# Comparison of the GRACE and TIMI Risk Scores in Predicting the Angiographic Severity of Coronary Artery Disease in Patients with non ST-elevation Myocardial Infarction

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## Abstract

***Key words:***
*Myocardial infarction, Coronary artery disease, TIMI risk score, GRACE risk score.*

***Background:*** *The superiority of the GRACE and TIMI risk scores in predicting the angiographic severity of coronary artery disease in patients with non ST-elevation myocardial infarction (NSTEMI) has not yet been established. This study was done to compare the GRACE and TIMI risk scores in predicting the angiographic severity of coronary artery disease in this group of patients.*

***Method:*** *The cross sectional study done in the Department of Cardiology, NICVD, Dhaka. The patients admitted with NSTEMI were evaluated to calculate the GRACE and TIMI risk score from April, 2015 to April, 2016. Coronary angiogram was done during index hospitalization and the severity of the coronary artery disease was assessed by vessel score and Gensini score.*

***Results:*** *Of 115 patients assessed, 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=0.59) correlated better than the TIMI score (r=0.52). The GRACE score presented area under the Receiver Operating Characteristic (ROC) curve of 0.844(95% CI = 0.774 – 0.914) significantly superior to the area under the ROC curve of 0.752(95% CI =0.658– 0.846) of the TIMI score for the difference between the two scores.*

***Conclusion:*** *Both the GRACE and TIMI scores had good predictive value in predicting the severity of coronary artery disease in the patients with NSTEMI but when both the scores were compared, the GRACE score was found to be superior and correlated better with the severity of coronary artery disease.*

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## 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 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]

NSTEMI currently accounts for about 50% of all myocardial infarctions. With the increased use of beta blockers and aspirin the incidence of NSTEMI is increasing.[3] The 6-month mortality rate in the patients with NSTEMI is about 6.2% and re-hospitalization rates over the 6 month is about 20%. This type of prognosis in patients with NSTEMI can be assessed by early risk stratification. Several risk scores are developed in predicting the outcomes in patients with acute coronary syndrome including NSTEMI. The most popular risk scores are the GRACE and TIMI risk scores. These risk scores calculate the patient's risk of mortality which depends on the severity of coronary artery disease and other comorbid conditions. But estimating the possible severity of coronary artery disease by these scores before performing coronary angiography may change the therapeutic decision and the timing or intensity of interventions.[4]

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Several international reports have shown an association between the GRACE score and the severity of coronary artery disease and several reports have also shown an association between the TIMI score and 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 and superiority of anyone over the other has not yet been established. The aim of this study was, therefore, to compare the performance of GRACE and TIMI risk scores in patients with NSTEMI to find out the score which can predict better the severity of coronary artery disease.

**Methods:**

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 115 patients, who presented in the Coronary Care Unit and Post Coronary Care Unit with non ST-elevation myocardial infarction were studied and the sampling was purposive type. The patients with NSTEMI who agreed to undergo subsequent coronary angiography during the period of index hospitalization after enrollment were included in the study. 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 the board of ethical review committee of the National Institute of Cardiovascular Diseases, Dhaka.

All patients were evaluated clinically at first presentation. Demographic data such as age, sex, occupation were recorded and noted. Risk factor including diabetes mellitus, smoking, hypertension, dyslipidemia and family history of premature coronary artery disease were noted. Drugs used before, during and after procedure were also noted. 12 lead resting ECG was done on admission and daily up to the discharge of the patient from the hospital at a paper speed of 25 mm/s and 10mm standardization. Cardiac troponin I, serum creatinine, random blood sugar was measured from the sample taken during admission into hospital. Troponin I concentration was measured by immunometric assay. The level of Troponin I >1ng/ml was considered as positive cardiac marker which was the upper reference limit (above the 99[th]centile) done by the machine "SIEMENS IMMULYTE 1000". The GRACE and TIMI scores were calculated by using the online GRACE and TIMI risk score calculator during admission into hospital.

The patients were divided into low risk (d"108), intermediate risk (109-140) and high risk (>140) groups according to the GRACE risk score. The patients were also divided into low risk (0-2), intermediate risk (3-4) and high risk (5-7) groups according to the TIMI risk score. 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. The severity of the coronary artery disease was assessed by vessel score and Gensini score. According to the vessel score, significant coronary artery disease was defined as e"70% stenosis in any of the three major epicardial coronary arteries or e" 50% stenosis in the left main coronary artery. The severity of CAD was defined as significant single, two or three vessel disease and significant left main coronary stenosis was scored as single vessel disease. The Gensini score was calculated from 14 coronary artery segments. The segments were scored according to their anatomical importance (ranging from 0.5 to 5) multiplied by the score regarding the maximum degree of obstruction (ranging from 1 to 100%).The points of the 14 segments are summed to yield a final score by using the following formula:

Total Gensini Score = Sum of Score (for % of stenosis) × Score for Vessel(s) involved.

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 d"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.[5]

Statistical analysis was performed using SPSS statistical software (version 19, SPSS Inc., Chicago, Illinois, USA). To test the association of GRACE and TIMI score with the severity of coronary artery disease, Pearson's correlation test used while 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 risk 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.

## Results:

The mean age of the study population was 52.2±9.2 years ranging from 26 to 75 years and most of the patients (38.3%) were belonged to 41-50 years of age. Male patients were predominant in study population which was 81%. Female patients were 19%. This study found smoking as the most prevalent (60.8%) risk factor for CAD. Among the other risk factors for CAD, the frequency of diabetes mellitus (56.6%) and hypertension (55.4%) were nearer to each other. 33.3% of the patients were dyslipidemic and 30.4% of the patients had positive family history of premature CAD.

In this study, among the GRACE score variables, mean heart rate was 80.3±15.3 beat per minute, and mean systolic blood pressure was 145.1±16.9 mm of Hg. The mean serum creatinine level was 1.49 ± 1.48 mg/dl and most of the patients were belonged to heart failure Killip class I (89.6%). We found 6.1% of the patients of Killip class II, 2.6% of the patients of Killip class III and 1.7% of the

patients of Killip class IV. Among the TIMI score variables, 23.5% patients had history of taking aspirin in last 7 days and 60% patients had ≥2 episodes of angina in last 24 hours.57.4% patients of the study were found of having ST depression of ≥0.5 mm, 17.4% patients having T wave inversion and 25.2% patients having no specific ST-T changes in contiguous leads on ECG. Most patients (71.3%) of the study had cardiac troponin-I in the range of 1-30 ng/ml.

The mean GRACE score of the study population was 139.56 ± 46.63 and when divided into low, intermediate and high risk group according to GRACE score, it was foundrespectively24.3%, 36.5% and 39.1% patients in each group (Table-I). The mean TIMI score of this study population was 3.28 ± 1.72 and when divided into low, intermediate and high risk group according to TIMI score, it was found 33.9%, 41.7% and 24.3% patients in each group respectively (Table-I).

The highest mean GRACE score (191.07 ± 35.98) was associated with high vessel score (vessel score=3) and in the low, intermediate and high GRACE score category, the mean Gensini score was 11.87±27.99, 27.64±25.43 and 42.02±20.17 respectively with p value < 0.001in both cases (Table-II and Table-III).

The mean GRACE score 156.31±53.39 was also associated significantly (p= < 0.001) with the Gensini score of >36 (moderate to severe CAD) (Table-IV).

**Table-I**

*Distribution of the study population according to GRACE and TIMI score (n=115).*

| GRACE score | Number | Percent (%) | TIMI score | Number | Percent (%) |
|---|---|---|---|---|---|
| Low (d''108) | 28 | 24.3 | Low (0-2) | 39 | 33.9 |
| Intermediate (109-140) | 42 | 36.5 | Intermediate (3-4) | 48 | 41.7 |
| High (>140) | 45 | 39.1 | High (5-7) | 28 | 24.3 |

**Table-II**

*Association between GRACE and TIMI score with number of vessels involvement (n=115).*

| Number of vessel involved | GRACE Score | | p value | TIMI score | | p value |
|---|---|---|---|---|---|---|
| | Mean | SD | | Mean | SD | |
| No vessel(n=14) | 90.48 | 18.36 | | 1.81 | 0.92 | |
| | | | <0.001[s] | | | <0.001[s] |
| Single vessel (n=29) | 116.45 | 18.99 | | 2.93 | 1.19 | |
| Double vessel (n=43) | 156.27 | 30.55 | | 3.97 | 1.15 | |
| Triple vessel (n=29) | 191.07 | 35.98 | | 4.28 | 0.92 | |

**Table-III**

*Association between the GRACE & TIMI risk score with Gensini score (n=115).*

| GRACE score | Gensini score | | p value | TIMIscore | Gensini score | | p value |
|---|---|---|---|---|---|---|---|
| | Mean | SD | | | Mean | SD | |
| Low (d"108) n=28 | 11.87 | 27.99 | | Low (0-2) (n=39) | 12.42 | 19.27 | |
| | | | <0.001[s] | | | | <0.001[s] |
| Intermediate (109-140) n=42 | 27.64 | 25.43 | | Intermediate 33.12 (3-4) (n=48) | 22.05 | | |
| High (>140) n=45 | 42.02 | 20.17 | | High (5-7) (n=28) | 46.78 | 29.91 | |

**Table-IV**

*Mean GRACE and TIMI score of the study population according to the Gensini score (n=115).*

| 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) (n=66) | 127.12±36.62 | 2.88±1.37 | <0.001[s] |
| Moderate to severe CAD Gensini score (>36)(n=49) | 156.31±53.39 | 4.05±1.16 | <0.001[s] |

This finding established the tendency towards severe coronary artery disease according to GRACE score tertile and mean GRACE score. The correlation co-efficient between GRACE risk score and Gensini score was r=0.59 (p = <0.001) for which the GRACE score was positively and significantly associated with the Gensini score (Fig.-1).
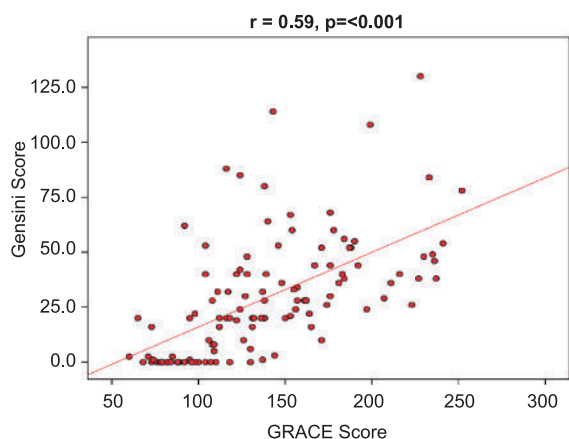


**Fig.-1:** *Pearson's correlation between GRACE score and Gensini score.*

The highest mean TIMI score (4.28 ± 0.92) was also associated with high vessel score (vessel score=3) that was statistically significant (p = < 0.001) and in the low, intermediate and high TIMI score category, the mean Gensini score was 12.42±19.27, 33.12±22.05 and 46.78±29.91 respectively with p value < 0.001(Table-II and Table-III).The mean TIMI score 4.05±1.16 was also associated significantly (p= < 0.001) with the Gensini score of >36 (moderate to severe CAD) (Table-IV). This finding established the tendency towards severe coronary artery disease according to TIMI score tertile and mean TIMI score. The correlation co-efficient between TIMI risk score and Gensini score was r=0.52 (p = <0.001) for which the TIMI score was positively and significantly associated with the Gensini score (Fig.-2).
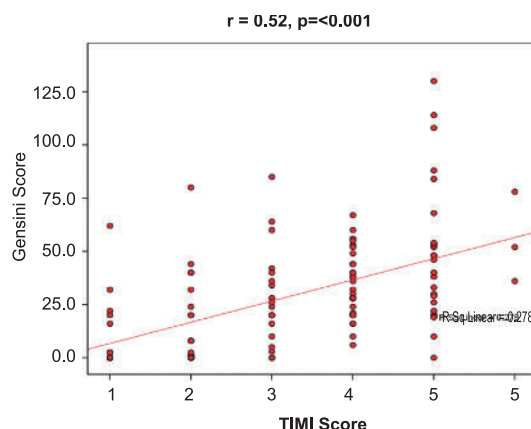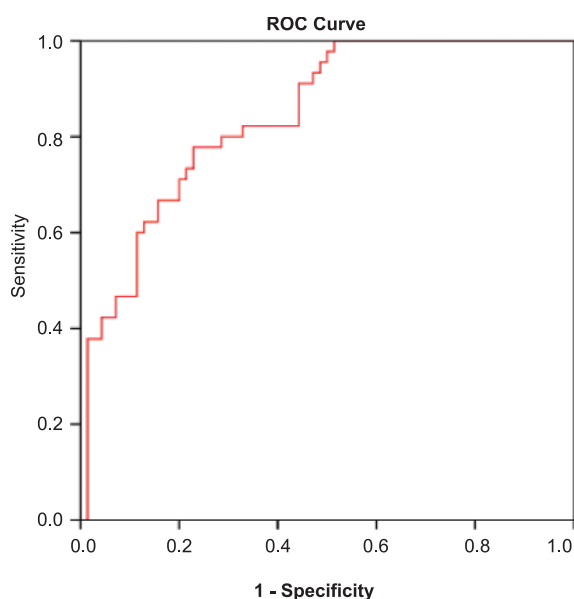


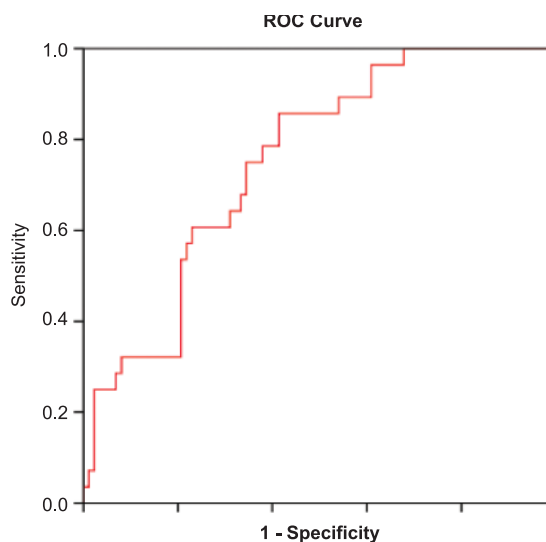**Fig.-2:** *Pearson's correlation between TIMI score and Gensini score.*

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 score (OR = 1.894) was strong predictor of the severity of CAD than the TIMI risk score (OR = 1.514).

In this study, correlation co-efficient between the GRACE score and Gensini score (r=0.59) was more than that of the TIMI score and Gensini score (r=0.52) (Fig.-1 and Fig.-2) and the receiver operating characteristic (ROC) curve showed that the area under ROC curve for GRACE score was 0.844 (95% CI = 0.774 – 0.914) (Fig.-3) and the area under ROC curve for TIMI score was 0.752 (95% CI = 0.658 – 0.846) (Fig.-4) in predicting the severity of coronary artery disease. The area under the ROC curve for both GRACE and TIMI risk score were statistically significant but the area for the GRACE score (0.844) was more than that of the TIMI score (0.752) and the difference was 0.092 (Fig.-3 and Fig.-4).



**ROC Curve**

**Area  Under the Curve = 0.752**
(95% CI = 0.658 – 0.846)

**Fig.-4:** *Receiver operating characteristic (ROC) curves for TIMI score in predicting the severity of CAD.*

As to consider a clinically relevant difference of at least 0.05 is necessary for superiority,[6] it established the superiority of the GRACE score to the TIMI score in predicting the angiographic severity of coronary artery disease in patients with NSTEMI.

**Discussion:**

Due to the heterogeneous nature of the population of patients with non-ST elevation myocardial infarction (NSTEMI), there is wide variation in terms of risk for the occurrence of death or recurrent ischemic events.[7] The risk stratification is important as it has been consistently proved that early coronary intervention in high-risk patients improves clinical outcomes. The main focus of this strategy is to evaluate the probability of occurrence of adverse events, analyzing data from the clinical history, physical examination, ECG findings and cardiac biomarkers.

The GRACE and the TIMI risk scores are the two most commonly used scores to risk-stratify for NSTEMI patients at presentation. The TIMI risk score incorporates seven variables, each having one point, while the GRACE risk score on the other hand is a more extensive scoring system, utilizing variables like age, heart rate, systolic blood pressure, creatinine (mg/dl), Killip class, cardiac arrest at admission, elevated cardiac markers and ST-



**ROC Curve**

**Area  Under the Curve = 0.844**
(95% CI = 0.774 – 0.914)

**Fig.-3:** *Receiver operating characteristic (ROC) curves for GRACE score in predicting the severity of CAD.*

segment deviation. In addition to predict the clinical outcome in NSTEMI, these scores have also been studied with regards to their correlation with the severity of CAD on coronary angiography.

This study, demonstrated the superiority of the GRACE risk score compared with the TIMI risk score in predicting the angiographic severity of coronary artery disease in patients with NSTEMI.

However, even when analyzed separately, both the GRACE and TIMI risk scores showed good performance in predicting the angiographic severity of coronary artery disease.

The usefulness of GRACE and TIMI risk scores in predicting the angiographic severity of CAD has been validated in several studies.[8-11] These studies showed an association of GRACE and TIMI risk scores with the angiographic severity of CAD in patients with NSTEMI. Those findings were validated by our study.

No local study, however, had been done to compare the GRACE and the TIMI risk scores with the severity of CAD and the international data available with regards to this comparison is also limited. A study showed that compared with the TIMI score, the GRACE score provides greater diagnostic information with regards to the extent of CAD in patients with NSTE-ACS, the discriminatory accuracy of GRACE score was superior to that of TIMI score.[12] The results of our study compare well between the two risk scores, suggesting that the GRACE score should be given preference in risk-stratifying for the patients with NSTEMI as it is associated with better assessment in predicting the severity of CAD.

In our study, we found that, correlation co-efficient between the GRACE score and the Gensini score (r=0.59) was more than that of the TIMI score (r=0.52) and area under the receiver operating characteristic (ROC) curve for both GRACE and TIMI risk score were statistically significant but the area for the GRACE score (0.844; 95% CI = 0.774 − 0.914) was more than that of the TIMI score (0.752; 95% CI = 0.658 − 0.846) and the difference between two areas under the curve (AUCs)was 0.092 which was statistically significant. It had been established that, the prediction of severity of coronary artery disease was significantly accurate for both the GRACE and TIMI scores and the strength of GRACE

score was more than that of TIMI score. Mahmood, et al. showed the better performance of the GRACE score than the TIMI score to predict the severity of CAD in NSTE-ACS patients of the Pakistani population which is consistent with our study.[12]

Though the GRACE score is more complex than the TIMI score, the ideal score should have a good balance between complexity and utility. Considering the relation between complexity and the accuracy in predicting the severity of coronary artery disease, it is favorable to the use of the GRACE score in the patients with non ST elevation myocardial infarction.

## Conclusion:

In conclusion, our study demonstrated that, both the GRACE and TIMI scores had good predictive value in predicting the severity of coronary artery disease in patients with NSTEMI but when both the scores were compared, the GRACE score was found to be superior and correlated better with the severity of coronary artery disease. Therefore, the GRACE risk score is more useful for better risk assessment and management of NSTEMI patients.

**Conflict of Interest - None.**

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