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GRACE RISK SCORE IN ACUTE CORONARY SYNDROME MORTALITY PREDICTION

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ABSTRACT **Importance:** Cardiovascular diseases are the leading global cause of death, projected by WHO to account for 33% of deaths by 2030, driven by lifestyle changes and rising rates in countries like India. Despite advances in treating acute myocardial infarction, mortality remains high, highlighting the need for effective risk assessment tools like the GRACE score, which is valued for its comprehensive, accessible, and validated risk prediction. **Objective:** To evaluate the risk of acute coronary syndrome (ACS) using the GRACE risk score to predict in-hospital mortality and identify associated risk factors. **Design:** This observational cross-sectional study was conducted from February to December 2022. **Setting:** This study was conducted in a tertiary care medical Centre- SRG hospital and Jhalawar Medical College, Jhalawar, India. **Participants:** 200 ACS patients having first incidence of acute coronary syndrome were selected by convenience sampling after obtaining their written informed consent. Patients were excluded if they had a known diagnosis of coronary artery disease (CAD), declined to provide consent, or were discharged before their data could be fully collected. **Exposure(s):** The exposures examined in the study included age, family history of ACS, smoking, dyslipidemia, and obesity. Main Outcome(s) and Measure(s): The study aimed to predict in-hospital mortality in ACS patients using the GRACE risk score, which demonstrated excellent discrimination. All fatalities were associated with high GRACE risk scores. **Results:** Out of 200 patients, 150 (75%) were male and 50 (25%) were female, with a mean age of 59.45 ±12.56 years. Fourteen patients (7%) died during hospital stay. The GRACE risk score had 100% sensitivity and high specificity (85.42% for NON-ST-Elevation ACS, 70% for ST-Elevation Myocardial Infarction) for predicting mortality. Its negative predictive value was 100%, and the positive predictive value was 25% for STEMI and 22.22% for NON-ST-Elevation ACS. The GRACE score showed excellent discrimination with a C-statistic of 0.99 and a 95% confidence interval of 115.742 – 151.221 ($p<0.001$). Elevated heart rate, low blood pressure, high serum creatinine, and Killip class 4 were significantly associated with in-hospital mortality ($p<0.001$). **Conclusions and Relevance:** this study demonstrates that the GRACE Risk Score is highly effective in predicting in-hospital mortality among patients with Acute Coronary Syndrome. Its accuracy in assessing risk underscores its utility as a crucial tool for identifying high-risk patients.

KEYWORDS :

INTRODUCTION

Cardiovascular diseases (CVDs) are now the leading global cause of death and are projected to account for 33% of deaths by 2030 as per WHO, driven by a shift from pestilence to lifestyle-related factors. Low- and middle-income countries, including India, are experiencing rapidly increasing CVD rates. In India, CVDs account for about 25% of deaths, with prevalence rates of over 10% in urban areas and 4.5% in rural areas[1,2]. Adverse lifestyle changes due to industrialization and urbanization contribute to rising CVD morbidity and mortality. Risk factors for CVD are largely derived from data in developed countries, highlighting the need for more localized research.

The survival of patients with acute myocardial infarction has improved significantly over the past 10 years with the advent of PCI and better utilization of aspirin, anticoagulants, and cardioprotective drugs. Despite this improvement, mortality rates after Myocardial infarction continue to demonstrate an early rise. Therefore, risk stratification is essential to identify high-risk patients. Risk assessment in patients with myocardial infarction is crucial as it guides subsequent management strategies and treatment decisions[3] like: Site of care (coronary care unit, monitoring step down care or out-patient setting), Type of therapy (medical, surgical/PCI/Gp IIb/IIIa inhibitors) and Long- and short-term prognosis.

There are so many risk scores to predict mortality and recurrent ischemic events. The TIMI (Thrombolysis In myocardial Ischemia) risk score[4] identifies seven independent risk factors. The PURSUIT risk score was developed in a multinational randomized clinical trial. The GRACE (Global Registry of Acute Coronary Events) risk score is more accurate[5,6] because it was derived from a multinational registry of unselected patients and includes hospitals in North America, South America, New Zealand, Europe, Asia and Australia. Risk assessment should be carried out at the time of hospital admission as it gives an idea about the probability of in-hospital death and also guides the appropriate treatment planning in cases of acute coronary syndrome.

While risk scores are recommended for managing acute coronary syndrome (ACS), their international use is limited due to accessibility issues and lack of availability at initial presentation. The GRACE risk score is an exception, as it is designed for emergency settings and is available on mobile devices[7]. Its user-friendly application, including a "pocket guide" by the European Society of Cardiology, is widely respected and helps clinicians combine this tool with their clinical judgment for patient care.

GRACE(Global Registry Of Acute Coronary Events) is an international observational program of outcomes for patients who were hospitalized with an acute coronary syndrome (ACS) in the 10 years from 1999. GRACE was conducted in nearly 250 hospitals in 30 countries, with a total of 102,341 patients[8]. The GRACE Score has been extensively validated prospectively and externally both[6,9]. NICE guidelines[10] recommend the GRACE risk score for risk stratification of patients with ACS. The score has been validated in greater than 20000 patients in multiple databases and is extremely well studied and supported. Many guidelines recommend more early invasive management for patients with high scores.

The GRACE Risk Score includes 8 parameters- Age, Heart rate, Systolic blood pressure, Killip class, Serum creatinine level, Cardiac arrest at hospital admission, ST segment deviation in ECG, Elevated serum cardiac markers. The total score is 372. Scores for GRACE models[11] were validated for 1) In-hospital mortality 2) death within 6 months from hospital admission or 3) death within 6 months of discharge.

Clinical parameters used earlier like the Framingham predictive models[12] were inadequate to determine the risk of heart attack or death. The GRACE program identified that survivors of 'non-ST elevation ACS' (previously perceived as minor or threatened heart attacks) had high long-term risks of death and recurrent heart attacks.

Pamela J. Bradshaw et al. conducted a validation study of the 'GRACE risk score in both indigenous and non-indigenous patients hospitalized with acute coronary syndrome'[11], involving 892 patients. The study found a significant association with age over 65 ($p = 0.001$) and elevated cardiac biomarkers ($p < 0.001$), while ST segment deviation

did not show a significant correlation. The model demonstrated good overall calibration from admission to six months, with a strong correlation between predicted and observed mortality. The C-statistic ranged from 0.75 to 0.79, indicating robust predictive accuracy.

In the study by Amar R. Prabhudesi, M.A. Srilakshmi, and Shamanna S. Iyengar, titled 'Validation of the GRACE Score for Prognosis in Indian Patients with Acute Coronary Syndromes'[13], 235 patients with acute coronary syndrome were analyzed for in-hospital mortality from all causes. The study identified significant associations between adverse events and lower systolic blood pressure (odds ratio [OR] 7.93, p = 0.005), ST segment deviation (OR 7.79, p = 0.002), and positive cardiac biomarkers (OR > 6.52, p = 0.01). Serum creatinine showed a trend towards statistical significance (OR 4.14, p = 0.005), while age over 50 years (OR 3.62, p = not significant) and Killip class 4 (OR 2.71, p = not significant) demonstrated good associations. The C-statistic for the GRACE score in this study group was 0.75, indicating good predictive accuracy.

Lim, W.J. et al. in their study 'Validation of the grace risk score for acute coronary syndrome patients in an Asian Medical Centre'[14], validated the GRACE score in 428 patients (≥18 years) admitted to the Hospital Sultanah Aminah Johor Bahru for ACS between January and April 2018. Survival status at 6 months post-discharge was assessed, and the GRACE score's calibration and discrimination were evaluated. Of the 428 patients, 92 had ST-elevation MI, 128 had non-STEMI, and 208 had unstable angina. By 6 months post-discharge, 66 patients (15%) had died. The GRACE score demonstrated good calibration and discrimination with an area under the ROC curve of 0.831 (95% CI [0.778–0.884]; p<0.001). The study supports routine use of the GRACE score in Asian ACS patients.

An observational study "Prognostic value of GRACE score for in-hospital and 6 months outcomes after non-ST elevation acute coronary syndrome" by Kumar D. et al included 300 patients with non-ST-elevation acute coronary syndrome (NSTE-ACS) aged over 30 years. High-risk patients had a higher mortality rate, with 10.5% dying during hospital stay and 11.8% within 6 months (p = 0.001 and p = 0.013). After adjusting for variables, diabetes, family history, and the GRACE score remained significant for in-hospital mortality, and age was significant for 6-month mortality. The c-statistic for in-hospital mortality was 0.80. The study concluded that GRACE risk score is effective in predicting both in-hospital and 6-month mortality in patients with NSTE-ACS[15].

Predictors of in-hospital mortality and major adverse cardiovascular events (MACE) highlight the need for quality improvements in acute coronary syndrome (ACS) care. Key areas include reducing the time from symptom onset to hospital presentation and addressing inappropriate thrombolytic use. Despite higher mortality and MACE rates associated with inappropriate thrombolytics, it does not affect the speed of care[16]. Using checklists to manage ACS patients can improve care quality efficiently. Therefore, accurate risk scoring systems are essential for better ACS management in India.

There is a notable lack of significant research focusing on the assessment of risk in acute coronary syndrome (ACS) using the GRACE Risk Score specifically for rural populations, such as those in Rajasthan. This gap in the literature prompted the need for a dedicated study to address this issue. Consequently, this cross-sectional study was undertaken with the primary objective of evaluating the effectiveness of the GRACE Risk Score in assessing ACS risk within this unique rural demographic. By examining the GRACE Risk Score's performance in a rural setting, this study aims to provide valuable insights and potentially improve risk stratification and management strategies for underserved populations.

MATERIAL AND METHODS

This observational cross-sectional study was conducted in the Department of Medicine, Jhalawar Medical College, Jhalawar and SRG hospital. The necessary clearances from the concerned departments and the institutional ethical committee had been taken prior to the start of the study.

A total of 200 patients who were admitted at Jhalawar Medical College & SRG hospital, Jhalawar from February 2022 to December 2022 were included in this study after obtaining their written informed consent. Patients included in the study were based on inclusion and exclusion criteria.

Inclusion & Exclusion Criteria

Patients who were diagnosed having first incidence of acute coronary syndrome were included. Patients were excluded if they had a known diagnosis of coronary artery disease (CAD), declined to provide consent, or were discharged before their data could be fully collected.

Data Collection

During the specified period, all patients with acute coronary syndrome admitted to SRG Hospital Jhalawar were screened for eligibility. After obtaining informed consent, patients meeting the study criteria were enrolled. Data collection was performed using a standardized proforma. This included a comprehensive history (both present and past), a thorough clinical examination covering vital signs and systemic evaluation, and recording of the patients' treatments. For STEMI patients, only those who received thrombolysis were included.

Key data points such as pulse, blood pressure, and Killip class were recorded. Serum creatinine levels were measured, and cardiac biomarkers, including troponin T or CK-MB, were assessed. Oral consent was obtained from all patients for a comprehensive clinical history, examination, and necessary laboratory investigations. The information gathered from each patient was then recorded in the designated proforma.

Demographic details, such as age and sex, along with presenting symptoms and risk factors (e.g., smoking, alcohol use, diabetes, hypertension, and family history of coronary artery disease) were recorded. A detailed physical examination was conducted, including both general and systemic assessments. Anthropometric measurements, including height, body weight, and BMI, were taken following standard guidelines. Vital signs were documented, and the GRACE Risk Score was calculated accordingly.

Calculation of GRACE score: Eight parameters are used for calculating GRACE score that includes:

1) Age
2) Heart Rate
3) Systolic Blood Pressure
4) Killip class
5) Serum Creatinine levels
6) Cardiac arrest at hospital admission
7) ST segment deviation in ECG
8) Elevated Serum Cardiac Markers (Cardiac Troponin or CK-MB)

Statistical Methods

Data Analysis:

Data was analysed using Statistical softwares namely SPSS 22.0, Stata 17.0 and Graph Pad. Microsoft Word and Excel softwares have been used to generate graphs, tables etc.

Statistical Methods:

In this study, descriptive statistical analysis was conducted.

Results for continuous variables are reported as mean ± standard deviation (SD) with the range (minimum-maximum), while results for categorical variables are presented as counts and percentages.

Cramer's V coefficient analysis has been carried out to find the association between risk factors and death of patients with acute coronary syndrome.

The significance levels are defined as follows:

- Significant : P value < 0.05,
- Strongly significant : P value < 0.01

OBSERVATIONS & RESULTS

Demographic Data: 200 cases of acute coronary syndrome admitted in Jhalawar Medical College & SRG hospital, Jhalawar, who gave informed consent and met the inclusion criteria were recruited. Out of these, 150 (75%) were males and 50 (25%) were females. The mean age of the cases was 59.45 ±12.56 years. The maximum number of cases in this study were in the age group between 60-69 years which was followed by age group of 50-59 years. The youngest case was 33 years old (male) and oldest case was 93 years old. The average age in males was 59.72 years, while the average age in females was 59.15 years.

100 patients (50%) had NON-STE ACS {includes NSTEMI and Unstable Angina}. Rest 100 patients (50%) had STEMI.

Table 1: Risk Factor Profile

PAST HISTORY	CASES	%
FAMILY HISTORY	52	26%
DYSLIPIDEMIA	92	46%
HYPERTENSION	88	44%
SMOKING	102	51%
ALCOHOL	86	43%
OBESITY	60	30%
TOBOCCO CHEWING	98	49%
DIABETES	40	20%

In this study group, smoking emerged as the most prevalent risk factor for acute coronary syndrome, affecting 51% of participants. Tobacco chewing was the second most common risk factor, present in 49% of the group, followed by dyslipidemia, which was observed in 46%.

Table 2: Association Of Various Parameters With Mortality

Attribute	Category	Number of Patients Expired	Percentage (%)	Results
Mortality Distributio n by Age	<30	0	0%	Age >50 is not significant for mortality but associated with adverse events (OR 4.65).
	30-39	0	0%	
	40-49	1	7.14%	
	50-59	1	7.14%	
	60-69	1	7.14%	
	70-79	6	42.80%	
	80-89	4	28.50%	
	>90	1	7.14%	
Heart Rate at Admission and Mortality	<50	0	0%	Heart rate >150 is highly significant (P < 0.01, OR 38.200, 95% CI: 16.085–90.723).
	50-69	0	0%	
	70-89	0	0%	
	90-109	1	7.10%	
	110-149	4	28.50%	
	150-199	9	64.20%	
	>200	0	0%	
Systolic Blood Pressure at Admission and Mortality	<80	8	57.10%	Systolic BP <90 mmHg is highly significant (P < 0.01, OR 60.667, 95% CI: 14.234–258.875).
	81-100	4	27.50%	
	101-119	0	0%	
	120-159	1	7.14%	
	160-199	1	7.14%	
	>200	0	0%	
Serum Creatinine and Mortality	0.8 - 1.19	0	0%	Serum creatinine >2 is highly significant (P < 0.01, OR 95.455, 95% CI: 18.693–480.500).
	1.20 - 1.58	0	0%	
	1.59 - 1.90	1	7.14%	
	2.0 - 3.99	10	71.40%	
	>4	3	21.40%	
Killip Class and Mortality	Class 1	1	7.14%	Killip Class 4 is highly significant (P < 0.01, OR 32, 95% CI: 14.559–70.336).
	Class 2	1	7.14%	
	Class 3	4	28.50%	
	Class 4	8	56.50%	
Duration from Admission to Mortality	<24 Hours	10	71.40%	Most deaths occurred within 24 hours of admission.
	1-2 Days	2	14.20%	
	2-3 Days	1	7.14%	
	3-4 Days	0	0%	
	4-5 Days	0	0%	
	5-6 Days	0	0%	
	>7 Days	1	7.14%	

In our study heart rate at the time of admission more than 150, Systolic blood pressure <90 mm Hg, Serum creatinine >2 and Killip class 4 is highly significant to predict mortality in our study.

Most death occurred within 24 hours from the admission time.

In our study, all four patients with a GRACE score ≥300 expired, indicating that a very high GRACE score (≥300) is associated with 100% mortality.

Table 3: Group Statistics

	Outcome	N	Mean	Std. Deviation	Std. Error Mean
GRACE SCORE	Dead	14	262.14	48.523	12.968
	Alive	186	128.66	31.018	2.274

Comparing mean scores between alive and dead
Mean difference 133.482
SE difference 8.995
95% CI 115.742 TO 151.221
P value <0.001
Grace Risk Score In Our Study Is Highly Significant To Calculate In-hospital Mortality.

DISCUSSION

Myocardial infarction is the leading cause of death in India, and global CVD deaths increased by 32% from 1990 to 2019. Coronary Heart Disease significantly contributes to global years of life lost and DALYs. Given poor survival rates for high-risk patients, precise risk estimation and early stratification are crucial for effective treatment and management of Acute Coronary Syndrome (ACS). While guidelines from ACC/AHA[17] and ESC recommend specific treatments for high-risk patients, cardiac catheterization is underused due to inadequate risk stratification. Although many risk scores have been developed, only a few are widely implemented.

The most popular risk scores are PURSUIT (Platelet glycoprotein 2b/3a in Unstable angina: Receptor Suppression Using Integrilin Therapy) and TIMI (Thrombolysis In Myocardial Infarction) risk scores, both derived from clinical trial populations, and the GRACE (Global Registry of Acute Coronary Events) risk score which was developed from an international registry.

The National Institute for Health and Care Excellence (NICE) evaluated all available risk scores for Acute Coronary Syndrome (ACS) using a diverse cohort of approximately 70,000 patients in the UK. The NICE guideline 94, released in 2010[10], along with guidelines from the European Society of Cardiology (ESC), American Heart Association (AHA), and American College of Cardiology (ACC) in 2012, recommended the use of the GRACE risk score due to its superior performance compared to other published risk assessment tools. Additionally, fifty-five countries have committed to adopting the ESC cardiovascular guidelines.

Risk Factors For Acute Coronary Syndrome And In Hospital Mortality

Among the various risk factors for acute coronary syndrome (ACS), smoking was the most prevalent in this study group, affecting 51% of participants. Dyslipidemia (46 %), Alcohol ingestion (43 %), Hypertension (44 %), Tobacco chewing (49 %), family history (26%) and diabetes (21%) were also much prevalent in the study group.

Analysis of the association between various risk factors and mortality in acute coronary syndrome was done using the Cramer's V Coefficient or Ø. Its value varies from 0 (no association between the variables) to 1 (complete association).

The analysis using Cramér's V coefficient showed weak associations for hypertension (0.14), diabetes (0.03), and alcohol consumption (0.08). Dyslipidemia (0.25), smoking (0.12), obesity (0.23), and family history of ACS (0.13) had moderate associations with mortality in acute coronary syndrome. None of the risk factors were strongly associated with mortality in our study.

Grace Risk Score And Acute Coronary Syndrome (ACS)

1. The GRACE Risk Score shows a statistically significant correlation with in-hospital mortality, with a p-value of less than 0.001. Patients who did not survive had an average GRACE Score of 262.14, while those who survived had an average score of 128.66.

2. Risk Categorization

Table 4: Comparison of In-Hospital Mortality with Grace Risk Score

GRACE RISK SCORE	NO OF PATIENTS with NON-STE-ACS	NO OF PATIENTS with STEMI	NO OF PATIENTS EXPIRED
LOW RISK CATEGORY 1 – 108 FOR NON STE-ACS 49-125 FOR STEMI	56	18	0
INTERMEDIATE RISK CATEGORY 109-140 FOR NON STE-ACS 126-154 FOR STEMI	26	34	0

HIGH RISK CATEGORY 141-372 FOR NON STE-ACS 155-319 FOR STEMI	18	48	4 IN NON STE- ACS 10 IN STEMI
TOTAL	100	100	14

GRACE score was high in STEMI and low in NON-STE ACS. Score more than 140 in NON-STE ACS and more than 154 in STEMI is considered as high risk.

All patients who expired had high GRACE risk scores, regardless of the type of myocardial infarction (MI) they experienced. The patients who are in high-risk category should get prompt and urgent care.

In our study, the GRACE risk score had 100% sensitivity and high specificity (85.42% for NON-ST-Elevation ACS, 70% for ST-Elevation Myocardial Infarction) for predicting mortality. Its negative predictive value was 100%, and the positive predictive value was 25% for STEMI and 22.22% for NON-ST-Elevation ACS.

Table No. 5: Comparison Of Grace Risk Score Of The Current Study With Literature.

STUDY	Number Of Patients	Significiant Parameters	Non-significant Parameters	C-statistic Value
Pamela J bradshaw, Sandrac Thompson11	892	Age>65, cardiac markers positivity	ST segment deviation	0.75-0.79
Amar.R.Prabhudesi S Iyrnger13	235	Systolic BP, ST segment deviation, cardiac marker positivity, serum creatinine	Killip class, age>50	0.75
Lim, W.J. et al14	428	Age>65, Dyslipidemia, Family history of Ischemic Heart Disease, Lower Systolic BP	Cardiac markers positivity, Smoking	>0.8
Kumar D, Ashok A15	300	Higher Age, diabetes mellitus	Obesity, Dyslipidemia, Smoking	0.80
Our study	200	Serum creatinine,Killip class,Heart rate,BP,	Age>50,cardiac markers positivity.	0.99

In our study, which examined 200 ACS patients for the combined endpoint of in-hospital mortality, several factors were significantly associated with adverse events: serum creatinine levels >2 mg/dl ($p<0.001$), heart rate >150 beats/min ($p<0.001$), systolic blood pressure <90 mmHg ($p<0.001$), and Killip class IV ($p<0.001$). Age >50 years ($p<0.110$) demonstrated a notable association with an odds ratio (OR) of 4.3. However, positivity for cardiac biomarkers was not significantly associated with adverse outcomes ($p=0.056$, OR 0.913). The overall GRACE score showed excellent discrimination for predicting in-hospital mortality ($p<0.001$), with a C-statistic of 0.99 and a 95% confidence interval of 115.742 – 151.221.

Key Findings Included:

1. The primary parameter studied was the GRACE Risk Score for predicting in-hospital mortality. The GRACE Risk Score demonstrated a statistically significant correlation with in-hospital mortality ($p<0.001$). The average GRACE Risk Score for deceased patients was 262.14, in contrast to 128.66 for those who survived.
2. Among the components of the GRACE Risk Score, heart rate, systolic blood pressure, serum creatinine, and Killip class all showed a statistically significant correlation with in-hospital mortality ($p<0.001$).
3. GRACE risk score had high sensitivity, high specificity, high negative predictive value, low positive predictive value for predicting mortality in high-risk patients.
4. GRACE risk score had higher specificity for NON-STE-ACS than STEMI.

CONCLUSIONS

This study demonstrates that the GRACE Risk Score is highly effective in predicting in-hospital mortality among patients with Acute Coronary Syndrome. Its accuracy in assessing risk underscores its utility as a crucial tool for identifying high-risk patients. Implementing the GRACE Risk Score routinely in hospital settings can help prioritize care and tailor treatment strategies to improve patient outcomes. By accurately stratifying risk, hospitals can better manage high-risk patients and potentially reduce overall mortality rates.

Limitations

There are a few limitations to this study that need to be mentioned.

- It included only 200 patients, which may affect generalizability compared to larger Western studies.
- Seriously ill patients were excluded due to consent issues, potentially introducing selection bias.
- Lack of follow-up after discharge limits long-term outcome assessment.
- All patients had ST-segment changes and no cardiac arrest at admission, so these factors couldn't be correlated with mortality.

KEY POINTS

Question: How effective is the GRACE risk score in evaluating the risk of acute coronary syndrome (ACS) and predicting in-hospital mortality?

Finding: In this cross-sectional study of 200 ACS patients, all fatalities had high GRACE risk scores. The GRACE score showed 100% sensitivity, high specificity (85.42% for NON-ST-Elevation ACS, 70% for STEMI), 100% negative predictive value, and low positive predictive value (25.00% for STEMI, 22.22% for NON-ST-Elevation ACS) for predicting mortality in high-risk patients.

Meaning: The GRACE Risk Score effectively predicts in-hospital mortality in Acute Coronary Syndrome patients, highlighting its value in identifying high-risk individuals.

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