

Performance of the Grace ACS Risk Score in Predicting in-Hospital and Six-Month Mortality in Patients with ACS: A Single Center Retrospective Cohort Study

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Introduction: The incidence of coronary heart disease (CHD) is rising globally. Despite the high burden of CHD in Africa, little is known about appropriate risk stratification systems that can be used to predict outcomes in patients with acute coronary syndromes (ACS) in this region.

Methodology: This was a single-center retrospective cohort study conducted at the Aga Khan University hospital. Data was explored descriptively by summarizing categorical variables using frequencies/percentages and continuous variables using medians and interquartile ranges. Risk groups and mortality were compared using Fisher's exact test or the chi-square test. The area under the receiver operating characteristic curve (AUROC), sensitivity, and specificity were obtained from a binary logistic regression model with mortality as the outcome of interest. The model fit was assessed using Hosmer-Lemeshow statistics. Analysis was performed using R version 4.3.2 (2023–10-31 ucrt) and p-value < 0.05 set as statistical significance.

Results: 378 participants were enrolled. NSTEMI was diagnosed in 48.4% of participants and STEMI in 51.6%. ACS in-hospital mortality was 2.11% and 6-months mortality was 12.70%. NSTEMI in-hospital mortality was 0.55% ($p = 0.45$) and 15.92% ($p = 0.028$) at 6-months. STEMI in-hospital mortality was 3.72% ($p < 0.001$) and 18.23% ($p < 0.001$) at 6-months. The AUROC curve for in-hospital mortality was 0.87 and 0.66 for 6-month mortality, demonstrating acceptable discriminatory capacity. Calibration of the score using the Hosmer-Lemeshow model fit was appropriate ($p = 0.999$).

Conclusion: The GRACE 2 score demonstrated good discriminative power and an acceptable goodness-of-fit for in-hospital outcomes in our setting, but was insufficiently accurate for reliably predicting 6-month post-discharge mortality.

Keywords: performance, GRACE score, in-hospital, 6 months, mortality

Background

A variety of risk prediction models have been developed to determine outcomes in patients with acute coronary syndromes (ACS). One such risk prediction model, the primary angioplasty in myocardial infarction (PAMI) risk score is a prognostic tool which reliably predicts immediate, in-hospital 30-day and 6-month mortality for STEMI.¹ Another risk score is the Grace score, which predicts in-hospital and 6-month post discharge mortality.²

The TIMI risk score was developed from the thrombolysis in myocardial infarction (TIMI) IIB trial and was then validated in important trials like TACTICS-TIMI 18 trial.^{3–6} The TIMI risk score is often used in conjunction with other prediction models to determine disposition of emergency department chest pain patients.^{7,8} The PURSUIT risk score is another prediction model which correlates with ejection fraction, angiographic severity of coronary artery disease, short- and long-term mortality of patients with non-ST-elevation acute myocardial infarction.^{9,10} The TIMI, PURSUIT, and



GRACE risk scores demonstrate good predictive accuracy for death or myocardial infarction at 1 year and identifies high-risk subsets of patients who will benefit most from myocardial revascularization at hospital presentation.^{11–14}

The GRACE score (2003) which was developed in a multinational registry of 11,389 ACS patients (Global Registry of Acute Coronary Events) as opposed to other risk prediction models, is noted for being more accurate in predicting long-term mortality.^{15,16} In 2014, the score was updated to GRACE 2.0 risk score and external validation of the GRACE 2.0 risk score in the contemporary all-comers GLOBAL LEADERS trial revealed that the GRACE 2.0 risk score is valuable in discriminating high risk ACS patients with improved accuracy in predicting in-hospital mortality.^{17,18} Improved outcomes in patients with ST-elevation myocardial infarction due to appropriate risk stratification during the last 20 years has been determined to be related to implementation of evidence-based treatments.^{19–23} The GRACE 2.0 score is a quick method for assessing cardiovascular risk to complement clinical assessment and can guide patient triage and management across the spectrum of patients with acute coronary syndromes.^{24–26}

Our study aimed to assess the performance of the GRACE 2.0 risk score for predicting in-hospital and 6-month post discharge mortality in a cohort of patients in a private referral hospital in Kenya where the ACS population may be skewed by socio-economic factors. The objective was to assess the relationship between predicted in-hospital and 6-month post discharge mortality in ACS patients (as per the GRACE 2.0 score) and the observed in-hospital and 6-month mortality.

Methods

Study Design and Setting

The study is a single-center retrospective cohort study, conducted at the Aga Khan University Hospital, Nairobi (AKUH, N). All patients who presented with ACS between January 2021 and December 2022 were included in the study.

At the Aga Khan University Hospital (AKUH), the management of acute coronary syndromes (ACS) follows internationally recognized guidelines while being tailored to the institution's resources and patient demographics. ACS encompasses a spectrum of clinical conditions that include unstable angina, non-ST elevation myocardial infarction (NSTEMI), and ST elevation myocardial infarction (STEMI). The approach for management of ACS at AKUH involves a multidisciplinary, evidence-based strategy to optimize patient outcomes. Established in 1958, the Aga Khan University Hospital is a modern 795-bed multispecialty tertiary care hospital. It is one of eight Joint Commission International (JCI) accredited hospitals in Africa. The hospital provides services to a large proportion of Kenya's population and also to neighboring countries such as Somalia, Sudan, and Uganda. Patients admitted to the hospital including those with ACS are registered and their data is captured using electronic health records managed by the hospital.

At AKUH, a provisional diagnosis of ACS is suspected based on presenting symptoms such as chest pain, shortness of breath, nausea, vomiting or sweating with background risk factors for coronary artery disease such as age, cigarette smoking, hypertension, type II diabetes and a family history of coronary artery disease. An immediate 12-lead ECG is usually obtained within ten minutes of arrival in the emergency room to determine the type of ACS and identify STEMI or NSTEMI.

Following a confirmed diagnosis of ACS, risk stratification is essential for guiding the management approach. AKUH Nairobi utilizes tools like the GRACE (Global Registry of Acute Coronary Events) score and the TIMI (Thrombolysis in Myocardial Infarction) risk score for this purpose. These scores help in determining not only the urgency of treatment (immediate versus delayed) but also the appropriate level of intervention (invasive or conservative).

Study Participants and Sample Size Determination

This data was obtained by chart review and review of data in two other electronic systems of the Aga Khan University Hospital – CARE 2020 and MEDITECH. Data of all patients who presented with ACS, defined by the third and fourth universal definitions of myocardial infarction,²⁷ between January 2021 to December 2022 were reviewed. The diagnosis of ACS was made based on clinical presentation, ECG findings and a rise or fall of high sensitivity troponin I or T.²⁸

Inclusion Criteria

Patients who presented with ACS (NSTEMI or NSTEMI) defined by the third and fourth universal definitions of myocardial infarction²⁷ during the study period were included in the study. Only patients with detectable lesions on coronary angiography, who had complete medical records from admission, through hospitalization and discharge, and at 6-months post discharge were included in the study.

Exclusion Criteria

Patients who were admitted with ACS and discharged from the hospital and who had no records of a hospital follow up visit 6-months post discharge were excluded from the study.

Patients who had incomplete data for calculation of the GRACE score at presentation were also excluded from the study.

Patients who did not have documented evidence of a follow up visit at 6 months were contacted by telephone regarding their wellbeing 6 months after discharge, and those who could not be reached by telephone were excluded from the study.

Patients who did not have detectable lesions in any of the coronary artery beds were not included in the final analysis.

A flow diagram illustrating selection of participants is shown in [Figure 1](#).

Study Variables

Dependent Variables

Mortality outcomes in different risk groups stratified by the GRACE 2.0 risk score (low risk, intermediate and high risk) in both STEMI and NSTEMI, during hospitalization and 6 months post discharge from the hospital. Mortality was the outcome of interest.

Independent Variables

Baseline demographics, comorbidities and risk factors for coronary artery disease, clinical parameters at presentation used for calculation of the GRACE 2.0 score, including ECG changes and biochemical parameters.

Data Collection and Management

All data was obtained from a review of medical records at the institution's medical records department. Data that was not found in the medical records department was obtained from electronic databases including CARE 2020 and MEDITECH.

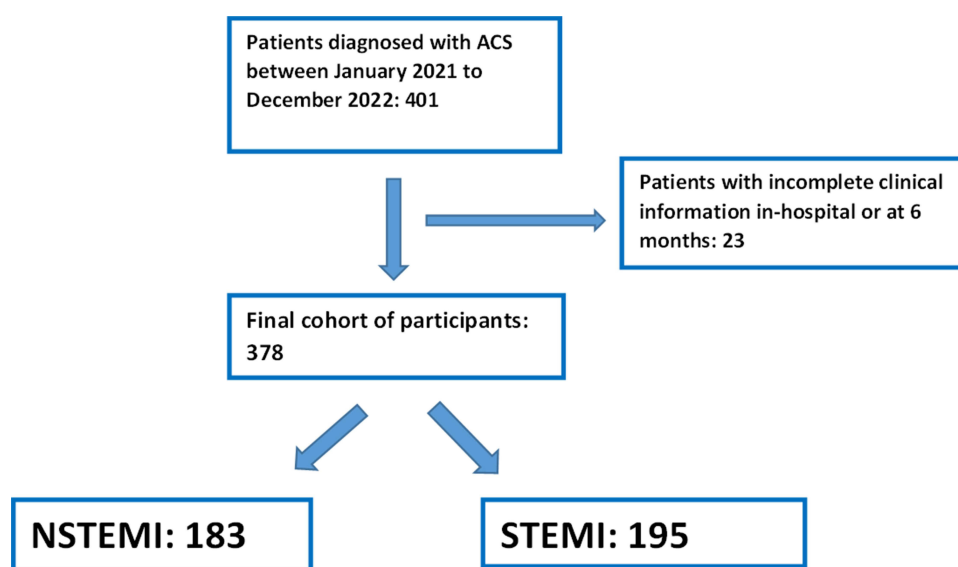


Figure 1 Flow diagram illustrating participant selection.

Data obtained included demographic characteristics, associated comorbidities and past medical history, clinical presentation symptoms, vital signs at diagnosis, ECG findings at diagnosis, cardiac troponin levels at diagnosis, serum creatinine at diagnosis, angiographic findings and interventions/treatment offered. A review of in-hospital course, discharge condition and six months follow up visit was also thoroughly assessed for in-patient and 6-month post discharge outcomes. These data were extracted by the primary investigator.

Data Analysis

Data was explored descriptively by summarizing categorical data using frequencies and percentages, while continuous variables were summarized using medians and interquartile ranges. The risk groups for STEMI and NSTEMI and mortality status were compared using Fisher's exact test or the chi-square test, depending on the observed cell counts.

Risk stratification was done using the GRACE 2.0 score from clinical parameters at the time of diagnosis.²³

Depending on the ACS type (NSTEMI versus STEMI), the patients were stratified into 3 levels of risk groups (low risk, intermediate risk and high risk) for in-patient outcomes (mortality) and 6-months' outcomes (mortality) based on the calculated GRACE 2.0 scores.

There are established predicted mortalities for the different risk groups (low risk, intermediate risk and high risk) for NSTEMI and STEMI, in-hospital and 6-months post discharge as stated in the development and validation cohorts of the GRACE 2.0 score.^{29,30}

Calibration

The model's calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test.^{31,32} This test is usually used for validating already existing or newly created models and it is equally useful for validating an existing logistical model with an external database, as is the case with our study.³¹ Ideally the test approximates a c statistic based on the difference between the observed mortality values (reality) and those predicted by the model for different risk groups. The smaller the statistical value of the c statistic, the better calibrated the model is, and generally, a p value > 0.05 indicates that the model is well adjusted to the data and therefore is a good predictor of patients' probability of death.³² The GRACE 2.0 score's calibration was assessed for the whole study cohort and subgroups representing the different ACS types (NSTEMI and STEMI).

Discrimination

GRACE 2.0 risk score discrimination denotes the score's ability to distinguish between patients who will be alive and those who will die in-hospital and six-months post discharge. The capacity for discrimination was analyzed by calculating the area under the ROC (receiver operating characteristic) curve (AUROC). The ROC curve is a plot of "1 – specificity (false positive rate)" as the x-axis and "sensitivity" as the y-axis and generally, a model with an AUC-ROC more than 0.5 and especially between 0.8 and 0.9 is considered to be a model with a good capacity for discrimination.³³ The area under the receiver operating characteristic curve (AUROC), sensitivity, and specificity were obtained from a binary logistic regression model with mortality as the outcome of interest.

All analysis was performed using R version 4.3.2 (2023–10-31 ucrt) and p-value < 0.05 set as statistical significance.

Ethical Clearance and Informed Consent

The study protocol was presented at the division of Cardiology, department of Medicine of Aga Khan University Hospital for approval, and was then submitted to the Aga Khan Institutional Scientific and Ethics Review committee (ISERC) for review. The study protocol was subsequently approved by the Aga Khan Institutional Scientific and Ethics Review committee (ISERC) with reference number: Ref: 2023/ISERC-130 (v2) of December 18, 2023. The Institutional Scientific and Ethic Review Committee (ISERC) of the Aga Khan University Hospital, Nairobi exempted individual Informed consent from study participants as the study design was purely based on extracting data from a registry and did not affect the rights and welfare of the patients. The study was conducted in line with study principles of the Aga Khan university Hospital Nairobi. The study complied with the Declaration of Helsinki.

Results

General Characteristics of the Study Population

The baseline demographic characteristics of the participants are summarized in Table 1. The study enrolled a total of 378 participants, the median age in years was 60 (IQR:51–69) and females were 281 (74.3%) of the total participants. Majority (n=315; 83.3%) of the participants were blacks. Asians and Caucasians constituted (n=4; 1.1%) and (n=59; 15.6%), respectively. The median body mass weight in kg/m² was 27.6 (IQR:24.0–31.2). The prevalence of hypertension, diabetes and dyslipidemia were 63.5% (n=240), 42.1% (n=159), and 69.6% (n=221), respectively. 221 (58.5%) of the participants were smokers, 117 (31.0%) had family history of CAD, 53 (14.0%) had previous MI, 19 (5.0%) had previous HF, 4 (1.1%) had previous cardiac surgery and 1 (0.3%) had previous non-cardiac surgery.

The GRACE 2.0 score was calculated from clinical characteristics of participants at presentation, which included age of the patient, heart rate at presentation, systolic blood pressure, creatinine at presentation, cardiac arrest at presentation or not, ST segment deviation on EKG, abnormal cardiac enzymes and Killip class at presentation. These clinical characteristics, the ACS type, in-hospital and 6-month post discharge risk stratification based on the GRACE 2.0 scores (low, intermediate and high risk groups), together with observed outcomes (mortality) and treatments offered are shown in Table 2.

The proportion of patients in the in-patient category decreased from low to high risk (there were more patients in the low-risk group and fewer patients in the high risk group) for both STEMI and NSTEMI. In the in-hospital NSTEMI group, participants classified as low risk were 100 (54.6%) and those in the high risk were 34 (18.6%). In the STEMI group, 87 (44.6%) of the participants were in the low-risk group, whilst 46 (23.6%) were in the high-risk group (p-value=0.15).

However, in the 6 month post discharge group, the proportion of patients increased with the severity of the risk with 47 (25.7%) classified as low risk and 67 (36.6%) classified as high risk among participants with NSTEMI. Among those with STEMI, 35 (17.9%) were in the low-risk group and 107 (54.9%) were in the high-risk group (p-value=0.002). This is shown in Table 3.

Overall (both STEMI and NSTEMI), in-hospital, the number of deaths increased from the low risk group to the high risk groups. There was no death in the low-risk groups, one death in the intermediate risk group and seven deaths in the high-risk group in both NSTEMI and STEMI (p-value < 0.001). Overall in-hospital mortality (STEMI and NSTEMI) was

Table 1 Baseline Variables of Study Participants

Baseline Characteristics	N = 378
Age in years, Median (IQR)	60.0 (51.0–69.0)
Sex, n (%)	
M	281 (74.3)
Race, n (%)	
Black	315 (83.3)
Asian	4 (1.1)
Caucasian	59 (15.6)
Body Mass Index, Median (IQR)	27.6 (24.0–31.2)
Hypertension, n (%)	240 (63.5)
Diabetes, n (%)	159 (42.1)
Dyslipidemia, n (%)	263 (69.6)
Smoking, n (%)	221 (58.5)
Family history of CAD, n (%)	117 (31.0)
Previous MI, n (%)	53 (14.0)
Previous HF, n (%)	19 (5.0)
Previous cardiac surgery, n (%)	4 (1.1)
Previous non-cardiac surgery, n (%)	1 (0.3)

Table 2 Clinical Characteristics of Study Participants

Characteristic	N = 378
Heart Rate (bpm), Median (IQR)	85.0 (71.0–99.0)
SBP (mmHg), Median (IQR)	130.0 (114.3–152.0)
Creatinine (μmol/L), Median (IQR)	91.0 (78.0–106.0)
Cardiac arrest at admission, n (%)	5 (1.3)
ST deviation on ECG, n (%)	282 (74.6)
Abnormal cardiac enzymes, n (%)	363 (96.0)
Killip Class, n (%)	
I	127 (33.6)
II	147 (38.9)
III	81 (21.4)
IV	23 (6.1)
Total score, Median (IQR)	119.5 (97.0–143.0)
ACS type, n (%)	
NSTEMI	183 (48.4)
STEMI	195 (51.6)
In-hospital risk group, n (%)	
Low risk	187 (49.5)
Intermediate	111 (29.4)
High risk	80 (21.2)
6-month risk category, n (%)	
Low risk	82 (21.7)
Intermediate	122 (32.3)
High risk	174 (46.0)
In-hospital survival status, n (%)	
Dead	8 (2.1)
Alive	370 (97.9)
Month 6 survival status, n (%)	
Dead	46 (12.7)
Alive	324 (85.7)
PCI, n (%)	
Medical management	111 (29.4)
Yes	251 (66.4)
CABG	16 (4.2)

Table 3 Risk Groups Stratified by ACS Type

Risk Groups	ACS Type		p-value ^q
	NSTEMI, N = 183	STEMI, N = 195	
In-patient risk group, n (%)			0.15
Low risk	100 (54.6)	87 (44.6)	
Intermediate	49 (26.8)	62 (31.8)	
High risk	34 (18.6)	46 (23.6)	
Six-months risk group, n (%)			0.002
Low risk	47 (25.7)	35 (17.9)	
Intermediate	69 (37.7)	53 (27.2)	
High risk	67 (36.6)	107 (54.9)	

Note: ^qPearson's Chi-squared test.

2.11%. 6-months' post discharge in both STEMI and NSTEMI, there were three deaths in the low risk group, 11 (10.0%) in the intermediate risk group, and 33 (19.7%) in the high risk group (p-value < 0.001). Overall mortality (STEMI and NSTEMI) 6-months post discharge was 12.70%. This is shown in [Table 4](#).

In-Hospital Mortality Outcomes

In the STEMI in-hospital category, there was no mortality in the low and intermediate risk groups. There were seven deaths (15.2%) in the high-risk group (p-value < 0.001). In-patient mortality in the STEMI category was 3.72%. In the NSTEMI in-hospital category, there was only one mortality in the intermediate risk group (p-value=0.45). In-patient mortality in the NSTEMI category was 0.55%. This is shown in [Table 5](#).

Six-Months Post Discharge Mortality Outcomes

In the STEMI category, 6-months post discharge, there was no death in the low-risk group. Four (7.8%) deaths were recorded in the intermediate risk group and 25 (24.5%) deaths were noted in the high-risk group (p-value < 0.001). Mortality 6-months post discharge in the STEMI category was 18.23%. In the NSTEMI category, 6-months post discharge, mortality increased from 6.4% among the low-risk group, to 10.2% among the intermediate group and 22.4% in the high-risk group (p-value=0.028). Mortality at 6 months post discharge in the NSTEMI category was 15.92%. This is shown in [Table 6](#).

Mortality 6 months post discharge in the low, intermediate and high risk groups for both STEMI and NSTEMI are shown in [Figure 2](#).

Table 4 Overall Mortality Status by Risk Groups (STEMI and NSTEMI)

In – Hospital	Low Risk	Intermediate Risk	High Risk	P - value [®]
Outcome	No (%)	No (%)	No (%)	
Dead	0 (0.00)	1 (0.9)	7 (8.8)	< 0.001
Alive	187 (100)	110 (99.1)	73 (91.3)	< 0.001
6-months post discharge	Low risk	Intermediate risk	High risk	P - value [®]
Outcome	No (%)	No (%)	No (%)	
Dead	3 (3.7)	11 (10.0)	33 (19.7)	< 0.001
Alive	79 (96.3)	110 (90.0)	134 (80.3)	< 0.001

Notes: [®]Fisher's exact test; Pearson's Chi-squared test.

Table 5 In-Hospital Mortality by Risk Groups

STEMI	Low Risk	Intermediate Risk	High Risk	P - value [®]
Outcome	No (%)	No (%)	No (%)	
Dead	0 (0.0)	0 (0.0)	7 (15.2)	< 0.001
Alive	87 (100)	62 (100)	39 (84.8)	< 0.001
NSTEMI	Low risk	Intermediate risk	High risk	P - value [®]
Outcome	No (%)	No (%)	No (%)	
Dead	0 (0.0)	1 (2.0)	0 (0.0)	0.45
Alive	100 (100)	48 (98.0)	34 (100.0)	

Notes: [®]Fisher's exact test; Pearson's Chi-squared test.

Table 6 Six-months Post Discharge Mortality by Risk Groups

STEMI	Low Risk	Intermediate Risk	High Risk	p - value^o
Outcome	No (%)	No (%)	No (%)	
Dead	0 (0.0)	4 (7.8)	25 (24.5)	< 0.001
Alive	35 (100)	47 (92.2)	77 (75.5)	
NSTEMI	Low risk	Intermediate risk	High risk	P - value^o
Outcome	No (%)	No (%)	No (%)	
Dead	3 (6.4)	7 (10.2)	15 (22.4)	0.028
Alive	44 (93.6)	61 (89.8)	52 (77.6)	

Notes: ^oFisher's exact test; Pearson's Chi-squared test.

Calibration of the GRACE 2 Score: Hosmer-Lemeshow Statistics

The Hosmer-Lemeshow (HL) goodness of fit test was used to calibrate the GRACE 2.0 score for prediction of in-hospital and 6-months mortality. The overall HL values of the GRACE score for prediction of in-hospital and 6-month mortality for NSTEMI and STEMI were both 0.999 which suggests a good model fit. The Hosmer-Lemeshow Characteristics are shown in Table 7.

Discriminatory Capacity of the GRACE 2 Score: Area Under the ROC Curve

The discriminatory capacity of the score (its ability to discriminate which patients will be alive or dead in-hospital and which patients will be alive or dead at 6 months post discharge) was determined by calculation of the area under the receiver operating curve (AUROC) using multivariable logistic regression. In the NSTEMI category, the area under the curve c-statistics was 0.65 (with a sensitivity and specificity of 0.67 and 0.60, respectively) for prediction of 6-month post discharge mortality. In the STEMI category, the area under the curve c-statistic was 0.70 (with a sensitivity and specificity of 0.51 and 0.86, respectively) for prediction of 6-month post discharge mortality. These are illustrated in Figure 3.

In summary, in the NSTEMI in-hospital category, there was 0% mortality observed in the low risk group, 1% in the intermediate risk group and 0% mortality in the high risk group (p value of 0.45), while at 6 months post discharge, there was a 3% observed mortality in the low risk group, 7% in the intermediate risk group, and 15% in the high risk group (p

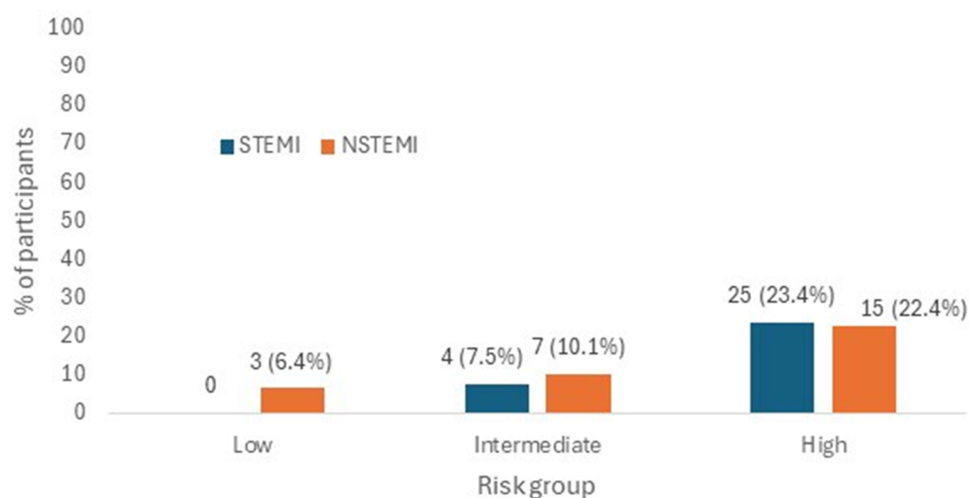


Figure 2 Mortality 6 months' post discharge in the low, intermediate and high risk groups for both STEMI and NSTEMI.

Table 7 Hosmer-Lemeshow Characteristics

Risk Category	Chi-Square	P value
NSTEMI: In-hospital	< 0.001	0.999
NSTEMI: 6 months	< 0.001	0.999
STEMI: In-hospital	< 0.001	0.999
STEMI: 6 months	< 0.001	0.999

Notes: NSTEMI: 0.999, STEMI: 0.999, Overall (STEMI and NSTEMI): 0.999.

value of 0.028). In the STEMI category, there was 0% observed mortality in both the low and the intermediate risk groups and 7% in the high risk group (p value < 0.001, while at 6 months post discharge, there was 0% observed mortality in the low risk group, 4% in the intermediate risk group and 25% in the high risk group (p value < 0.001).

The discriminatory capacity of the GRACE score was acceptable: the area under the ROC curve for the whole cohort (NSTEMI and STEMI) for in-hospital mortality was 0.87 and 0.66 for 6-months' mortality. The calibration of the GRACE risk score was admissible, with a Hosmer-Lemeshow value (p value 0.999) indicating a good model fit for predicting in-hospital and 6-month post discharge mortality in both STEMI and NSTEMI.

Discussion

To the best of our knowledge, this is the first study in Kenya and Africa that has assessed the performance of the GRACE 2.0 risk score in determining in-hospital and 6-month post discharge mortality in a cohort of ACS patients attending a private referral hospital. This study demonstrated the validity of using the GRACE 2.0 ACS risk score in stratification of patients with ACS in the region.

The median age of the participants was 60 years, which is quite similar to the median age in a cohort of patients who were admitted with ACS in another African setting.³⁴ Males constituted 74.3% (n= 281) of the participants, while females were 25.7% (n = 97). This is representative of data from the ACS QUIK trial that aimed to explore sex differences and inequalities in terms of medical management and cardiovascular disease (CVD) outcomes in a low/middle-income country (LMIC), where reports are scarce. In the ACS QUIK trial, a total of 5191 (24.3%) patients were women.³⁴

In our study, 48.8% of the patients were diagnosed with NSTEMI and patients diagnosed with STEMI were 51.6%. Previous cohorts in our hospital have shown more STEMI than NSTEMI, but as has been demonstrated elsewhere, as the population matures the number of NSTEMI tend to increase.³⁵ Other studies in Africa have demonstrated similar findings, with a higher proportion of ACS patients presenting with STEMI as in Côte d'Ivoire, where it was documented that 71.5% of patients diagnosed with ACS presented with STEMI in one study.³⁶ Previous studies in Kenya have also shown a higher proportion of patients (57.1%) presenting with STEMI.³⁷

In our study, the 6-month post discharge mortality rate of 12.7% was higher than the rates observed in the development (4.8%) and validation cohorts (4.7%) of the GRACE 2.0 score which involved a multinational registry, involving 94 hospitals in 14 countries, that used data from the Global Registry of Acute Coronary Events (GRACE) to develop and validate a multivariable stepwise regression model for death during 6-months post discharge.^{38–41} This higher rate of mortality from our study was consistent in both the STEMI and NSTEMI subgroups. Our study also demonstrated an in-hospital mortality rate of 2.11%, which is slightly higher compared to a value of 2.1% obtained in the validation cohort.⁴¹ The higher in-hospital mortality in our setting could be due to late presentations and being a referral center.

The AUC c-statistics from this study (for both categories of patients, NSTEMI and STEMI) for in-hospital mortality was 0.87, with a sensitivity of 0.80 and a specificity of 0.87. In an external validation of the GRACE 2.0 risk score and the risk-treatment paradox in patients with acute coronary syndrome by Niels M R van der Sangen, a discriminative

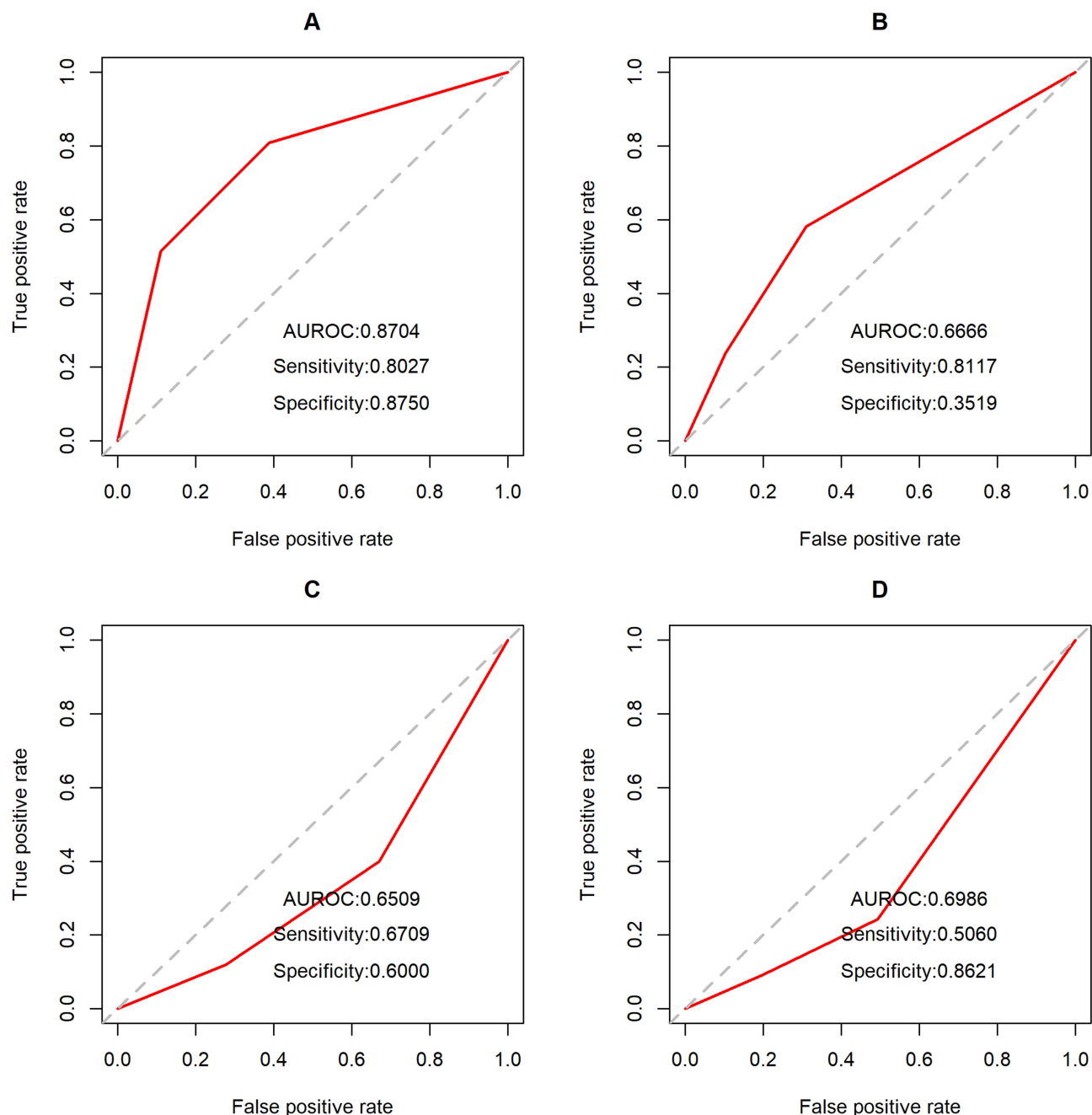


Figure 3 AUROC curves. **(A)** In-patient mortality (NSTEMI and STEMI). **(B)** 6-months' post discharge mortality (NSTEMI and STEMI). **(C)** 6-months' post discharge mortality (NSTEMI). **(D)** 6-months' post discharge mortality (STEMI).

power of 0.86 (c-statistic: 0.86; 95% CI: 0.83 to 0.90) was obtained and reflected good predictive power of the GRACE score for in-hospital mortality.⁴²

The AUC c-statistics for both categories (NSTEMI and STEMI) for 6 month post discharge mortality was 0.66 with a sensitivity of 0.81 and a specificity of 0.35. This indicates only limited discriminatory power, suggesting that the model is insufficiently accurate for reliably predicting 6-month mortality in our study. In another study, by Emad Abu-Assi et al, titled “validation of the GRACE Risk Score for Predicting Death Within 6 Months of Follow-Up in a Contemporary Cohort of Patients with Acute Coronary Syndrome”, they demonstrated that the validated model shows an adequate capacity for discrimination, with an overall in-hospital AUC c-statistic of 0.86, and an AUC of 0.902 for STEMI and 0.855 for NSTEMI.⁴³ In our study, several factors including missing patient data, a single center cohort and narrow age

range of study participants could have resulted in the lower c-statistic value of 0.66. Our overall in-patient AUC of 0.87 was similar to the AUC of 0.86 obtained by Emad Abu-Assi et al. From the study by Emad Abu-Assi et al, as from our study, it is determined that the GRACE 2.0 risk score for predicting in-hospital mortality is valid and can be used in patients with ACS.⁴³

In our study, at 6 months post discharge in a subgroup analysis, the AUC c-statistic for the NSTEMI group for mortality was 0.65, with a sensitivity of 0.67 and a specificity of 0.60, while the AUC c-statistic for mortality in the STEMI subgroup was 0.69 with a sensitivity of 0.5 and a specificity of 0.86. This suggests that the GRACE score demonstrates better discriminative power and accuracy for prediction of 6-month post discharge mortality in STEMI than in NSTEMI. Gale et al, however, demonstrated an AUC c-statistic for 6 month mortality of 0.8 in their multi-center study in the United Kingdom.⁴⁴

In another study, titled “validation of the Grace risk score to predict in-hospital and 6-months” post-discharge mortality in patients with acute coronary syndrome, Vítor Boniatti Neves et al, demonstrated that the risk model had satisfactory ability to predict both in-hospital mortality, with an area under the curve (AUC) of 0.76 (95% confidence interval [CI], 0.57–0.95; $p = 0.014$), and 6-month post-discharge mortality, with AUC of 0.78 (95% CI, 0.62–0.94).⁴⁵ Their value of in-hospital AUC of 0.76 was somewhat different from what we obtained in this study (0.87) for in-hospital mortality, and their value of 0.78 for 6-month post discharge mortality was somewhat close to the value of 0.66 we obtained in our study.

Limitations of the Study

This study set out to determine the validity of the GRACE 2.0 risk stratification system in the management of patients with ACS in a contemporary setting. It was important to conduct this survey, as the GRACE 2.0 risk scoring system is well integrated in the assessment of ACS patients in our setting and risk stratification based on the scoring system is robustly utilized in decision making during management of patients with ACS.

However, several limitations were encountered during this survey. The retrospective nature of the survey itself is a limiting factor, as clinical parameters for the determination of the GRACE score could have been incompletely documented therefore affecting the number of participants who were finally studied as patients with incomplete data were excluded from the study.

It was noted that several patients who were hospitalized for ACS did not show up at 6 months for a review and information about the welfare of these patients 6 months after discharge was unavailable. This led to a diminution in the sample size or number of participants.

There was no exploratory analysis of the impact of the prescribed pharmacological and interventional treatments. Given the retrospective nature of the study, medication compliance before the 6 month review could not be accurately accounted for.

The predictive power of the score could not be appropriately tested in a subgroup analysis for in-hospital mortality in both NSTEMI and STEMI categories due to lack of in-hospital mortalities in the low and high risk groups of NSTEMI and in the low and intermediate risk groups of STEMI. As a result, appropriate AUC c-statistic values could not be obtained for in-hospital mortality for NSTEMI and STEMI.

Conclusion

The GRACE 2.0 score demonstrated good performance in predicting in-hospital mortality in the combined STEMI and NSTEMI cohorts with good acceptability in our setting. For 6-month post-discharge mortality in the combined STEMI and NSTEMI cohorts, the model showed only modest ability to distinguish between individuals with and without the outcome. The in-patient mortality rate of ACS patients (NSTEMI and STEMI) was similar to the rate noted in the validation cohort of the GRACE 2.0 score, however, the observed mortality six months post discharge was higher in our study compared to the validation cohort. The lower discriminatory power of the model for 6-month post discharge mortality as observed in our study (AUC c-statistic of 0.66), could be attributed to single center cohorts and missing patient data. Generally, the GRACE 2.0 score illustrated an overall satisfactory discriminative power and goodness-of-fit for prediction of in-patient mortality, but demonstrated limited or insufficient discriminatory power for prediction of 6-month post discharge mortality in our study.

What is Known About This Topic

- In-hospital mortality as predicted by the GRACE 2.0 score from ACS is 2.1%, from the validation cohort of the GRACE 2.0 score, while mortality 6 months post discharge is 4.7%.
- In patients with NSTEMI, in-hospital, predicted mortality amongst patients classified as low risk (GRACE 2.0 score of 1–108) is less than 1%, predicted mortality in the intermediate risk group (GRACE 2.0 score of 109–140) is 1–3% and predicted mortality in the high risk category (GRACE 2.0 score 141–372) is > 3%, while at 6 months post discharge, predicted mortality in patients classified as low risk (GRACE 2.0 score 1–88) is < 3%, predicted mortality in the intermediate risk group (GRACE 2.0 score 89–118) is 3–8%, while predicted mortality in the high risk group (GRACE 2.0 Score 119–263) is > 8%.
- In patients with STEMI, in-hospital, predicted mortality in patients classified as low risk (GRACE 2.0 score 49–125) is < 2%, predicted mortality in the intermediate risk group (GRACE 2.0 score 126–154) is 2–5% and predicted mortality in the high risk group (GRACE 2.0 score 155–319) is > 5%, while at 6 months post discharge, predicted mortality in those classified as low risk (GRACE 2.0 score 27–99) is < 4.4%, predicted mortality in the intermediate risk group (GRACE 2.0 score 100–127) is 4.5–11%, and predicted mortality in the high risk group (GRACE 2.0 score 128–263) is > 11%.

What This Study Adds

The key additional finding from this study was the 6 month post discharge mortality rate. This study demonstrated a rate of in-hospital mortality in ACS patients of 2.11% which is similar compared to the in-hospital mortality obtained in the validation cohort of the GRACE 2.0 risk score (2.1%). However, our study demonstrated a higher 6 month post discharge mortality in ACS patients of 12.7% compared to 4.7% obtained in the validation cohort of the GRACE 2.0 score. This higher mortality rate at 6 months post discharge indicates the need for early presentation, early referrals, adequate risk stratification upon presentation and early implementation of appropriate treatment to optimize outcomes and reduce mortality in our setting.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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The authors report no conflict of interest in this work.

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