9)	127 (76.6)	
Dyslipidemia			
Present	6 (16.7)	60 (36.1)	0.023
Absent	30 (83.3)	106 (63.9)	
Killip class			
I	34 (94.4)	118 (71.0)	0.013
II	2 (5.6)	40 (24.4)	
III	0	8 (4.8)	
ST deviation			
Present	13 (36.1)	92 (55.4)	0.035
Absent	23 (63.9)	74 (44.6)	
T inversion			
Present	21 (58.3)	112 (67.4)	0.031
Absent	15 (41.7)	54 (32.6)	

CAD=Coronary artery disease

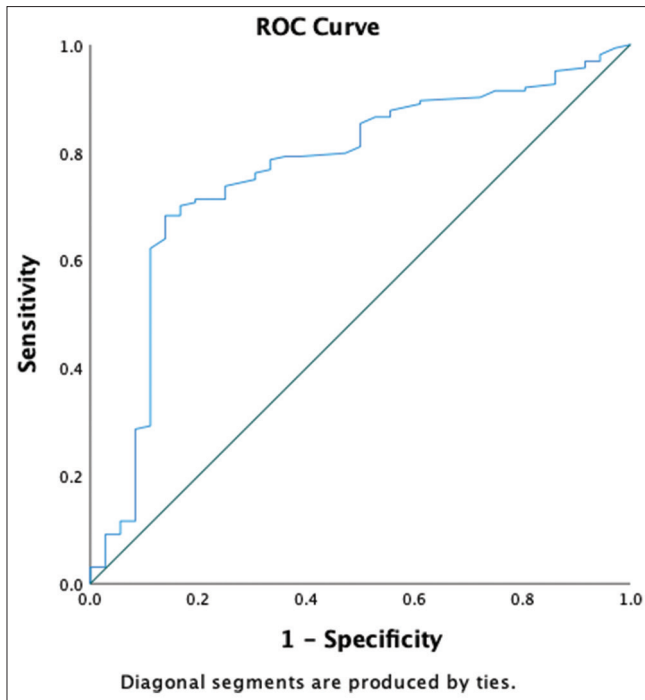


Figure 1: Receiver operating characteristic curve showing predictive ability of Global Registry of Acute Coronary Events score for severity

Mahmood *et al.*^[19] showed that GRACE score was superior to TIMI risk score in predicting extent of CAD in NSTEMI-ACS which was similar to the result of our study.

Bekler *et al.*^[20] found that there was a positive significant correlation between the GRACE and the syntax score ($r = 0.427$, $P < 0.001$) but not with TIMI score. However, in our study, we compared these scores with the Gensini score and vessel score.

Hammami *et al.*^[21] found in their study that both GRACE and TIMI scores can predict obstructive CAD moderately well but not severity of CAD.

Ascenzo *et al.*^[22] a meta-analysis of 40 derivation studies on 216,552 patients and 42 validation studies on 31,625 patients, showed that TIMI and GRACE are the risk scores that up until now have been most extensively investigated, with GRACE score superior in predicting the severity compared to TIMI score.

For prognostication, the GRACE score is better than TIMI risk score in patients of NSTEMI-ACS.^[8,23] However, TIMI risk score may be a better predictor of severity of CAD.^[24] This is explained by variables such as prior CAD stenosis $>50\%$, use of aspirin, and risk factors (hypertension, diabetes, family history, and dyslipidemia). Age, heart rate, blood pressure, heart failure class, cardiac arrest at presentation, and serum creatinine are not included in TIMI score. However, these parameters are included in the GRACE score. TIMI score consists of dichotomous variables. Age, heart rate, blood pressure, serum creatinine are continuous variables which make the GRACE score better predictor of severity of CAD than the TIMI score in patients of NSTEMI-ACS.^[11,25]

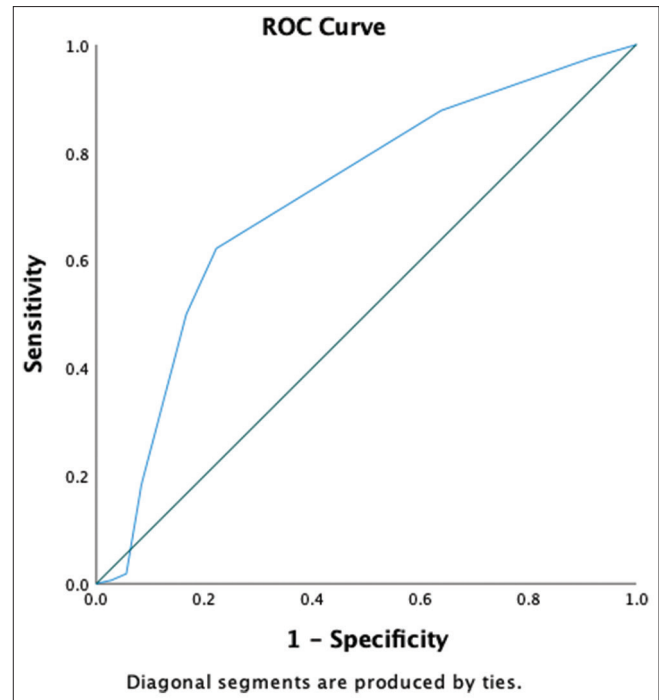


Figure 2: Receiver operating characteristic curve showing predictive ability of Thrombolysis in Myocardial Infarction score for severity

According to ESC guidelines, early invasive strategy (< 24 hour) was adopted for patients with GRACE score >140 and delayed invasive strategy (24–72 h) implemented for patients with GRACE score 109–140, and TIMI score ≥ 2 . An ischemia guided strategy recommended for patients with GRACE score < 109 and TIMI score ≤ 1 .^[26,27] Angiographic severity is an independent predictor of major cardiovascular events. We found a good association between high GRACE score and high TIMI score with angiographic severity. Hence, patients with high scores may get benefit from early invasive therapy.

Limitations

This evaluation was based on a small number of patients involving only one center. Normal coronaries were prespecified by angiogram without any IVUS evaluation.

CONCLUSIONS

Both the GRACE and TIMI risk scores had a high predictive capacity for angiographic severity of CAD in patients with NSTEMI-ACS, and the GRACE score was found to be better in assessing the severity than TIMI score. Patients with high-risk GRACE and TIMI scores at admission may get benefit from an early intervention approach to treatment.

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Conflicts of interest

There are no conflicts of interest.

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