

ORIGINAL ARTICLE

THE PREDICTIVE UTILITY OF GRACE SCORE FOR OBSTRUCTIVE CORONARY ARTERY DISEASE IN PATIENTS WITH NON ST ELEVATION MYOCARDIAL INFARCTION

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Objectives: The objective of this study was to determine the predictive value of GRACE score for predicting obstructive coronary artery disease in patients with non ST-segment elevation myocardial infarction (NSTEMI).

Methodology: This cross-sectional study was conducted at the largest public sector cardiac care center of the Pakistan between January 2020 and June 2020. In this study, we included adult patients diagnosed with NSTEMI and correlation of GRACE score was assessed with angiographic finding of obstructive CAD defined as $\geq 50\%$ stenosis in the left main or $\geq 70\%$ stenosis in other coronary arteries.

Results: A total of 227 patients were included in this study, out of whom 72.2% (164) were male patients and mean age was 55.77 ± 9.15 years. Mean GRACE score was found to be 95.89 ± 21.15 . On coronary angiography obstructive CAD was present in 84.6% (192) of the patients. Area under the curve for predicting obstructive CAD was 0.669 [0.552 to 0.785]. The optimal cutoff value of GRACE score was ≥ 84 with sensitivity of 79.7% [73.3% to 85.1%] and specificity of 57.1% [39.3% to 73.7%]. GRACE score of ≥ 84 was found to be an independent predictor of obstructive CAD with odds ratio of 4.33 [1.61 - 11.64; $p=0.004$] adjusted for gender, age, hypertension, diabetes, family history of CAD, and smoking.

Conclusion: GRACE score has a moderate predictive value in predicting obstructive CAD in patients with NSTEMI. The optimal cutoff value of 84 is an independent predictor with good sensitivity but moderate specificity in predicting obstructive CAD.

Keywords: coronary artery disease, acute myocardial infarction, non ST-segment elevation myocardial infarction, GRACE score, risk stratification, obstructive coronary artery disease

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INTRODUCTION

Coronary artery disease (CAD) is among leading causes of premature life losses around the world. Acute coronary syndrome (ACS) is the most common clinical manifestation of CAD comprises of acute myocardial infarction (AMI), with and without ST segment elevation, and unstable angina pectoris. ACS consisted of patients with heterogeneous clinical spectrum with substantially varying outcomes and hospital course. Hence, management guidelines recommend risk stratification at individualized level to determine the prognosis and to optimize the planning and management of the patients.¹

Effective risk stratification of ACS patients, especially non ST-segment elevation myocardial infarction (NSTEMI), has become the cornerstone of management of the patients considering the varying prognosis and increased risk of re-hospitalization due to recurrence of myocardial infarction (MI). Various

risk stratification modalities have been proposed notably Global Registry of Acute Coronary Events (GRACE) score, Framingham Risk score, and Thrombolysis in Myocardial Infarction (TIMI) score.¹ Both European and American clinical practice guidelines endorse use of either TIMI or GRACE score for risk stratification of short- and mid-term outcome of these patients.²⁻⁴ However, clinical evidence and literature is very limited regarding use of these scores for the prediction of the extent and severity of CAD. A reliable prediction of coronary anatomy before any invasive assessment, such as coronary angiography, can have great implications in clinical decision making regarding timing and intensity of therapeutic management as well as interventions. Such strategy can help us in identifying patients requiring more aggressive management to improve outcomes or, conversely, to avoid unnecessary invasive procedures in patients with non-obstructive CAD.

Although GRACE risk score is an important and validated modality for assessing prognosis but clinical evidence regarding its predictive utility for discriminating anatomical extent of CAD is scarce. Therefore, aim of this study was to determine the predictive value of GRACE score for predicting obstructive coronary artery disease in patients with non ST-segment elevation myocardial infarction (NSTEMI).

METHODOLOGY

This cross-sectional study was conducted at the largest public sector cardiac care center of the Pakistan between January 2020 and June 2020. Required number of consecutive patients fulfilling the inclusion criteria were included in this study. Consent for participation was obtained from all the patients and approval for the study was obtained from the ethical review committee of the institution. Inclusion criteria for the study were adult patients of either gender, between 18 to 80 years of age, diagnosed with non-ST segment elevation myocardial infarction (NSTEMI), and undergone coronary angiography. Patients who refused to participate in the study, patients with prior history of cardiac related surgery or intervention, previously diagnosed with obstructive coronary artery disease (CAD), current diagnosis of ST-elevation myocardial infarction (STEMI) or new left bundle branch block, and patients with chest pain of proven non-ischemic etiology (such as takotsubo syndrome or myocarditis) were excluded from the study.

Diagnosis of NSTEMI was made based on history, presentation, ECG findings, and cardiac enzymes. Demographic details and information regarding pre-existing co-morbid conditions were obtained for all the patients. Global Registry for Acute Coronary Events (GRACE) score (2.0) was calculated based on age, heart rate, systolic blood pressure, Killip class, cardiac arrest, ST-segment deviation, serum creatinine, and initial cardiac biomarker status available at <https://www.mdcalc.com/grace-acs-risk-mortality-calculator>. All the patients underwent routine coronary angiography and all the procedures were performed and interpreted by the consultant cardiologist. Obstructive CAD was defined as $\geq 50\%$ stenosis in the left main or $\geq 70\%$ stenosis in other coronary arteries. Routine management was unaltered and all the patients received management as per the guidelines and institutional protocol. Data were collected on a pre-defined structured proforma.

Sample size for the study was calculated considering the expected AUC of 0.59⁵ for GRACE score to predict obstructive coronary artery disease at 95%

confidence level and 6% margin of error. The minimum required sample size was calculated to be $n=167$. Data analysis were performed with the help of IBM SPSS version 21. Data points were summarized with appropriate summary statistics such as mean \pm standard deviation (SD) or frequency (%). The predictive utility of GRACE score was assessed by performing the receiver operating characteristic (ROC) curves analysis taken GRACE score as test variable and dichotomous variable of presence or absence of obstructive CAD as state variable. Area under the curve (AUC) along with 95% confidence interval (CI) were computed and prediction value of GRACE score was deemed to be significant when the AUC was statistically different from 0.5. The optimal cutoff value of GRACE score for the prediction of obstructive CAD was obtained using Youden's index and accuracy, sensitivity, specificity, positive predictive value, and negative predictive value at the computed cutoff value were calculated. Multivariate binary logistic regression analysis was performed taken dichotomous variable of presence or absence of obstructive CAD as dependent variable and demographic characteristics, co-morbid conditions and GRACE score as independent variables. Odds ratio (OR) along with 95% CI was reported and p -value ≤ 0.05 was taken as significance criteria throughout the analysis.

RESULTS

A total of 227 patients were included in this study, out of whom 72.2% (164) were male patients and mean age was 55.77 ± 9.15 years. Most of the patients (90.7%) were in Killip class I at presentation, there were only four patients (1.8%) were in Killip class III and no patient was in Killip class IV. Most common pre-existing co-morbid condition was hypertension (84.6%) followed by diabetes mellitus (39.6%). Mean GRACE score was found to be 95.89 ± 21.15 . Demographic and clinical characteristics are presented in Table 1.

Table 1: Demographic and clinical characteristics

Characteristics	Total
Total (N)	227
Gender	
Male	72.2% (164)
Female	27.8% (63)
Age (years)	55.77 \pm 9.15
≤ 50 years	34.4% (78)
51 to 70 years	59.9% (136)
> 70 years	5.7% (13)
Height (cm)	153.03 \pm 45.09
Weight (kg)	71.95 \pm 11.21
KILLIP Class	

I	90.7% (206)
II	7.5% (17)
III	1.8% (4)
IV	0% (0)
Heart rate (bpm)	82.06 ± 13.08
Systolic blood pressure (mmHg)	134.42 ± 16.62
Serum creatinine (ng/dL)	1.04 ± 0.31
Risk factors	
Hypertension	84.6% (192)
Diabetes	39.6% (90)
Family history of CAD	10.1% (23)
Smoking	18.5% (42)
Obesity	7.9% (18)
GRACE Score	95.89 ± 21.15

CAD = coronary artery diseases

On coronary angiography obstructive CAD was present in 84.6% (192) of the patients out of which 25.5% (49) had single vessel disease, 28.1% (54) had two vessel disease, and 46.4% (89) had three vessel disease. The ROC analysis (Figure 1) revealed significant predictive value of the GRACE score for predicting obstructive CAD with AUC of 0.669 [95% CI; 0.552 to 0.785]. The optimal cutoff value of GRACE score was computed to be ≥ 84 with overall all accuracy of 76.2% [95% CI; 70.1% to 81.6%] in discriminating obstructive CAD with sensitivity of 79.7% [95% CI; 73.3% to 85.1%] and specificity of 57.1% [95% CI; 39.3% to 73.7%]. Angiographic findings and diagnostic accuracy of GRACE score at the calculated optimal cutoff value are presented in Table 2.

Table 2: Angiographic findings and diagnostic accuracy of GRACE score

	Total	GRACE Score		P-value
		< 84	≥ 84	
Total (N)	227	59	168	-
Obstructive CAD				
No	15.4% (35)	33.9% (20)	8.9% (15)	<0.001*
Yes	84.6% (192)	66.1% (39)	91.1% (153)	
Number of vessels involved				
Single vessel	25.5% (49)	33.3% (13)	23.5% (36)	0.454
Two vessels	28.1% (54)	25.6% (10)	28.8% (44)	
Three vessels	46.4% (89)	41% (16)	47.7% (73)	
Left main involvement	12% (23)	15.4% (6)	11.1% (17)	0.463
Diagnostic accuracy assessment for obstructive CAD				
Accuracy	76.2% [95% CI; 70.1% to 81.6%]			
Sensitivity	79.7% [95% CI; 73.3% to 85.1%]			
Specificity	57.1% [95% CI; 39.3% to 73.7%]			
Positive Predictive Value	91.1% [95% CI; 87.4% to 93.8%]			
Negative Predictive Value	33.9% [95% CI; 25.6% to 43.4%]			

CAD = coronary artery diseases, CI = confidence interval

*significant at 5%

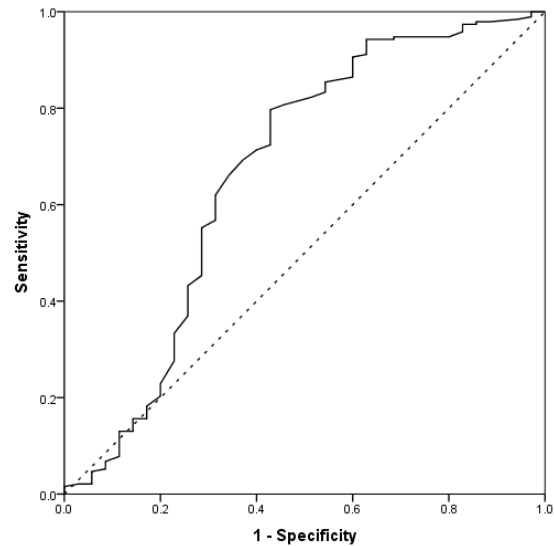


Figure 1: ROC curve analysis of GRACE score for obstructive CAD

AUC = 0.669 [0.552 to 0.785]; p=0.001

The optimal cut-off value based on Youden's index in ≥ 84

GRACE score of ≥ 84 was found to be an independent predictor of obstructive CAD with odds ratio of 4.33 [95% CI: 1.61 - 11.64; p=0.004] adjusted for gender, age (years), hypertension, diabetes mellitus, family history of CAD, and smoking. Multivariate binary logistic regression analysis for obstructive CAD is presented in Table 3.

Table 2: Multivariate binary logistic regression analysis for obstructive CAD

Parameter	Odds Ratio (OR)	95% CI	P-value
Male	1.12	0.46 - 2.69	0.805
Age (years)	1.01	0.96 - 1.06	0.686
Hypertension	4.3	1.44 - 12.88	0.009*
Diabetes Mellitus	3.36	1.25 - 9.03	0.016*
Positive Family History of CAD	1.56	0.32 - 7.63	0.583
Smoking	9.27	1.75 - 49.16	0.009*
GRACE score ≥ 84	4.33	1.61 - 11.64	0.004*
Constant	0.18	-	0.212

CAD = coronary artery diseases, CI = confidence interval

*significant at 5%

DISCUSSION

This study was conducted with the aim of assessing the predictive value of GRACE score for predicting obstructive CAD in patients with NSTEMI and it was observed that GRACE score showed moderate accuracy in discriminating obstructive CAD with AUC of 0.669 [95% CI: 0.552 to 0.785; p=0.001]. The optimal cutoff vale of GRACE score was determined to be ≥ 84 , which was found to be an independent

predictor of obstructive CAD with good sensitivity of 79.7% and moderate specificity of 57.1%. Various studies have observed the similar association between GRACE score and extent of CAD in full spectrum of ACS and also specific to the NSTEMI patients.

A study conducted by Roy SS et al.⁶ included 205 patients with NSTEMI and reported positive correlation between GRACE score and severity of CAD, furthermore, study reported superiority of GRACE score over TIMI score in predicting severity of CAD. Similar finding of superiority of GRACE score over TIMI score has been reported in a comparative study of both the scores for predicting the severity of CAD in another study conducted by Roy SS et al.⁷ Hammami R et al.⁵ reported their observations from the study of 238 consecutive NSTEMI patients regarding relationship between GRACE score and extent of CAD, a moderate accuracy in predicting obstructed CAD has been reported with AUC of 0.599 and GRACE score has sensitivity of 57% and specificity of 61.8% at the cutoff value of 120. However, weak association was observed between the score and severity of CAD, hence, conclusion was made that the score has better predictive power in discriminating obstructive CAD but not severity of CAD. Rahman ME et al.⁸ conducted a study of 50 NSTEMI patients and reported positive and significant relationship between GRACE score and coronary artery stenosis. Further at the cutoff value of 135, GRACE score was reported to have sensitive of 82.4% and specificity of 75.8% in predicting severe CAD. Similarly, Cakar MA et al.⁹ in their study tertiles 245 NSTEMI patients to low-, intermediate-, and high risk groups and reported significant association of GRACE score with severity and extent of coronary artery stenosis.

A study conducted by Mahmood M et al.¹⁰ in our local population also reported good predictive value of GRACE and TIMI score in predicting the extent of the disease, however, this study also claimed superiority of GRACE score over TIMI score. Various other studies in the spectrum of acute coronary syndrome had similar observations.^{1,11-13} However, one of the largest study in this context so far by dos Santos Viana M et al.¹⁴ have argued the association of GRACE score with extent of anatomical coronary disease before angiogram, study included a total of 733 patients out of which 81% had obstructive CAD and reported AUC for GRACE score was 0.65 for predicting severe disease and at the cutoff value of 103 it has 67% and 50% sensitivity and specificity, further, GRACE score was reported to have weak correlation of 0.36 with SYNTAX score. Therefore, role of GRACE score was recommended to limit to prognostic assessments.

Single center experience and relatively smaller sample size are the key limitations of this study, furthermore, study objective was specific to assessment of utility of GRACE score for predicting presence of obstructive CAD only, therefore, no conclusion could be drawn regarding the relationship of GRACE score and severity of CAD.

CONCLUSION

GRACE score has a moderate predictive value in predicting obstructive CAD in patients with NSTEMI. The optimal cut-off value of 84 is an independent predictor with good sensitivity but moderate specificity in predicting obstructive CAD. Hence, this score can be used as a screening tool but its clinical utility for predicting extent of CAD is limited.

AUTHORS' CONTRIBUTION

HI, TS, and MK: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. BA, MK, GSS, AH, and SM: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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