GRACE and TIMI risk scores in predicting the angiographic severity of non-ST elevation acute coronary syndrome

Sharadindu Shekhar Roy*, S.T.M. Abu Azam, Md. Khalequzzaman, Mohammad Ullah, Mohammad Arifur Rahman
Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh

Abstract

Aims: We aimed to compare the GRACE and TIMI risk scores in patients with non-ST elevation acute coronary syndrome for their accuracy in predicting the angiographic severity of coronary artery disease.

Method: The cross-sectional study done in the Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh from April, 2015–April, 2016. The patients admitted with non-ST elevation acute coronary syndrome were evaluated to calculate the GRACE and TIMI risk score.

Coronary angiogram was done during index hospitalization and the severity of coronary artery disease was assessed by vessel score and Gensini score.

Results: Of 205 patients, a positive correlation of the vessel score and Gensini score was observed with both the GRACE and TIMI risk scores (p < 0.001) and the GRACE score (r = 0.55) correlated better than the TIMI score (r = 0.51). The GRACE score presented area under the Receiver Operating Characteristic (ROC) curve (0.943; 95% CI = 0.893–0.993) significantly superior to the area under the ROC curve (0.892; 95% CI = 0.853–0.937) of the TIMI score.

Conclusion: Both the GRACE and TIMI risk scores had good predictive value in assessment the severity of coronary artery disease in patients with non-ST elevation acute coronary syndrome, when they were compared, the GRACE score was found to be superior to the TIMI score.

© 2018 Published by Elsevier B.V. on behalf of Cardiological Society of India. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Cardiovascular diseases account for more than 17 million deaths globally each year. This figure is expected to grow to 23.6 million by the year 2030. Coronary artery disease (CAD) alone caused 7 million deaths worldwide in 2010 and it is an increase of 35% since 1990.1 The incidence of non-ST elevation acute coronary syndrome to ST elevation myocardial infarction is increasing, probably as a result of demographic changes in the population, including progressively increasing numbers of older persons and higher rates of diabetes mellitus.2

Prognosis in patients with non-ST elevation acute coronary syndrome can be assessed by early risk stratification. Several risk scores are developed in predicting the outcomes in patients with acute coronary syndrome. The most popular risk scores are the GRACE and TIMI scores.3 These two scoring systems yield the scores from some clinical parameters obtained from patient’s history, physical examination and investigations during admission.

The GRACE score has been derived from Global Registry of Acute Coronary Events (GRACE) registry and it has been published as an online risk calculator (http://www.outcomes-umassmed.org/grace/). This score has eight variables (Age, Heart Rate, Systolic BP, Killip Class of HF, Cardiac arrest at admission, S. Creatinine, ST segment deviation on ECG and elevated cardiac biomarker) with the scoring from 2 to 372. The TIMI score has been derived from Thrombolysis In Myocardial Infarction (TIMI) IIB trial and has also been published as online TIMI risk score calculator (http://www.timi.org). This score has seven variables (Age, Prior CAD, Risk factors, History of Angina episodes in 24 h, History of Aspirin intake, ST segment deviation on ECG and elevated cardiac biomarker) with the scoring from 0 to 7. Both the scores calculate the patient’s risk of mortality and they are not intended to identify the severity of coronary artery disease. But estimating the possible severity of CAD by these scores before performing coronary angiography may change the therapeutic decision and the timing or intensity of interventions.4 Vessel score and Gensini score are the two scoring systems which are being widely used in assessment of the severity of coronary artery disease. Vessel score describes significant coronary artery disease as ≥70% stenosis in any of the major epicardial coronary arteries or ≥50%...
stenosis in the left main coronary artery.\textsuperscript{5} Gensini score calculates the severity of CAD from 14 coronary artery segments.\textsuperscript{7} The segments are scored from 0.5 to 5 according to their anatomical importance and is multiplied by the score regarding the maximum degree of obstruction ranging from 1 to 100\% and the points of the 14 segments are summed to yield a final score by using the following formula: Gensini Score = Sum of Scores (Score for\% of stenosis \times Score for vessel/vessels involved).\textsuperscript{8}

Several international reports have shown positive correlation of GRACE and TIMI risk scores with the severity of coronary artery disease but regarding the comparison of these scores in predicting the severity of coronary artery disease, the available international data is limited. The superiority of anyone has not yet been established.

2. Methods

2.1. Participants and study design

This cross sectional, analytical study was done in the Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh from April, 2015 to April, 2016. A total of 205 patients with non-ST elevation acute coronary syndrome were studied who agreed to undergo coronary angiography during the period of index hospitalization. The patients with history of prior myocardial infarction, valvular heart diseases, congenital heart diseases, cardiomyopathy, suspected myocarditis or pericarditis and who underwent prior PCI or CABG were excluded from the study. The study protocol was approved by ethical review committee of the National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.

2.2. Procedure

After enrollment, all patients were evaluated clinically at first presentation. Demographic data such as age, sex and occupation were recorded. Risk factor including diabetes, smoking, hypertension, dyslipidemia and family history of premature CAD were noted. Drugs used previously were also noted. A 12-lead resting ECG was done on admission at a paper speed of 25 mm/s and 10 mm standardization. Cardiac troponin I, serum creatinine, random blood sugar were measured from the sample taken during admission. Troponin I concentration was measured by immunometric assay in our institute and the level of more than 1 ng/ml was considered as positive cardiac marker. The GRACE and TIMI scores were calculated by using the online calculator (http://www.outcomes-umassmed.org/grace and http://www.timi.org) during hospital admission. Coronary angiogram was done during index hospitalization. All coronary angiograms were evaluated by two experienced cardiologists who were blind to the GRACE and TIMI risk score of individual patient and the severity of coronary artery disease was assessed by vessel score and Gensini score.

2.3. Definition

The patients were divided into low (≤108), intermediate (109–140) and high (>140) risk groups according to the GRACE risk score. The patients were also divided into low (0–2), intermediate (3–4) and high (5–7) risk groups according to the TIMI risk score. The severity of CAD was classified as no (vessel score = 0), single (vessel score = 1), double (vessel score = 2) and triple (vessel score = 3) vessel disease. After Gensini score was determined, 36 points was chosen as an appropriate cut-off value and patients were divided into two groups, those with a Gensini score ≤36 were considered as absent or mild coronary artery disease and those with a Gensini score >36 were considered as moderate to severe coronary artery disease.\textsuperscript{9}

2.4. Statistical analysis

Statistical analysis was performed by using SPSS statistical software (version 19, SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean and standard deviation and categorical variables as frequency and percentage. Quantitative variables were analyzed by Student’s t-test and ANOVA. Categorical variables were analyzed by chi-square test. To test the association of GRACE and TIMI score with the severity of coronary artery disease, Pearson’s correlation test used while multivariate logistic regression was used to demonstrate the strength of the influence of the GRACE and TIMI scores. The receiver operating characteristics (ROC) curve was used to test the strength of the scores in predicting the angiographic severity of coronary artery disease. P value of less than 0.05 was considered as significant. The area under the ROC curve of 0.5 and the difference between the areas under the ROC curve of at least 0.05 for superiority was defined as statistical significance.

3. Results

The mean age of the study population was 51.8 ± 9.1 years. Male patients were predominant (80\%). This study found smoking as the most prevalent (74.6\%) risk factor. Among the other risk factors, the frequency of hypertension (69.3\%) and diabetes mellitus (57.1\%) were nearer to each other. 28.9\% patients had positive family history of premature CAD and 33.7\% patients were dyslipidemic. Among the GRACE score variables, mean heart rate was 80.2 ± 15.0 beats per minute, and mean systolic blood pressure was 145.2 ± 16.5 mm of Hg. The mean serum creatinine was 1.31 ± 0.62 mg/dl and most of the patients were belonged to Killip Class-I (90.6\%). Among the TIMI score variables, 22.9\% patients had history of taking aspirin in last 7 days and 58\% patients had ≥2 episodes of angina in last 24 h. 59\% patients of the study population were found of having ST depression of ≥0.5 mm, 18\% patients having T wave inversion and 23\% patients having no specific ST-T changes in contiguous leads on ECG. Troponin-I was negative in 43.9\% patients. Among them of positive biomarker, most of the patients had got the value of Troponin-I <30 ng/ml.

The mean GRACE score of the study population was 139.02 ± 46.71. According to the GRACE score, patients were divided into low, intermediate and high-risk group and it was found 24.9\%, 36.1\% and 39.0\% in each group respectively. The mean TIMI score of this study population was 3.24 ± 1.41. According to the TIMI score, it was found, 34.6\%, 42.0\% and 23.4\% patients in low, intermediate and high-risk group respectively.

The highest mean GRACE score (189.55 ± 36.94) was associated with high vessel score (vessel score = 3). In the low, intermediate and high GRACE score category, the mean Gensini score was 29.19 ± 28.67, 31.38 ± 25.19 and 42.87 ± 20.95 respectively with p value <0.001 (Tables 1 and 2). The mean GRACE score

| Number of vessel involved | GRACE Score | p value | TIMI score | p value |
|---------------------------|-------------|---------|------------|---------|
|                           | Mean | SD   |          | Mean | SD |
| No vessel (n = 22)         | 94.77 | 14.51 | **<0.001** | 1.86 | 1.03 | **<0.001** |
| Single vessel (n = 51)     | 115.67 | 19.32 | 2.88 | 1.19 |
| Double vessel (n = 81)     | 133.94 | 43.37 | 3.22 | 1.47 |
| Triple vessel (n = 51)     | 189.55 | 36.94 | 4.24 | 0.91 |
Table 2
Association between the GRACE & TIMI risk score with Gensini score (n = 205).

| GRACE score | Gensini score | p value | TIMI score | Gensini score | p value |
|-------------|---------------|---------|------------|---------------|---------|
| Low (≤108) | 29.19 | 28.67 | <0.001 | Low (0–2) | 26.13 | 20.15 | <0.001 |
| Intermediate (109–140) | 31.38 | 25.19 | Intermediate (3–4) | 35.12 | 22.06 | |
| High (>140) | 42.87 | 20.95 | High (5–7) | 49.29 | 30.78 | |

Table 3
Mean GRACE and TIMI score of the study population according to the Gensini score (n = 205).

| Severity of CAD by Gensini score | Mean ± SD of GRACE score | Mean ± SD of TIMI score | p value |
|-------------------------------|--------------------------|-------------------------|---------|
| None or mild CAD Gensini score (≤36) | 125.66 ± 35.60 | 3.01 ± 1.31 | <0.001 |
| (n = 112) | | | |
| Moderate to severe CAD Gensini score (>36) | 155.12 ± 53.18 | 3.53 ± 1.49 | <0.001 |
| (n = 93) | | | |

155.12 ± 53.18 was associated significantly (p = < 0.001) with the Gensini score of >36 (Table 3).

The highest mean TIMI score (4.24 ± 0.91) was also associated with high vessel score (vessel score = 3). In the low, intermediate and high TIMI score category, the mean Gensini score was 26.13 ± 20.15, 35.12 ± 22.06 and 49.29 ± 30.78 respectively with p value <0.001 (Tables 1 and 2). The mean TIMI score 3.53 ± 1.49 was associated significantly (p = <0.001) with the Gensini score of >36 (Table 3). These findings established the tendency towards severe coronary artery disease according to GRACE and TIMI score tertile and mean GRACE and mean TIMI score. The correlation coefficient between GRACE and TIMI risk score with the Gensini score were 0.55 (p = < 0.001) and 0.51 (p = < 0.001) respectively for which both the scores were positively and significantly associated with the Gensini score.

Multivariate logistic regression analysis of the study after adjusting the risk factors for CAD revealed that independently the GRACE and TIMI scores could predict the severity of coronary artery disease and the GRACE risk score (OR = 1.914) was strong predictor of the severity of CAD than the TIMI score (OR = 1.556).

The correlation co-efficient between the GRACE score and Gensini score (r = 0.55) was more than that of the TIMI score and Gensini score. The receiver operating characteristic (ROC) curve showed that the area under curve for GRACE score was 0.943 (95% CI = 0.893–0.993) (Fig. 1) and the area under curve for TIMI score was 0.892 (95% CI = 0.853–0.937) (Fig. 2) in predicting the severity of coronary artery disease. The area under the ROC curve for both the scores were statistically significant but the area for the GRACE score was more than that of the TIMI score. The difference between two areas was 0.051 (Figs. 1 and 2). As to consider a difference of at least 0.05 is necessary for superiority,10 it established the superiority of the GRACE score to the TIMI score in predicting the angiographic severity of coronary artery disease in patients with non-ST elevation acute coronary syndrome.

4. Discussion

Due to the heterogeneous nature of the population of patients with non-ST elevation acute coronary syndrome, there is wide variation in terms of risk for the occurrence of death or recurrent ischemic events. The risk stratification is important as it has been consistently proved that early coronary intervention in high-risk patients improves clinical outcomes.11

The GRACE and TIMI scores are two most commonly used risk scores in risk stratification for the patients with non-ST elevation acute coronary syndrome at first presentation. In addition to predict the clinical outcomes, these scores have been studied for their association with the severity of coronary artery disease in some studies which have showed a positive correlation of these two risk scores with the angiographic severity of non-ST elevation acute coronary syndrome.12,13

This study, based on the patients with non-ST elevation acute coronary syndrome undergoing coronary angiography during the period of index hospitalization in the National Institute of Cardiovascular Diseases, Dhaka, Bangladesh from April 2015 to April 2016, demonstrated the superiority of the GRACE score compared with the TIMI score in predicting the angiographic severity of coronary artery disease. Barbosa et al, in 2012 reported that the degree of association of GRACE and TIMI score with the angiographic severity of CAD was not sufficient to make the scores as accurate predictor14 but the results of our study compared well between these two scores, suggesting that the GRACE score should be given preference in risk-stratifying for the patients with non-ST
elevation acute coronary syndrome as it performed better in predicting the severity of disease. Mahmood et al, 2013 compared these two scores in predicting the extent of CAD in patients with non-ST elevation acute coronary syndrome and they showed the better performance of GRACE score which was consistent with the result of our study.15

In our study, we found that, correlation co-efficient between the GRACE score and the Gensini score (r = 0.55) was more than that of the TIMI score (r = 0.51). Area under the receiver operating characteristic (ROC) curve for both GRACE and TIMI score were statistically significant but area for the GRACE score (0.943; 95% CI = 0.893–0.993) was more than that of the TIMI score (0.892; 95% CI = 0.853–0.937). The difference between two areas under the curve (AUCs) was 0.051 which was statistically significant to establish better performance for the accuracy of GRACE score than TIMI score in predicting the angiographic severity of coronary artery disease in patients with non-ST elevation acute coronary syndrome.

Although, some variables of TIMI score like risk factor status, prior coronary artery disease, prior aspirin intake and the experience of angina in 24 h are indicative of extension of coronary artery disease, it does not include any measurement of heart rate, blood pressure, heart failure, cardiac arrest at presentation and renal function. This score has no continuous variable. On the other hand, The GRACE score measures some parameters like, age, heart rate, systolic blood pressure and renal insufficiency as a continuous variable. It also includes heart failure and cardiac arrest at presentation. All are potential advantage of the GRACE score over the TIMI score to make the GRACE score stronger than the TIMI score in predicting the angiographic severity of non-ST elevation acute coronary syndrome.

4.1. Study limitations

Though adequate number of study population was used, we believe that it is still limited to generalize the results and it was conducted in a single center.

5. Conclusion

Both GRACE and TIMI risk scores had good predictive accuracy in assessment the severity of coronary artery disease in patients with non-ST elevation acute coronary syndrome but when they were compared, the GRACE score was found to be superior to the TIMI score. Nevertheless, further studies with large number of patients with multicenter approach are needed to assess this comparison.

Conflict of interest

No conflict of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgments

We thank Prof. Abdullah Al Shaﬁ Majumder (Ex-Director and Professor, NICVD, Dhaka, Bangladesh) and Prof. Md. Afzalur Rahman (Director and Professor, NICVD, Dhaka, Bangladesh), for their valuable support for the completion of this research.

References

1. Wong ND. Epidemiological studies of CHD and the evolution of preventive cardiology. Nat Rev Cardiol. 2014;11(5):276–289.
2. Giugliano RP, Cannon CP, Braunwald E. Non-ST elevation acute coronary syndromes. In: Mann DL, Zipes DP, Libby P, Bonow RO, eds. Braunwald’s heart disease: a textbook of cardiovascular medicine. 10th ed. Philadelphia: Elsevier; 2015:1155–1174.
3. Amsterdam EA, Wenger NK, Brindis RG, et al. AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes. J Am Coll Cardiol. 2014;64(24):e139–e228.
4. Roffi M, Patrono C, Collet JP, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2016;37:267–315.
5. Neeland IJ, Patel RS, Estehardi P, et al. Coronary angiographic scoring systems: an evaluation of their equivalence and validity. Am Heart J. 2012;164(4):547–552.
6. Chaitman BR, Bourassa MG, Davis K, et al. Angiographic prevalence of high-risk coronary artery disease in patient subsets. Circulation. 1981;64(2):360–367.
7. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol. 1983;51(3):606.
8. Huang G, Zhao J, Du H, et al. Coronary score adds prognostic information for patients with acute coronary syndrome. Circ J. 2010;74(3):490–495.
9. Ling S, Shu-Zheng Li. Association between non-alcoholic fatty liver disease and coronary artery disease severity. Chin Med J (Engl). 2011;124(6):867–872.
10. Correia LCL, Freitas R, Bittencourt AP, et al. Prognostic value of GRACE score versus TIMI score in acute coronary syndromes. Arq Bras Cardiol. 2010;94(5):576–582.
11. Santos ES, Filho LFA, Fonseca DM, et al. Correlation of risk scores with Coronary anatomy in non-ST-elevation acute coronary syndrome. Arq Bras Cardiol. 2013;100(2):511–517.
12. Cakar MA, Sahinkus S, Aydin E, et al. Relation between the GRACE score and severity of atherosclerosis in acute coronary syndrome. J Cardiol. 2014;63(1):24–28.
13. Lakhani MS, Qadir F, Hanif B, et al. Correlation of thrombolysis in myocardial infarction (TIMI) risk score with extent of coronary artery disease in patients with acute coronary syndrome. J Pak Med Assoc. 2010;60(1):197–200.
14. Barbosa CE, Viana M, Brito M, et al. Accuracy of the GRACE and TIMI scores in predicting the angiographic severity of acute coronary syndrome. Arq Bras Cardiol. 2012;99(3):818–824.
15. Mahmood M, Achakzai AS, Akhtar P, Zaman KS. Comparison of the TIMI and the GRACE risk scores with the extent of coronary artery disease in patients with non-ST-elevation acute coronary syndrome. J Pak Med Assoc. 2013;63(6):691–695.