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ORIGINAL ARTICLE – OPEN ACCESS

The Prognostic Value of the GRACE Score for Acute Kidney Injury in Patients with ST Elevation Myocardial Infarction Complicated with Cardiogenic Shock

Mert İlker Hayıroğlu[1], Tufan Çınar[1], Ahmet İlker Tekkeşin[2]

ABSTRACT

Objective: The Global Registry of Acute Coronary Events (GRACE) risk score has been proposed in predicting short-term death in patients who are diagnosed with acute coronary syndrome. The aim of the present study was to investigate the significance of the GRACE score for acute kidney injury (AKI) in patients with cardiogenic shock (CS)–ST elevation myocardial infarction (STEMI) who were treated with primary percutaneous coronary intervention (PPCI).

Materials and Methods: We retrospectively examined a total of 492 consecutive patients with CS–STEMI who had undergone PPCI. The GRACE score was calculated for each patient. Patients were stratified by tertiles (T1, T2, and T3) according to the GRACE score, and the incidence of AKI was compared between the groups.

Results: In univariate analysis, the incidence of AKI was significantly higher for patients allocated into the T3 group than for patients in the T1 group (odds ratio (OR) 2.8, 95% confidence interval (CI) 1.8–4.1, p<0.001). Following including all confounding variables, participants in the T3 group had a 3.1-fold higher incidence of AKI (OR 3.1, 95% CI 1.9–5.4, p<0.001). In a receiver operating characteristic curve analysis, the GRACE score of the area under the curve value for AKI was 0.70 (95% CI 0.65–0.74, p<0.001) with 69.2% sensitivity and 68.8% specificity.

Conclusion: The GRACE score provides an independent prognostic marker of AKI in patients with CS related with STEMI. Based on our data, we propose that the GRACE score is a simple and clinically applicable directive tool for rapid risk stratification of AKI in patients with STEMI complicated with CS.

Keywords: GRACE, acute kidney injury, prognostic value, cardiogenic shock

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[1]Department of Cardiology, Health Sciences University, Sultan Abdülhamid Han Training and Research Hospital, İstanbul, Turkey
[2]Department of Cardiology, Health Sciences University, Siyami Ersek Training and Research Hospital, İstanbul, Turkey

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Correspondence Tufan Çınar, Department of Cardiology, Health Sciences University, Sultan Abdülhamid Han Training and Research Hospital, İstanbul, Turkey
Phone: +90 216 542 20 20
e-mail: drtufancinar@gmail.com

INTRODUCTION

Acute kidney injury (AKI) is an acute medical emergency that is associated with significant morbidity and mortality in patients with acute coronary syndrome (ACS) (1). Principally, patients presenting with cardiogenic shock (CS) have a higher risk of AKI due to the inability of the left ventricle to supply an adequate blood flow to the kidneys (2). Prior studies demonstrated that some risk factors, such as chronic renal failure, elderliness, and hemodynamic status upon admission, are independent predictors of AKI in patients with CS (3, 4). Although tissue hypoperfusion and venous congestion are the main underlying pathophysiologic mechanisms of the worsening of renal function among these patients, other mechanisms, such as the increase in systemic inflammatory response and the activation of neurohormonal responses, may also play a significant role (5). Since patients presenting with CS often have higher mortality rates, the deterioration of renal functions in this condition may further aggravate the cardiac damage that is responsible for the higher incidence of death (6). Hence, an early recognition to initiate some therapeutic modalities including early continuous renal replacement therapy or mechanical circulatory support may improve survival among these patients (7, 8).

The Global Registry of Acute Coronary Events (GRACE) score is a guideline-based risk calculator that has been proven to be useful to determine the risk of in-hospital and short-term deaths in patients diagnosed with ACS (9, 10). It estimates the risk of death using some clinical variables, such as age, Killip class examination findings, and serum creatinine upon admission. As previously mentioned, some components of the GRACE score have been found to be related to the occurrence of AKI in patients with CS. Therefore, we hypothesized that the GRACE score may have an appreciable value for the occurrence of AKI in patients presenting with CS secondary to ST elevation myocardial infarction (STEMI).

MATERIALS and METHODS

A total of 492 consecutive patients with CS–STEMI who were treated with primary percutaneous coronary intervention from January 2013 to January 2017 in a tertiary heart center were included in this retrospective

study. Patients aged <18 years and pregnant, having been treated with thrombolytic drugs, with active infection(s) and malignancy, and having undergone emergency aorta coronary bypass grafting were excluded from the study. In addition, patients who died within 24 h following admission were excluded. Patient's baseline demographic characteristics and laboratory findings from the hospital's electronic database were collected. All of the patients received the standard medical therapy according to the current guidelines. The GRACE score was calculated for each patient using an online calculator. In the GRACE score, age, heart rate, systolic blood pressure, creatinine, cardiac arrest at admission, ST segment deviation on electrocardiography, abnormal cardiac enzymes, and Killip class were noted. The study was approved by the ethics committee of Haydarpasa Numune Training and Research Hospital (date 8/4/2019, no. HNEAH-KAEK 2019/KK/46) in accordance with the principles of the Declaration of Helsinki. There was no need for written informed consent due to the retrospective design of the study, and it was not obtained.

In all of the patients, venous samples were collected at admission to the emergency department. A Coulter LH 780 hematology analyzer (Beckman Coulter Inc., Brea, CA, USA) was used to evaluate all basic hematologic parameters. Biochemical measurements were performed using Siemens kit and calibrators (Siemens Healthcare Diagnostic GmbH, Marburg, Germany). All of the patients underwent a detailed echocardiographic examination by a trained cardiologist. The Simpson method was used to estimate the left ventricle ejection fraction (LVEF).

All coronary angiographies were performed by experienced interventional cardiologists via the femoral artery within 90 min. All of the patients received the standard antiplatelet regimen of 300 mg acetylsalicylic acid along with a loading dose of either 300–600 mg clopidogrel or 180 mg of ticagrelor before the procedure. In accordance with hospital protocol, the choice of infusion of glycoprotein IIb/IIIa inhibitors and the use of either a drug-eluting stent or a bare metal stent were left to the operator's discretion. In case of a high coronary thrombus burden, manual thrombectomy was not mandatory as per hospital protocol. In all procedures, a nonionic, iso-osmolar, contrast material was used.

STEMI was defined using the universal definition provided in the myocardial infarction guideline of the European Society of Cardiology (11). CS was accepted as a systolic blood pressure of <90 mm Hg that was not responsive to fluid and/or inotropic resuscitation or a systolic blood pressure drop ≥40 mm Hg for >15 min without new-onset arrhythmia, hypovolemia, or sepsis (12). Dopamine infusion was the first treatment option in CS in our department, and noradrenalin infusion was concomitantly started if hemodynamic collapse did not solely recover with dopamine infusion. AKI was accepted as an increase of serum creatinine level ≥0.5 mg/dL or 25% increase of serum creatinine from baseline within 48 h following the contrast administration (13). The Modification of Diet in Renal Disease equation was used to determine the estimated glomerular filtration rate (GFR). Chronic kidney disease was defined as decreased kidney function as shown by a GFR of <60 mL/min/1.73 m^2 or markers of kidney damage or both of at least 3 months duration, regardless of the underlying cause (14).

IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Chicago, IL, USA) was used for statistical analysis. First, the study population was sectioned into three tertiles (T1, T2, and T3) based on the GRACE score. The Kolmogorov–Smirnov test was used to assess the distribution pattern. Continuous variables with normal distribution were analyzed using the variance test. Continuous variables with normal distribution were expressed as mean±standard deviation. Categorical data were expressed as number of cases and percentages. The Fisher's exact test or χ^2 test was used to compare the categorical parameters. The ANOVA test was performed to compare the groups. As a posthoc analysis, Tukey's method was preferred. The odds ratio assessed the relative risk of AKI of the T3 group compared with the T1 and the T2 groups. Multiple binary logistic regression was performed for multiple analyses. Multiple models included all relevant confounders in multiple analyses as predictors of AKI. Model I was unadjusted, and model II was adjusted for all confounders. The goodness-of-fit test presented adequate calibration for model II (Hosmer–Lemeshow goodness-of-fit=9.176, p=0.328). The variables included in model II were gender, hypertension, diabetes mellitus, hyperlipidemia, smoking, chronic renal failure, previous cerebrovascular accident, myocardial infarction, PCI, peripheral artery disease (PAD), chronic obstructive pulmonary disease (COPD), atrial fibrillation, anterior myocardial infraction, culprit artery, type of stent, multivessel intervention, thrombus aspiration, laboratory parameters including baseline serum creatinine, blood urea nitrogen, and hemoglobin, and echocardiographic parameters including LVEF, left ventricular diastolic diameter, left ventricle systolic diameter, pulmonary artery systolic pressure, and tricuspid annular plane systolic excursion. A receiver operating characteristic (ROC) curve analysis was utilized to determine the optimal value of the GRACE score for predicting AKI. A two-tailed p value of <0.05 was considered as statistically significant.

RESULTS

The mean age of the study population was 69±13 years, and a total of 185 (37.6%) patients were female. Baseline demographic features and interventional data of all patients are depicted in Table 1. The frequency of diabetes mellitus, hyperlipidemia, current smoker, previous cerebrovascular accident, myocardial infarction, PCI, PAD, COPD, cardiopulmonary arrest at admission, and anterior myocardial infarction was not different between the groups (p>0.05 for each). In contrast, the frequency of hypertension, chronic renal failure, and atrial fibrillation was significantly elevated in patients allocated into the T3 group (p<0.05 for each). The groups were indifferent with respect to systolic arterial pressure and heart rate upon admission (p>0.05 for each). The right coronary artery as the infarct-related artery and multivessel involvement were significantly elevated in patients in the T3 group (p<0.05 for each). The choice of drug-eluting stent was more common in high GRACE score patients. The mean GRACE score was 171.8±13.8 for the T1 group, whereas it was 201.5±6.2 and 222.0±7.5 for the T2 and T3 groups, respectively (p<0.001 for comparison of each group).

Laboratory and echocardiographic findings of each group are shown in Table 2. Comparison of echocardiographic parameters did not differ between the groups (p>0.05 for each). Patients in the T3 group had lower hemoglobin levels and higher creatinine

Table 1. Baseline demographic characteristics and angiographic data of all patients

	GRACE score						p
	T1 (n=164)		T2 (n=164)		T3 (n=164)		
	n	%	n	%	n	%	
Age, years	60±12		68±9		76±10		<0.001
Male gender	112	68.3	100	61.0	95	57.9	0.138
Hypertension	63	38.4	82	50.0	89	54.3	0.012
Diabetes mellitus	46	28.0	65	39.6	54	32.9	0.083
Hyperlipidemia	41	25.0	36	22.0	39	23.1	0.807
Current smoker	65	39.6	56	34.1	52	31.7	0.306
Chronic renal failure	20	12.2	20	12.2	45	27.4	<0.001
Previous CVA	7	4.3	5	3.0	8	4.9	0.694
Previous MI	27	16.5	22	13.4	36	22.0	0.117
Previous PCI	37	22.6	36	22.0	40	24.4	0.861
PAD	10	6.1	12	7.3	8	4.9	0.653
COPD	7	4.3	10	6.1	14	8.5	0.280
CPA	39	23.8	35	21.3	53	32.3	0.058
Atrial fibrillation	20	12.2	14	8.5	6	3.7	0.018
Anterior MI	99	60.4	95	57.9	113	68.9	0.098
At admission							
Systolic blood pressure, mmHg	70.4±10.0		69.9±9.4		70.1±9.5		0.843
Heart rate, beats per minute	91.1±21.4		91.8±20.2		96.7±20.7		0.178
Culprit artery							
LMCA	7	4.3	9	5.5	7	4.3	0.833
LAD	92	56.1	86	52.4	106	64.6	0.072
CX	22	13.4	16	9.8	20	12.2	0.579
RCA	50	30.5	62	37.8	38	23.2	0.016
Additional ≥70% stenosis to culprit artery							
LAD and/or branches	70	42.7	75	45.7	53	32.3	0.034
CX and/or branches	84	51.2	81	49.4	82	50.0	0.945
RCA and/or branches	58	35.4	56	34.1	62	37.8	0.781
Intervened coronary artery							
LMCA	7	4.3	6	3.7	6	3.7	0.947
LAD	79	48.2	69	42.1	78	47.6	0.912
CX	18	11.0	7	4.3	16	9.8	0.065
RCA	41	25.0	47	28.7	31	18.9	0.114
Multivessel	19	11.6	35	21.3	33	20.1	0.041
PTCA	130	79.3	120	73.2	116	70.7	0.189
Stent (DES)	141	86.0	147	89.6	131	79.9	0.043
Stent number >1	49	29.9	51	31.1	50	30.5	0.972
Non-compliant balloon usage	66	40.2	66	40.2	66	40.2	1.000
Thrombus aspiration	7	4.3	8	4.9	16	9.8	0.081
Tirofiban usage	72	43.9	73	44.5	83	50.6	0.404
GRACE score	171.8±13.8		201.5±6.2		222.0±7.5		<0.001
Acute kidney injury	52	31.7	84	51.2	109	66.5	<0.001

Continuous variables are presented as mean±SD, nominal variables presented as frequency (%). CVA: Indicates cerebrovascular accident; PAD: Peripheral arterial disease; COPD: Chronic obstructive pulmonary disease; CPA: CardioPulmonary arrest; MI: Myocardial infarction; LMCA: Left main coronary artery; LAD: Left anterior descending artery; CX: Circumflex artery; RCA: Right coronary artery; PTCA: Percutaneous transluminal coronary angioplasty; DES: Drug eluting stent; PCI: Percutaneous coronary intervention; GRACE: Global registry of acute coronary events

Table 2. Echocardiographic and laboratory findings of all patients

	GRACE score			
	T1 (n=164)	T2 (n=164)	T3 (n=164)	p
LVEF, %	33.0±10.0	31.9±8.9	31.5±10.0	0.105
LVEDD, cm	5.38±0.46	5.37±0.46	5.47±0.53	0.061
LVESD, cm	4.17±0.62	4.19±0.58	4.33±0.71	0.050
PASP, mmHg	26.9±8.1	26.1±7.3	28.8±10.0	0.153
Tapse, cm	1.82±0.26	1.76±0.23	1.76±0.20	0.051
MR ≥+3, n (%)	27 (16.5)	22 (13.4)	31 (18.9)	0.402
TR ≥+3, n (%)	6 (3.7)	10 (6.1)	14 (8.5)	0.182
Hemoglobin, g/dL	13.4±2.8	12.5±2.0	12.2±1.8	<0.001
Leucocyte, x10^3/µ/L	16.2±6.3	15.6±5.4	15.2±5.0	0.719
Platelet, x10^3/µ/L	256.1±87.5	256.7±94.6	248.4±100.1	0.447
Glucose, mg/dL	127.7±42.2	130.6±40.3	131.2±49.0	0.629
Creatinine, mg/dL	1.11±0.33	1.13±0.48	1.27±0.60	0.004
BUN, mg/dL	29.3±14.4	30.2±15.1	35.0±18.6	0.011
ALT, U/L	68.1±85.6	90.0±189.7	70.3±121.2	0.087
AST, U/L	216.5±251.2	231.4±310.7	180.4±174.5	0.411
Lactate, mmol/L	4.58±3.43	4.68±3.30	4.92±3.65	0.768
pH	7.32±0.10	7.31±0.12	7.31±0.12	0.627
pCO_2	35.4±7.8	34.3±7.9	34.0±7.6	0.106
pO_2 97.3±54.7	87.3±31.5	96.3±41.1	0.058	

Continuous variables are presented as mean±SD; nominal variables presented as frequency (%). LVEF: Indicates left ventricle ejection fraction; LVEDD: Left ventricle end-diastolic diameter; LVESD: Left ventricle end-systolic diameter; PASP: Pulmonary artery systolic pressure; MR: Mitral regurgitation; TR: tricuspid regurgitation; GRACE: Global registry of acute coronary events

Table 3. In-hospital event rates and multiple binary logistic regression models for in-hospital mortality and AKI by GRACE score tertiles

	GRACE score		
	T1	T2	T3
In-hospital mortality			
Number of deaths	57	74	90
Mortality, %	34.8	45.1	54.9
Mortality, OR (%95 CI)			
Model I: unadjusted	1 [Reference]	1.5 (0.9–2.4)	1.8 (1.2–2.6)
Model II: adjusted for all covariates[a]	1 [Reference]	1.9 (1.0–3.5)	2.1 (1.3–3.5)
Acute kidney injury			
Number of events	52	84	109
Events, %	31.7	51.2	66.5
Events, OR (%95 CI)			
Model I: unadjusted	1 [Reference]	2.3 (1.4–3.5)	2.8 (1.8–4.1)
Model II: adjusted for all covariates[a]	1 [Reference]	2.5 (1.5–4.1)	3.1 (1.9–5.4)

OR: Odds ratio; CI: Confidence interval; AKI: Acute kidney injury; GRACE: Global registry of acute coronary events. [a]Includes gender; hypertension; diabetes mellitus; hyperlipidemia; current smoking; chronic renal failure; previous cerebrovascular accident; previous myocardial infarction; previous percutaneous coronary intervention; peripheral artery disease; chronic obstructive lung disease; atrial fibrillation; anterior myocardial infarction; percutaneous coronary transluminal angioplasty; culprit artery; drug-eluting stent; multivessel intervention; thrombus aspiration; the first measurement during hospitalization of the following laboratory values including baseline serum creatinine, blood urea nitrogen, hemoglobin; the left ventricle ejection fraction; left ventricle diastolic diameter; the left ventricular systolic diameter; pulmonary artery systolic pressure; and tricuspid annular plane systolic excursion

and blood urea nitrogen levels than those in the T1 and T2 groups (p<0.05 for each).

The incidence rate of AKI and in-hospital mortality rates according to the groups are shown in Table 3. Of note, patients in the T3 groups had higher in-hospital deaths than those in the T1 and the T2 groups (54.9% vs. 45.1% vs. 34.8%). The unadjusted risk of AKI was 2.8 (95% confidence interval (CI) 1.8–4.1) for patients in the T3 group. In addition, adjusted risk including all covariables for AKI was 3.1 (95% CI 1.9–5.5) for patients in the T3 group. In a ROC curve analysis, the area under the curve of the GRACE score was 0.70 (95% CI 0.65–0.74, p<0.001). The optimal value of the GRACE score for AKI was found to be 200.5 with 69.2% sensitivity and 68.8% specificity (Fig. 1)

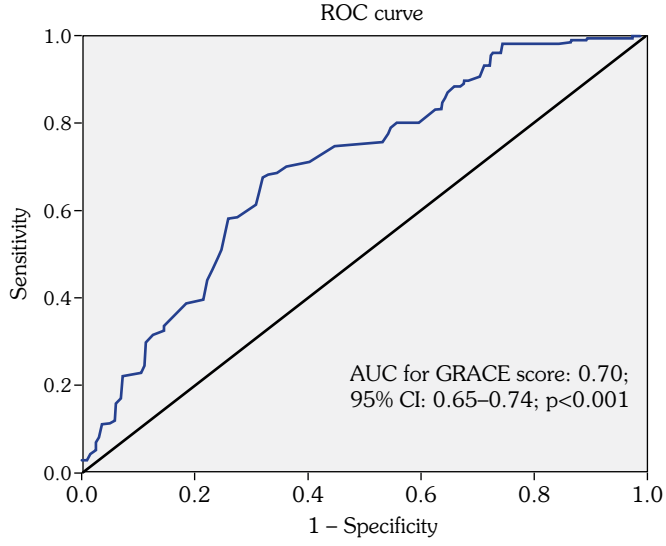

Figure 1. A ROC curve analysis showed that the area under the curve value of the GRACE score for acute kidney injury was 0.70 (95% CI 0.65–0.74, p<0.001)

ROC: Receiver operating characteristic; GRACE: Global Registry of Acute Coronary Events; CI: Confidence interval; AUC: Area under the curve

DISCUSSION

In the present study, we observed that after adjusting all potential confounders, patients with CS with high GRACE score have three-fold higher incidence of AKI than those with an intermediate and low GRACE score. To the best of our knowledge, this is the first study in the literature to show that the GRACE score may have a prognostic value for AKI in patients presenting with CS.

CS is a state of medical emergency characterized by a reduce blood flow to multiple vital organs including the kidneys due to the ex-

tensive damage of the ventricle (15). Although CS may be caused by a variety of cardiovascular conditions, the most common reason is STEMI (15). Although there have been great improvements in pharmacological treatment and reperfusion therapy of patients with CS in the last two decades, the mortality rate among these patients still remains to be high (16). Additionally, this condition is frequently complicated with the deterioration of renal functions that has been related with further increase in mortality rates (17, 18). Hence, adequate intravenous hydration, timely start of continuous renal replacement therapy, and mechanical circulatory support would be crucial steps after identification of these patients.

The GRACE score is derived from the GRACE registry that included >100,000 patients in 30 countries (19). This score determines the risk by including the appropriate number of points for each of the eight variables into the calculation (e.g., age, heart rate, systolic blood pressure, and serum creatinine). In previous studies, this risk score has been proven to be useful to estimate the risk of short- and long-term deaths in patients presenting with ACS (9, 10). In addition, several previous studies have extended the role of this risk tool to other clinical conditions, such as pulmonary embolism, heart failure, and stroke (20–22). Additionally, in a recent prospective study, which included 209 consecutive patients with STEMI, Koonsiripaiboon et al. revealed that patients with a high GRACE score may have higher risk of CS than those with a low GRACE score upon admission (23). Although the GRACE score has been extensively investigated in different cardiovascular conditions, data regarding the suitability of the GRACE score to predict AKI in patients with CS have not been tested before. Based on the study findings, we observed that patients whose GRACE score was higher had also elevated risk of AKI in addition to the increase in-hospital mortality rates. As the possible explanations of our study findings, we considered that patients with a high GRACE score were older patients with chronic renal failure and had higher Killip class; hence, these patients might be at higher risk of AKI because all of these variables have been shown as an independent predictor of AKI in patients with CS in previous studies (3, 4, 17, 18). In addition, a well-known risk model that is developed and validated for the assessment of AKI includes similar variables (24).

With respect to clinical applicability, our results may point up to significant findings because the GRACE score is a simple tool that can be obtained after the first medical evaluation. According to the study findings, patients with high-risk GRACE score should be closely followed up for the development of AKI since some early prophylactic treatment modalities may improve survival among these patients. However, the definitive recommendations could not be given because our study had a retrospective design. Therefore, prospective studies with larger population are necessary to understand the exact role of the GRACE score to predict AKI in patients with CS.

Study Limitations

The present study has limitations. First, our study had a retrospective and observational design with the possibility of selection bias. Second, we only included patients with CS due to STEMI; hence, our result might not be generalized to all patients with CS. Third, even though all potential confounders were included in a multiple model, there might be some unmeasurable confounders that might affect the result of the study. Fourth, the component of the GRACE score, namely systolic blood pressure, was obtained by a noninvasive method. Fifth, other well-known risk scores, such as the thrombolysis in myocardial infarction and the primary angioplasty in myocardial infarction, were not evaluated and compared with the GRACE score in our study. Sixth, the contrast media volume, which is an important contributor for the development of AKI, was not evaluated in the study due to the missing data. Seventh, there are limited data with respect to intravenous hydration and statin therapy following the reference procedure.

CONCLUSION

We showed that patients with CS with an elevated GRACE score might have higher risk of AKI. To the best of our knowledge, this is the first study in the literature to demonstrate the relationship between the GRACE score and AKI in patients with STEMI complicated with CS.

Ethics Committee Approval: The ethics committee of Haydarpaşa Numune Training and Research Hospital approved the protocol of the current study (Date 8/4/2019, No. HNEAH-KAEK 2019/KK/46).

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Author Contributions: Concept – MİH, TÇ; Design – MİH; Supervision – AİT; Resource – MİH, TÇ; Materials – MİH, TÇ; Data Collection and/or Processing – MİH, TÇ; Analysis and/or Interpretation – MİH, AİT; Literature Search – TÇ, AİT; Writing – MİH, TÇ; Critical Reviews – AİT.

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