

GRACE and TIMI scores in predicting the extension of coronary artery disease in patients with non-ST elevation myocardial infarction

ST yükselmesiz miyokard enfarktüsü hastalarında koroner arter hastalığı yaygınlığının GRACE ve TIMI skorlarıyla öngörülmesi

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ABSTRACT

Objective: We aimed to assess the correlation of TIMI and GRACE risk scores with the SYNTAX score as the surrogate of severity and extent of coronary artery disease.

Methods: Patients with non-ST elevation myocardial infarction admitted to our emergency department and undergoing coronary angiography were considered for this study. TIMI and GRACE risk scores were calculated, and coronary artery disease severity and extension were assessed by using the SYNTAX score algorithm.

Results: We assessed 145 patients (mean age 59.41±11.04 years, 29% female). Based on the GRACE risk score for in-hospital deaths, the SYNTAX risk score was 12.22±8.70 for the low-risk group, 16.66±8.01 for the intermediate-risk group, and 22.48±11.42 for the high-risk group (ANOVA, p<0.0001). There were significant positive correlations between the SYNTAX score and GRACE scores (r=0.414, p<0.0001). The SYNTAX score also had a significant but weaker correlation with the TIMI score (r=0.271, p=0.001). The GRACE score showed good discriminatory capacity between the patients with and without a high-risk (>33) SYNTAX score, with an area under the ROC curve of 0.804 (CI 0.660-0.948, p=0.002); however, the TIMI score showed no predictive capacity and had an area under the ROC curve of 0.532 (CI 0.358-0.749, p=0.749).

Conclusion: A GRACE score indicating high risk may be helpful in predicting patients with severe extended coronary artery disease

Key words: Coronary artery disease, non-ST elevation myocardial infarction, risk scores

ÖZET

Amaç: TIMI ve GRACE risk skorlarının koroner arter hastalığının ciddiyetinin ve yaygınlığının bir göstergesi olan SYNTAX skoru ile korelasyonunu değerlendirmeyi amaçladık.

Yöntemler: ST elevasyonsuz miyokard infarktüsü nedeniyle acilimize başvuran ve koroner anjiyografi yapılan hastalar çalışmaya alındı. TIMI ve GRACE risk skorları hesaplandı, koroner arter hastalığının ciddiyeti ve yaygınlığı SYNTAX skor algoritması kullanılarak değerlendirildi.

Bulgular: 145 hastayı (ortalama yaş 59,41±11.04 yıl, %29 bayan) değerlendirdik. GRACE risk skoru baz alındığında hastane içi ölüm için düşük riskli grupta SYNTAX skoru 12,22±8,70, orta riskli olanlarda 16,66±8,01, yüksek riskli olanlarda 22,48±11,42 idi (ANOVA, p<0,0001). SYNTAX skorları ve GRACE skorları arasında anlamlı pozitif korelasyon vardı (r=0,414, p<0,0001). SYNTAX skoru ile TIMI skoru arasında anlamlı ama daha zayıf bir korelasyon vardı (r=0,271, p=0,001). GRACE skoru yüksek (>33) SYNTAX skoru olan ve olmayan hastalar için iyi bir ayırt etme kapasitesi göstermiştir, ROC eğrisi altında alan 0,804 (CI 0,660-0,948, p=0,002); fakat TIMI skoru ayırt etme kapasitesi göstermedi, ROC eğrisi altındaki alan 0,532 (CI 0,358-0,749, p=0,749) idi.

Sonuç: Yüksek GRACE risk skoru ciddi ve yaygın koroner arter hastalığı olan hastaları öngörmede faydalı olabilir.

Anahtar kelimeler: Koroner arter hastalığı, ST elevasyonsuz miyokard infarktüsü, risk skoru

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INTRODUCTION

Patients with hospital admission due to non-ST elevation myocardial infarction (NSTMI) have a wide variation in their disease severity, which ranges according to clinical and laboratory characteristics [1]. Thus, risk stratification is essential for adequate clinical decision-making. The Thrombolysis In Myocardial Infarction (TIMI) and Global Registry of Acute Coronary Events (GRACE) risk scores are the most commonly used, and their prognostic value have been validated in multiple clinical trials [1-3]. The most attractive aspect of these risk scores are that they can be estimated at the bedside with easy to obtain clinical, laboratory, and electrocardiographic parameters.

The Synergy between PCI with TAXUS and Cardiac Surgery (SYNTAX) score is a lesion-based scoring system. This score has been successfully validated with clinical studies [4]. Not only can this scoring system quantify coronary anatomy complexity but it also has the ability to objectively identify which patients with complex coronary artery disease (CAD) are suitable for PCI [5,6]. Preoperative clopidogrel use in patients who are candidates for coronary artery bypass graft (CABG) is a major concern for cardiologists and surgeons [7,8]. Estimating the coronary anatomy before angiography is performed could be useful in clinical practice to predict the likelihood of a patient having coronary anatomy amenable to CABG. In this regard, our aim in this study is to assess the correlation of TIMI and GRACE risk scores with the SYNTAX score as the surrogate of severity and extent of coronary artery disease.

METHODS

Patient population

This was a single-center prospective study. After applying the exclusion criteria, a total of 145 NSTMI patients undergoing coronary angiography were recruited from February to June 2013. NSTMI was defined as new-onset or worsening chest pain occurring at rest or with minimal exertion with positive cardiac markers (troponin value above the 99th percentile) and without ST segment elevation. Patients with ST segment elevation at admission, new left bundle branch block, percutaneous coronary

intervention in the previous 6 months, or previous CABG were excluded from the study.

TIMI and GRACE scores

The TIMI risk score consists of the following seven variables: age >65 years, aspirin use in the past 7 days, presence of >3 coronary artery disease risk factors, known >50% coronary artery stenoses, >2 anginal episodes in the past 24 hours, ST segment changes, and positive cardiac biomarkers. The presence of each variable adds one point to the total score that ranges from zero to seven; the score gives a 14-day risk of all-cause mortality, new or recurrent myocardial infarction (MI), or severe recurrent ischemia requiring urgent revascularization [1].

GRACE consists of the following eight variables at admission: age, heart rate, systolic blood pressure, plasma creatinine, Killip class, ST-segment deviation, elevated myocardial necrosis marker, and cardiac arrest at admission. In-hospital percutaneous coronary intervention (PCI), coronary artery bypass grafting surgery, and past MI history are also added to the score when calculating the discharge GRACE score. For calculating the score electrocardiographic records of the first 6 hours, the first plasma creatinine value and the troponin measures for the first 12 hours were used. Troponin T or I above the 99th percentile were used to show elevation of the cardiac markers. The final score can range from zero to 372 [3].

Coronary angiography and the SYNTAX score

Coronary angiography was performed for each of the study population, and coronary artery disease severity and extension was assessed by an experienced invasive cardiologist who used the SYNTAX score algorithm [5,6].

Statistical Analysis

Patients' characteristics and laboratory values were presented as proportions for dichotomous variables and means \pm standard deviation for continuous variables. The associations between the SYNTAX score and patient characteristics or laboratory parameters were assessed by Pearson or Spearman correlation tests. To assess the association between the GRACE score or TIMI risk score and the SYNTAX score, some analyses were used. First, the linear associa-

tion of each risk score with the SYNTAX score was assessed by use of Pearson's correlation test. Second, ANOVA with the post-hoc Tukey test was used to compare SYNTAX score values between low-, intermediate-, and high-risk groups based on the GRACE risk score for death in the hospital and the TIMI risk score. Third, the receiver-operating characteristics (ROC) curve was used to test the predictive accuracy of the risk scores with respect to the presence of high risk (>33) or low risk (<22) based on the SYNTAX score. Significant prediction was accepted when the area under the ROC curve was significantly different from 0.5. A p value <0.05 was accepted as statistically significant. All analyses were performed with SPSS 17.0 for Windows.

RESULTS

We assessed 145 patients (mean age 59.41±11.04 years, 29% female) for the study. During hospitalization, 66 (45.5%) patients underwent PCI, 10 (6.9%) patients underwent CABG, and only one (0.7%) patient died because of cardiogenic shock. Clinical characteristics and laboratory values of the study population are presented in the Table 1.

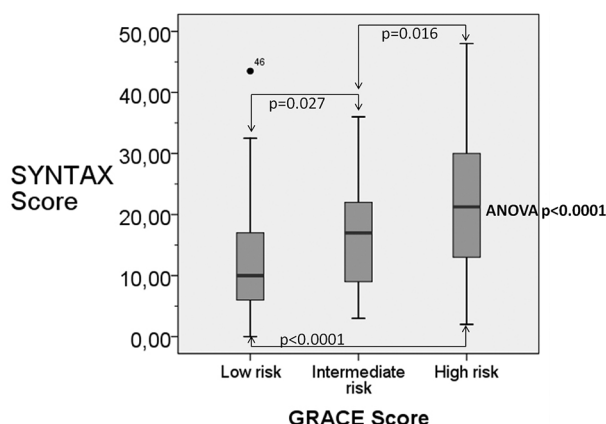


Figure 1. The comparison of SYNTAX score between risk groups based on the GRACE score.

Based on the GRACE score for in-hospital deaths, 62 (42.8%) patients were included in the low-risk (1-108) group, 53 (36.6%) in the intermediate-risk (109-140) group, and 30 (20.7%) in the high-risk (141-372) group. The mean TIMI risk score of the study population was 3.58±1.20. Based on the TIMI risk score, 27 (18.6%) patients were

in the low-risk (0-2) group, 86 (59.3%) were in the intermediate-risk (3-4) group, and 24 (16.6%) were in the high-risk (>5) group.

Table 1. Demographic and Clinical Characteristics and Laboratory Values of the Study Group

	Study group (n=145)
Age, years	59.41 ± 11.04
Female, n (%)	42 (29.0)
Diabetes mellitus, n (%)	40 (27.6)
Hypertension, n (%)	79 (54.5)
Hypercholesterolemia, n (%)	47 (32.4)
Smoking, n (%)	66 (45.5)
Family history, n (%)	31 (21.4)
CAD history, n (%)	36 (24.8)
PCI in hospital, n (%)	66 (45.5)
CABG in hospital, n (%)	10 (6.9)
Laboratory values	
Basal creatinine, mg/dL	0.94 ± 0.31
eGFR, mL/min/1.73 m ²	82.48 ± 24.67
BUN, mg/dL	18.40 ± 11.44
Glucose, mg/dL	136.13 ± 63.77
Total cholesterol, mg/dL	196.23 ± 46.30
LDL, mg/dL	129.17 ± 39.22
HDL, mg/dL	39.33 ± 9.48
Triglyceride, mg/dL	187.23 ± 99.62
Troponin T,	1.17 ± 1.80
CK-MB,	37.64 ± 62.67
WBC, × 10 ³ /μl	9.51 ± 2.95
Hemoglobin, g/dl	13.63 ± 2.19
Platelet count, × 10 ³ /μl	266.25 ± 79.73
MPV, fL	8.56 ± 0.93

CAD, coronary artery disease; PCI, percutaneous coronary intervention; CABG, coronary artery by-pass grafting; eGFR, estimated glomerular filtration rate; BUN, blood urea nitrogen; LDL, low density lipoprotein; HDL, high density lipoprotein; CK-MB, creatinine kinase-myocardial band; WBC, white blood cell; MPV, mean platelet volume.

The analysis of coronary angiography showed that the mean SYNTAX score of the study population was 15.97±9.82. When the patients were divided into the risk groups based on the intervals given in the original paper, 5112 patients (77.2%) were in the low-risk (<22) group, 24 (16.6%) were in the intermediate-risk (22-33) group, and 9 (6.2%) were in the high-risk (>33) group.

Based on the GRACE risk score for in-hospital deaths, the SYNTAX risk score was 12.22 ± 8.70 in the low-risk group, 16.66 ± 8.01 in the intermediate-risk group, and 22.48 ± 11.42 in high-risk group (ANOVA, $p < 0.0001$) (Figure 1). Post-hoc Tukey analysis showed that the low-risk group had a significantly lower SYNTAX score than the intermediate- and high-risk groups ($p = 0.027$ versus $p < 0.0001$, respectively). The SYNTAX score of the intermediate-risk group was also significantly different from the SYNTAX score of the high-risk group ($p = 0.016$). Based on the TIMI risk score, the SYNTAX risk score was 12.87 ± 9.91 in the low-risk group, 16.01 ± 10.38 in the intermediate-risk group, and 18.48 ± 7.47 in the high-risk group. The difference between the risk groups did not reach statistical significance (ANOVA, $p = 0.091$).

There were significant positive correlations between the SYNTAX score and GRACE scores of the study population calculated at admission for in-hospital deaths ($r = 0.414$, $p < 0.0001$) (Figure 2). The SYNTAX score also had a significant but weaker correlation with the TIMI score ($r = 0.271$, $p = 0.001$).

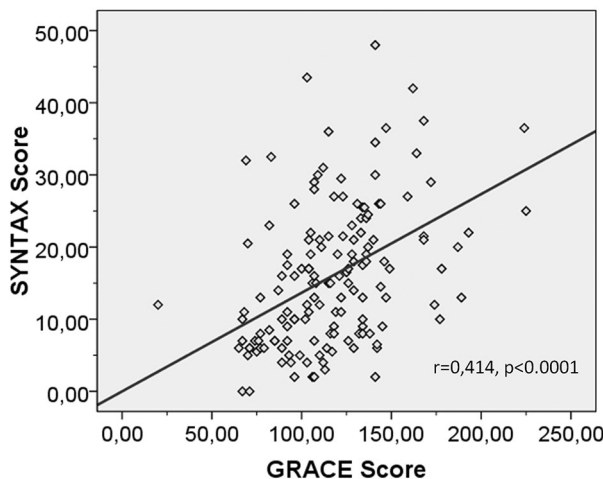


Figure 2. The correlation between the GRACE score and the SYNTAX score.

The GRACE score of the study population calculated at admission for in-hospital deaths showed good discriminatory capacity between the patients with and without a high-risk (>33) SYNTAX score, with an area under the ROC curve of 0.804 (CI 0.660-0.948, $p = 0.002$) (Figure 3). The GRACE score of the study population showed poor predic-

tive capacity between the patients with and without a low-risk (<22) SYNTAX score, with areas under the ROC curve of 0.695 (CI 0.594-0.796, $p = 0.001$) (Figure 4). The TIMI score of the study population showed no predictive capacity between the patients with and without a high-risk (>33) SYNTAX score and with and without a low-risk (<22) SYNTAX score. Areas under the ROC curve were 0.532 (CI 0.358-0.749, $p = 0.749$) and 0.582 (CI 0.473-0.691, $p = 0.152$), respectively (Figures 3 and 4).

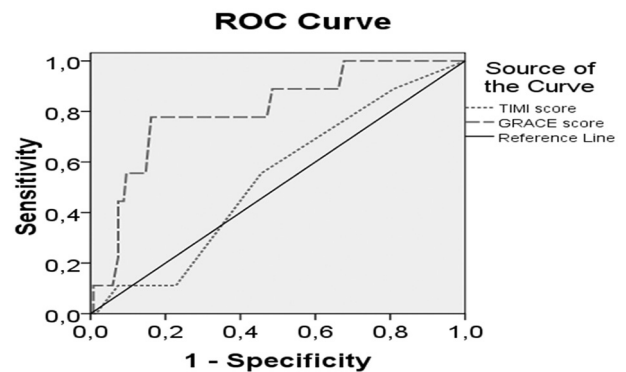


Figure 3. The ROC curves of the GRACE and TIMI scores for detecting high risk (>33) SYNTAX score (the area under the ROC curve of 0.804 [CI 0.660-0.948, $p = 0.002$] for GRACE score and the area under the ROC curve of 0.532 (CI 0.358-0.749, $p = 0.749$) for TIMI score)].

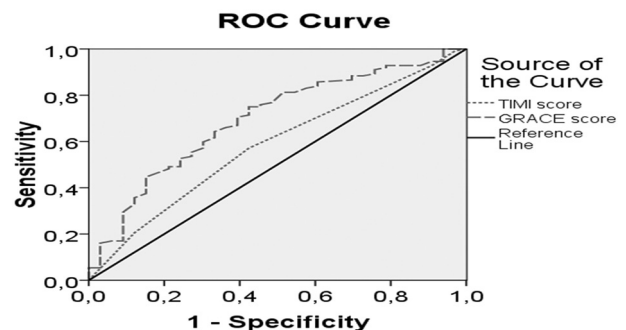


Figure 4. The ROC curves of the GRACE and TIMI scores for detecting low risk (<22) SYNTAX score (the area under the ROC curve of 0.695 (CI 0.594-0.796, $p = 0.001$) for GRACE score and the area under the ROC curve of 0.582 (CI 0.473-0.691, $p = 0.152$) for TIMI score).

DISCUSSION

Our study results indicated that the TIMI score is of no use in predicting severe extended CAD, whereas the relationship between the GRACE and SYNTAX scores may have some clinical implications.

In contrast to the reports of Garcia et al. and Mega et al. [9,10], the TIMI risk score, with its weak association to the SYNTAX score, does not appear to be a good candidate in predicting the extension and severity of CAD. From our point of view, these contradictory results can be explained as follows. First, a positive association does not mean accuracy, which should be assessed by tests of calibration and discriminatory capacity of extended severe disease versus non-severe disease. Although a statistically significant association was observed, the TIMI score was not able to differentiate between SYNTAX score risk tertiles (ANOVA, $p=0.091$). The area under the ROC curve of the TIMI score was not statistically significant either. Second, the definition of multivessel disease that was used for extended severe CAD in the above mentioned studies, which was described as a quantitative variable (SYNTAX score) in our study, is another reason for the discrepancy with our results [9,10]. Barbosa et al. [11] used another quantitative variable for measuring the severe extension of CAD, namely the Gensini score, and stated the same results as ours with respect to the TIMI score.

The GRACE score has shown a greater prognostic value as compared with that of the TIMI score [2,9]. This greater prognostic value was translated into a better discriminatory capacity in our study. The area under the ROC curve of the GRACE score in our study population showed good discriminatory capacity between the patients with and without a high-risk (>33) SYNTAX score. This result may have a clinical implication. The latest ESC guideline of 2011 recommends an early invasive strategy (<24 hours) in NSTMI patients of high risk (GRACE score >140) [12]. This guideline also states that “the revascularization strategy should be based on the clinical status as well as the SYNTAX score” [11]. A SYNTAX score ≥ 33 also includes left main patients in whom CABG is the only treatment option [13-15]. Based on our results, patients with a GRACE score of >140 have a good possibility of achieving a SYNTAX score ≥ 33 . Therefore, we speculate that these patients should not be given clopidogrel, at least not before angiography is performed.

In conclusion, a GRACE score indicating a high risk may be helpful in predicting patients with

severe extended CAD in whom CABG is the only treatment modality.

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