

Global Registry of Acute Coronary Events (GRACE) Risk Score as a Predictor of In-hospital Mortality for Acute Coronary Syndrome in Trinidad and Tobago

M Chin¹, T Cummings², C Thomas², T Seemungal¹

ABSTRACT

Objective: To determine whether risk stratification using the Global Registry of Acute Coronary Events (GRACE) risk score is a predictor of in-hospital mortality for patients with acute coronary syndrome (ACS) in a multi-ethnic Caribbean population.

Method: During a six-month period, all patients meeting the GRACE diagnostic criteria for one of the acute coronary syndromes were entered into a prospective single-centre study at one of the major public hospitals in Trinidad and Tobago. Clinical data, the GRACE risk score and in-hospital morbidity and mortality were recorded. Patients were placed into three GRACE risk categories: low, intermediate or high risk.

Results: There were 372 patients (mean age 63 years; males 56% and females 44%; hypertension 69%, diabetes mellitus 58%, positive smoking history 43%, previous myocardial infarction 34%), of which 25% were ST-segment elevation myocardial infarction, 56% non-ST-segment myocardial infarction and 19% unstable angina pectoris. In-hospital mortality was 8.3%. There were 35%, 33% and 32% of patients in the high, intermediate and low GRACE risk categories, respectively. The GRACE risk score demonstrated good discrimination (C statistic 0.82, 95% CI 0.755, 0.879; $p < 0.001$) and good calibration (Hosmer-Lemeshow; $p = 0.096$) for in-hospital mortality in this ACS cohort.

Conclusion: The GRACE risk score was found to be a reliable predictor of in-hospital mortality in this ACS population and therefore can be used to identify those high-risk patients who may benefit from aggressive management strategies, thereby allowing for more effective use of limited resources.

Keywords: Acute coronary syndrome, age, cardiac arrest, creatinine, GRACE risk score, in-hospital mortality, Killip score, Trinidad and Tobago

La Puntuación de Riesgo del Registro Global de Eventos Coronarios Agudos (GRACE) como Predictor de Mortalidad Intrahospitalaria a Causa del Síndrome Coronario Agudo en Trinidad y Tobago

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RESUMEN

Objetivo: Determinar si la estratificación de la puntuación de riesgo usando el Registro Global de Eventos Coronarios Agudos (GRACE), es un predictor de la mortalidad intrahospitalaria en pacientes con síndrome coronario agudo (SCA) en una población multi-étnica del Caribe.

Método: Por un período de seis meses, todos los pacientes que satisfacían los criterios diagnósticos de GRACE en relación con alguno de los síndromes coronarios agudos, pasaron a formar parte de un estudio prospectivo de monocéntrico en uno de los principales hospitales públicos de Trinidad y Tobago. Se registraron los datos clínicos, la puntuación de riesgo de GRACE, y la morbilidad y mortalidad intrahospitalarias. Los pacientes fueron colocados en tres categorías de riesgo de GRACE: bajo, intermedio y alto.

Resultados: Hubo 372 pacientes (edad promedio 63 años; varones 56% y mujeres 44%; hipertensión arterial 69%, diabetes mellitus 58%, historia de tabaquismo positiva 43%, infarto de miocardio previo 34%), de los cuales 25% tuvieron infarto del miocardio con elevación del segmento ST, 56% infarto del

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miocardio sin elevación del segmento ST, y 19% angina de pecho inestable. La mortalidad intrahospitalaria fue de 8.3%. Hubo 35%, 33% y 32% de los pacientes en las categorías de riesgo de GRACE alta, intermedia y baja, respectivamente. La puntuación de riesgo de GRACE demostró buena discriminación (C estadística 0.82, 95% IC 0.755, 0879; $p < 0.001$) y buena calibración (Hosmer-Lemeshow; $p = 0.096$) para la mortalidad intrahospitalaria en esta cohorte de SCA.

Conclusión: Se halló que la puntuación de riesgo de GRACE es un predictor fiable de la mortalidad intrahospitalaria en esta población de SCA, y por lo tanto puede utilizarse para identificar a aquellos pacientes de alto riesgo que pueden beneficiarse de estrategias de tratamiento agresivas, lo que permite un uso más eficaz de los limitados recursos.

Palabras claves: Síndrome coronario agudo, edad, paro cardíaco, creatinina, puntuación de riesgo de GRACE, mortalidad intrahospitalaria, puntuación de Killip, Trinidad y Tobago

West Indian Med J 2016; 65 (1): 53

INTRODUCTION

Acute coronary syndrome (ACS) is responsible for half of all cardiovascular deaths worldwide (1). The survival of hospitalized ACS patients is dependent on multiple factors. The current American Heart Association/American College of Cardiology (AHA/ACC) and European Society of Cardiology (ESC) guidelines recommend the use of various risk scores as suitable and sufficiently accurate guides for risk stratification to identify high-risk patients who are more likely to benefit from an early invasive strategy *versus* a conservative strategy (2, 3). This is beneficial in resource-poor countries as limited resources could be utilized on those high-risk patients who are likely to benefit the most. The Global Registry of Acute Coronary Events (GRACE) risk score can be used for risk stratification of the whole spectrum of ACS (4, 5). It was derived from the GRACE registry which was a large, multinational, observational study of hospitalized patients with suspected ACS involving 94 hospitals in 14 countries. The eight factors which contained most (70%) of the prognostic information used to create the GRACE risk model include: Killip class, age, systolic blood pressure, resuscitated cardiac arrest, positive initial cardiac biomarkers, creatinine, ST-segment deviation and heart rate, which are all taken at admission. Taking into consideration the geographic and population differences that may exist in other countries compared to the GRACE registry population which was predominantly Caucasian, it is important to validate the GRACE score in countries and populations that may be different. This was done in multiple countries and in countries such as Singapore which has a predominantly multi-ethnic Asian population, the GRACE risk score systematically underestimated the risk of absolute mortality; as such, high-risk patients were inappropriately classified as low risk (6, 7). In order to reflect observed mortality and improve mortality estimation in this population, recalibration of the GRACE risk score was required. For Trinidad and Tobago, which consists of a multi-ethnic population of predominantly Afro-Trinidadians and Indo-Trinidadians (South Asians), as well as a high prevalence of cardiac risk factors such as diabetes mellitus and hypertension, it is important to

determine whether the GRACE risk score could be a predictor of in-hospital mortality in this ACS population before being widely recommended for use. The GRACE risk score has not previously been validated in any Caribbean population.

The primary objective of this study was to determine whether the GRACE risk score is a predictor of in-hospital mortality in a predominantly Afro-Trinidadian and Indo-Trinidadian multi-ethnic population of patients with ACS in a major hospital in Trinidad and Tobago.

SUBJECTS AND METHODS

This study was a prospective, single-centre, cross-sectional study which was carried out at one of the major hospitals, Eric Williams Medical Sciences Complex (EWMSC), in Trinidad and Tobago. It was conducted during the period of November 1, 2011 to April 30, 2012. The Ethics Committee of the University of the West Indies granted permission for this study to be conducted. Written, informed consent was obtained from all living patients or their relatives in the case of those who died.

Patients who were admitted to the Accident and Emergency Department of the EWMSC during the study period and diagnosed with one of the acute coronary syndromes according to the GRACE diagnostic criteria (5) by the admitting medical consultant were included in this study. Patients must have been more than 18 years of age, alive at the time of admission and must have had symptoms of acute cardiac ischaemia within 24 hours of presentation. Patients with symptoms of acute cardiac ischaemia who died within 24 hours of hospitalization, but did not meet the GRACE diagnostic requirements for one of the acute coronary syndromes were included providing they had all parameters to calculate the GRACE risk score and cause of death was confirmed by post mortem to be from acute myocardial infarction.

The following patients were excluded: patients with significant non-cardiac co-morbidity, motor vehicle accident, severe gastrointestinal bleeding, trauma or surgery that precipitated the ACS; patients who were initially entered into the study with a presumptive diagnosis of ACS, but later found not

to have ACS by the admitting consultant or research member; those with insufficient data to calculate the GRACE risk score; patients readmitted within the study period (six months); patients who did not give consent or those that took self-discharge from hospital. Symptoms of acute cardiac ischaemia within 24 hours of admission to hospital included: cardiac type chest pain, angina equivalent symptoms and recurrent chest pain [atypical chest pain] (8).

GRACE ACS definitions (5)

ST-segment elevation myocardial infarction (STEMI): symptoms of acute cardiac ischaemia, new or presumed new persistent ST-elevation of more than 1 mm (> 0.1 mV) in 2 or more contiguous leads in all leads except V2-V3, where it should be more than 2 mm (> 0.2 mV) or new onset left bundle branch block and positive cardiac enzymes.

Non-ST-segment elevation myocardial infarction (NSTEMI): symptoms of acute cardiac ischemia; no new ST-segment elevation seen on the index electrocardiogram (ECG) or on any subsequent ECG and positive cardiac enzymes.

Unstable angina pectoris (USAP): symptoms of acute cardiac ischaemia; negative cardiac enzymes during hospital stay and at least one of the definitions for at least one of the following: history of coronary artery disease, new documentation of coronary artery disease and ECG changes suggestive of acute cardiac ischaemia (5).

Data collection

Patients included in the study were followed-up from admission to discharge or in-hospital death (all-cause mortality, primary outcome) and data were obtained from the patient and the medical charts using a data collection tool. Clinical data obtained included: demographic information, prior diagnosed medical conditions, previous cardiac investigations and interventions, physical examination findings, laboratory findings such as creatinine and serial cardiac enzymes (Troponin I, Troponin T and creatinine kinase MB), serial electrocardiographic findings, medical treatment received in-hospital, interventions done in hospital, complications and the GRACE parameters (Table 1). Standardized definitions as used in the GRACE study were used for all clinical diagnoses and in patient complications (5).

Table 1: The various parameters in the GRACE risk categories of this study population and the original GRACE registry

| Parameter | Low risk (n = 119) | Intermediate risk (n = 124) | High risk (n = 129) | All (n = 372) | GRACE registry |
|---|-----------------------|--------------------------------|------------------------|---------------|-------------------|
| Age, (mean, year) | 52 | 62.3 | 72 | 62.7 | 66 (56, 75) |
| Male (%) | 68.1 | 51.6 | 50.4 | 56.5 | 66.5 |
| Ethnicity (%) | | | | | |
| Afro-Trinidadian | 16.8 | 19.4 | 25.6 | 20.7 | – |
| Indo-Trinidadian | 73.9 | 75 | 68.2 | 72.3 | – |
| Other | 6.2 | 5.6 | 9.2 | 7.0 | – |
| Type of ACS (%) | | | | | |
| STEMI | 21.8 | 26.6 | 27.1 | 25.3 | 31.9 |
| NSTEMI | 38.7 | 59.7 | 68.2 | 55.9 | 27.0 |
| USAP | 39.5 | 13.7 | 4.7 | 18.8 | 41.1 |
| Symptoms (%) | | | | | |
| Cardiac type chest pain | 80.7 | 71.8 | 62 | 71.2 | – |
| Angina equivalent | 7.6 | 16.1 | 35.7 | 20.2 | – |
| Recurrent chest pain | 11.7 | 12.1 | 9.3 | 8.6 | – |
| Medical history | | | | | |
| Hypertension | 62.2 | 75 | 69.8 | 69.1 | 57.8 |
| Diabetes mellitus | 47.1 | 61.3 | 63.6 | 57.5 | 23.3 |
| History of hyperlipidaemia | 39.5 | 32.3 | 21.7 | 30.9 | 43.6 |
| Previous MI | 36.1 | 33.1 | 31.8 | 33.6 | 32 |
| Previous PCI | 7.6 | 9.7 | 2.3 | 6.5 | 14 |
| Previous CABG | 5.9 | 4.8 | 2.3 | 4.3 | 8.0 |
| Previous diagnostic angiogram of CAD | 14.3 | 12.1 | 7.8 | 11.3 | – |
| Congestive heart failure | 0.8 | – | 2.3 | 1.1 | 11.0 |
| Current/previous smoking | 39.4 | 31.3 | 29.4 | 43.0 | – |
| Family history of CAD | 24.4 | 17.7 | 9.3 | 16.9 | – |
| Chronic kidney disease | 2.5 | 4 | 11.6 | 6.2 | – |

Table 1(Cont'd) : The various parameters in the GRACE risk categories of this study population and the original GRACE registry

| GRACE risk parameters | | | | | |
|---|----------------|-----------------|----------------|------------------|----------------|
| Heart rate (median [25, 75], beat/min) | 77 (67, 92) | 84 (71, 95) | 90 (70, 110) | 83 (70, 100) | 76 (65, 90) |
| Systolic blood pressure (median [25, 75], mmHg) | 147 (129, 173) | 139 (118, 163) | 137 (115, 154) | 140.5 (121, 161) | 140 (120, 160) |
| Killip class | | | | | |
| Class 1 | 94.1 | 81.3 | 39.5 | 71.0 | 82.7 |
| Class 2 | 5.9 | 16.1 | 43.4 | 22.3 | 13.2 |
| Class 3 | – | 1.6 | 15.5 | 5.9 | 3.1 |
| Class 4 | – | 0.8 | 1.6 | 0.8 | 1.0 |
| Resuscitated cardiac arrest at admission | – | – | 4.7 | 1.6 | 1.5 |
| Positive cardiac enzymes | 52.1 | 79.0 | 88.4 | 73.7 | 31.6 |
| ST deviation | 26.9 | 40.3 | 65.1 | 44.6 | 54.1 |
| Creatinine (median [25, 75] mg/dL) | 0.9 (0.7, 1.1) | 1.0 (0.8, 1.24) | 1.2 (0.8, 1.7) | 1.0 (0.8, 1.3) | 0.88 |
| GRACE risk score | 93 (80, 100) | 128 (119, 136) | 172 (161, 193) | 129 (101, 162) | – |
| Inpatient medical treatment | | | | | |
| Aspirin | 98.3 | 99.2 | 97.7 | 98.4 | 93.6 |
| Clopidogrel | 99.2 | 100 | 98.4 | 99.2 | 31.8 |
| Low molecular weight heparin | 99.2 | 98.4 | 98.4 | 98.7 | 44.2 |
| Nitrates | 97.5 | 98.4 | 87.6 | 98.4 | – |
| Statins | 95.8 | 95.2 | 91.5 | 94.1 | 49.3 |
| Beta blockers | 97.5 | 94.4 | 98.4 | 92.5 | 80.6 |
| ACE-inhibitors | 96.6 | 94.4 | 91.5 | 92.7 | 56.4 |
| Diuretics | 4.2 | 10.5 | 34.9 | 16.9 | – |
| Calcium channel blockers | 3.4 | 8.1 | 5.4 | 5.6 | 27.5 |
| STEMI receiving thrombolytic therapy | 76.9 | 57.6 | 54.3 | 61.7 | 47.0 |
| Inpatient procedures | | | | | |
| Inpatient angiogram | 11.8 | 12.9 | 7.0 | 10.5 | 49.1 |
| Inpatient PCI | 2.5 | 0.8 | 0.8 | 1.3 | 26.6 |
| Inpatient CABG | 0.8 | 0.8 | 0.8 | 0.8 | 5.0 |
| Inhospital complications | | | | | |
| Recurrent symptoms of cardiac ischaemia | 21.6 | 13.7 | 14.7 | 16.7 | 34.5 |
| Clinical heart failure | 2.5 | 10.5 | 40.3 | 18.3 | 14.4 |
| Cardiogenic shock | 1.7 | 0.8 | 6.2 | 3.0 | 4.5 |
| Ventricular tachycardia | – | – | 2.3 | 0.8 | 5.0 |
| Major bleed | – | – | 0.8 | 0.3 | 3.6 |
| Atrial fibrillation | 0.8 | – | – | 0.3 | 8.7 |
| Cerebrovascular accident | – | – | 0.8 | 0.3 | 0.9 |
| Outcome | | | | | |
| Discharge | 100 | 96.0 | 79.8 | 91.7 | 95.0 |
| Death | – | 4.0 | 20.2 | 8.3 | 5.0 |
| Duration of hospital stay (day {range}) | 6 (5, 10) | 6 (5, 9) | 6 (5, 10) | 6 (5, 9) | 6.3 |

GRACE: Global registry of acute coronary events; ACS: acute coronary syndrome; STEMI: ST-segment elevation myocardial infarction; NSTEMI: non-ST-segment elevation myocardial infarction; USAP: unstable angina pectoris; MI: myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft surgery; CAD: coronary artery disease; ACE: angiotensin converting enzyme

The eight GRACE risk parameters at admission included: age, systolic blood pressure and heart rate; Killip class based on physical examination findings of the lung fields, jugular venous pressure (JVP) and systolic blood pressure by the admitting physicians as defined by Killip and Kimball *et al* (9); ST deviation (ST depression or ST elevation on ECG); positive cardiac enzymes (elevated Troponin I, T or CKMB using hospital reference values); resuscitated cardiac arrest and baseline creatinine.

The GRACE risk score for each patient was calculated using the eight variables in an online GRACE risk score calculator from the official GRACE website (10). Patients were placed into risk categories based on their risk score and type of ACS. For NSTEMI/USAP, the values for low risk, intermediate and high risk were 1 to 108, 109 to 140 and 141 to 372, respectively. For the STEMI patients, the values for low, intermediate and high risk were 49 to 125, 126 to 154 and 155 to 319, respectively.

Statistical analysis

Data were analysed using SPSS (version 19 for Windows). Data which were normally distributed were summarized by mean (standard deviation, SD) and data not normally distributed were summarized by median (25th percentile, 75th percentile). Normally distributed continuous variables were compared by use of the *t*-test. Relationships between binary coded variables were examined using the Chi-squared test. Odds ratios and 95% confidence intervals were used to determine the association between the eight GRACE risk parameters and in-hospital mortality using binary logistic regression analysis.

The sample size for this study was estimated using simple random sampling. In order to test the GRACE risk score, we obtained an ACS population similar to that of the GRACE registry (38% STEMI and 62% NSTEMI/USAP patients). We used the larger portion of ACS patients (62% NSTEMI/USAP patients) as the estimated prevalence of the variable to calculate the sample size with an acceptable margin of error at 5% which yielded a sample size of 362 patients.

Calibration and discrimination

GRACE risk score discrimination is the ability to distinguish between patients who will die in hospital and those who will survive. This was done for the entire ACS cohort and analysed by calculating the area under the ROC (receiver operating characteristic) curve (AUC-ROC). Values of 0.7 to 0.8 show acceptable discrimination, values of 0.8 to 0.9 indicate good discrimination and values of ≥ 0.9 show outstanding discrimination.

Hosmer-Lemeshow goodness-of-fit test was used on the entire ACS cohort to evaluate the model's calibration. This test is used to validate newly created models and also existing logistical models with an external database as done in this

study. A *p* value of < 0.05 indicates that the model is well adjusted to the data and therefore is a good predictor of patient's probability of death.

RESULTS

A total of 384 patients met the criteria for inclusion but 12 patients were excluded for the following reasons: four patients took self-discharge, six patients did not give consent and for two patients, data collected were insufficient to calculate the GRACE risk score. Three of the twelve patients who were excluded died in hospital and included: two patients with insufficient data to calculate the GRACE risk score and consent was not obtained for one. Of the 372 patients analysed, there were 94 (25.3%) STEMI, 208 (55.9%) NSTEMI and 70 (18.8%) USAP patients. There were 129 (34.7%), 124 (33.3%) and 119 (32%) patients in the high, intermediate and low GRACE risk categories, respectively. Three hundred and forty-one (91.7%) patients were discharged from hospital and 31 (8.3%) patients died in hospital.

Baseline characteristics and relation with mortality

Baselines characteristics and comparison to the GRACE registry can be seen in Table 1. The mean (SD) age was 63 (12.8) years with fewer females (43.5%) compared to males (56.5%). The mean age for those that died while in hospital [mean (SD) = 71 (12.7 years)] was significantly higher than those that were discharged [mean = 62 years, $p < 0.001$; Table 2]. There were more Indo-Trinidadians (72.3%) compared to Afro-Trinidadians (20.7%) and mixed ethnicity (6.7%). The death rate was higher in the mixed ethnicity (12%) compared to the Indo-Trinidadian (8.2%) and Afro-Trinidadian (7.8%) patients, however, this difference was not statistically significant ($p > 0.05$).

Table 2: The various parameters in the outcome groups (death and discharge)

| Parameter | Discharge | Death | <i>P</i> value |
|----------------------------------|-----------|-------|----------------|
| Age (mean, year) | 62 | 71 | < 0.001 |
| Male | 56.9 | 51.6 | 0.057 |
| Ethnicity (%) | | | |
| Afro-Trinidadian | 20.8 | 19.4 | > 0.05 |
| Indo-Trinidadian | 72.4 | 71.0 | > 0.05 |
| Other | 6.7 | 9.7 | > 0.05 |
| Type of ACS (%) | | | |
| STEMI | 25.2 | 25.8 | – |
| NSTEMI | 54.3 | 74.2 | 0.015 |
| USAP | 20.5 | – | 0.015 |
| GRACE risk categories (%) | | | |
| High | 30.2 | 83.9 | < 0.001 |
| Intermediate | 34.9 | 16.1 | < 0.001 |
| Low | 34.9 | 0 | < 0.001 |
| Symptoms (%) | | | |
| Cardiac type chest pain | 72.7 | 54.8 | 0.006 |
| Angina equivalent | 18.2 | 41.9 | |
| Recurrent chest pain | 9.1 | 3.2 | |

Table 2 (Cont') : The various parameters in the outcome groups (death and discharge)

| | | | |
|--|----------------|----------------|---------|
| Medical history (%) | | | |
| Hypertension | 68.9 | 71 | > 0.05 |
| Diabetes mellitus | 58.1 | 51.6 | > 0.05 |
| History of hyperlipidaemia | 32 | 9.7 | 0.008 |
| Previous MI | 34.6 | 22.6 | > 0.05 |
| Previous PCI | 6.7 | 3.2 | > 0.05 |
| Previous CABG | 4.4 | 3.2 | > 0.05 |
| Previous diagnostic angiogram of CAD | 11.7 | 6.5 | > 0.05 |
| Congestion heart failure | 0.9 | 3.2 | > 0.05 |
| Current/previous smoking | 44.6 | 25.8 | 0.043 |
| Family history of CAD | 18.2 | 3.2 | 0.034 |
| Chronic kidney disease | 4.4 | 25.8 | < 0.001 |
| GRACE risk parameters | | | |
| Heart rate (beats per minute) | 83 (70, 99) | 90 (71, 113) | > 0.05 |
| Systolic blood pressure (mmHg) | 140 (122, 161) | 144 (113, 176) | > 0.05 |
| Killip class (%) | | | |
| Class 1 | 74.2 | 35.5 | – |
| Class 2 | 21.1 | 35.5 | – |
| Class 3 | 4.4 | 22.6 | – |
| Class 4 | 0.3 | 6.5 | – |
| Killip class 2 or more | 25.8 | 64.5 | < 0.001 |
| Cardiac arrest (%) | 0.3 | 16.1 | < 0.001 |
| Positive cardiac enzymes (%) | 73.0 | 80.6 | > 0.05 |
| ST deviation (%) | 44.0 | 51.6 | > 0.05 |
| Creatinine (mg/dL) | 1 (0.8, 1.2) | 1.3 (0.9, 2.4) | 0.01 |
| GRACE risk score | 128 | 172 | < 0.001 |
| Inhospital complications | | | |
| (% Recurrent symptoms of | | | |
| cardiac ischaemia | 16.7 | 16.1 | > 0.05 |
| Clinical heart failure | 14.1 | 64.5 | < 0.001 |
| Cardiogenic shock | 0.9 | 29.0 | < 0.001 |
| Ventricular tachycardia | 0.9 | – | > 0.05 |
| Major bleed | – | 0.3 | > 0.05 |
| Atrial fibrillation | 0.3 | 0.3 | > 0.05 |
| Inpatient medical treatment (%) | | | |
| Aspirin | 98.2 | 100.0 | > 0.05 |
| Clopidogrel | 99.4 | 96.8 | > 0.05 |
| Low molecular weight heparin | 98.8 | 96.8 | > 0.05 |
| Nitrates | 98.5 | 96.8 | > 0.05 |
| Statins | 95.9 | 74.2 | < 0.001 |
| Beta blockers | 95.0 | 64.5 | < 0.001 |
| ACE-inhibitors | 95.3 | 64.5 | < 0.001 |
| Diuretics | 14.1 | 48.4 | < 0.001 |
| Calcium channel blockers | 5.9 | 3.2 | > 0.05 |
| Thrombolytic therapy | 10.9 | 3.2 | > 0.05 |
| Inpatient procedures (%) | | | |
| Inpatient angiogram | 12.6 | – | 0.036 |
| Inpatient PCI | 1.5 | – | > 0.05 |
| Inpatient CABG | 0.9 | – | > 0.05 |
| Outcome | | | |
| Duration of hospital stay (days [range]) | 6 (5, 10) | 3 (1, 4) | < 0.001 |

GRACE: Global registry of acute coronary events; ACS: acute coronary syndrome; STEMI: ST-segment elevation myocardial infarction; NSTEMI: non-ST-segment elevation myocardial infarction; USAP: unstable angina pectoris; MI: myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft surgery; CAD: coronary artery disease; ACE: angiotensin converting enzyme

The most common medical illnesses were hypertension (69.1%) and diabetes mellitus (57.5%). There was a high prevalence of diabetes mellitus (63.6%) in the high-risk GRACE category. Chronic kidney disease occurred in 25.8% of patients who died in-hospital compared to 4.4% in those who were discharged ($p < 0.001$).

GRACE risk parameters and relation with mortality

Of the eight GRACE independent variables used to calculate the GRACE risk score, age, ST deviation, Killip class, cardiac arrest at admission and creatinine at admission were found to be predictors of in-hospital mortality (Table 3), while heart rate, systolic blood pressure and elevated cardiac enzymes at admission were not.

Table 3: Odds ratio for the eight prognostic factors used in the GRACE risk score in this study

| GRACE parameter | Odds ratio (95% CI) | P value |
|---------------------------------------|----------------------|---------|
| Age | 1.047 (1.01, 1.09) | 0.024 |
| Heart rate at admission | 0.99 (0.97, 1.01) | 0.40 |
| Systolic blood pressure at admission | 1.00 (0.99, 1.02) | 0.75 |
| Creatinine at admission | 1.79 (1.24, 2.59) | 0.002 |
| Positive cardiac enzymes at admission | 0.66 (0.21, 2.10) | 0.49 |
| ST segment deviation at admission | 3.42 (1.24, 9.44) | 0.018 |
| Killip class at admission | 2.74 (1.51, 4.99) | 0.001 |
| Cardiac arrest at admission | 79.27 (7.63, 822.98) | < 0.001 |

The median GRACE risk score was 129. There were significantly more in-hospital deaths in the high-risk category (20.2%) than the intermediate-risk category (4.4%, $p < 0.001$) but no deaths in the low-risk GRACE category (Figure).

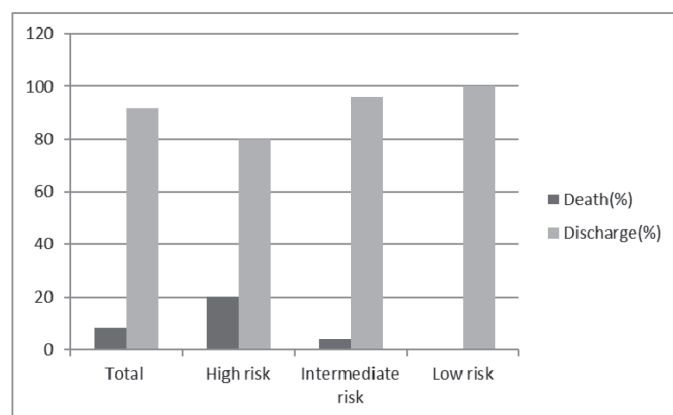


Figure: Comparison of the outcome (in-hospital death versus discharged alive) in high-risk, intermediate-risk and low-risk categories.

The median GRACE risk score for patients who died in hospital (172) was significantly higher than for those that were discharged (128, $p < 0.001$). Most of the patients (83.9%) who died in hospital were in the GRACE high-risk category compared to those who were discharged (30.2%, $p < 0.001$). As the GRACE risk score increased, the predicted probability of in-hospital mortality increased (odds ratio 1.027 (1.018, 1.037);

$p < 0.001$). The GRACE risk score demonstrated good discrimination (C statistic 0.82, 95% CI 0.755, 0.879; $p < 0.001$) and good calibration (Hosmer-Lemeshow); $p = 0.096$) for in-hospital mortality.

Treatment received and outcomes in hospital

Sixty-two per cent of STEMI patients received thrombolytic therapy, 10.5% of patients had an inpatient coronary angiogram, 1.3% had inpatient percutaneous coronary intervention (PCI; non-primary) and 0.8% inpatient coronary artery bypass graft surgery (CAB G). The most common in-hospital complications were heart failure (18.3%), recurrent symptoms of cardiac ischaemia (16.7%), and cardiogenic shock (3%). Significantly more patients who died in hospital had heart failure (64.5% versus 14.1%; $p < 0.001$) and cardiogenic shock (29% versus 0.9%; $p < 0.001$) compared to those who were discharged.

DISCUSSION

This study tested the performance of the GRACE risk score derived from a predominantly Caucasian population (GRACE registry) in a multi-ethnic Caribbean ACS population consisting predominantly of Indo-Trinidadians (70%) and Afro-Trinidadians (21%) with a high prevalence of hypertension (69% versus 58%) and diabetes mellitus (57.5% versus 23.3%). The GRACE risk score used the C index to accurately discriminate between in-hospital ACS survivors and non-survivors. A C index of 0.82 refers to an 82% chance that the non-survivor had a higher GRACE risk score than the survivor. The Hosmer-Lemeshow test showed an insignificant difference between the predicted and observed mortality and therefore good calibration for the GRACE risk score which is essential for reliable risk assessment.

The variables which were found to have the highest predictive probability of in-hospital mortality were cardiac arrest at admission and Killip class. The independent variables which were not found to be predictors were systolic blood pressure, heart rate and positive cardiac enzymes at admission. There were more patients in this cohort with positive cardiac enzymes compared to the GRACE registry; this was seen in other studies with similar trends of positive cardiac enzymes not being found to be a predictor of in-hospital mortality.

The overall in-hospital mortality was 8.3% and in-hospital mortality after 24 hours from presentation was higher than the original GRACE registry (5.9% versus 4.9%). Compared to other studies such as GRACE Canada (6), the overall mortality was higher (8.3% versus 3.4%). The reasons for this higher mortality are likely secondary to the higher prevalence of cardiac risk factors such as diabetes mellitus and much lower rates of coronary angiogram with revascularization in this population compared to other studies. In the GRACE registry, the in-hospital mortality rate for ACS patients with diabetes was almost double that of those patients without diabetes. In a study of outcomes in a diabetic ACS population, Franklin *et al* found that diabetic patients with ACS tended to be older,

female, more likely to have multi-vessel disease and have left ventricular failure, which are all associated with more adverse outcomes (11). Our study did not find diabetes mellitus to be a predictor of in-hospital mortality though the study was not powered to detect this; however, it is possible that the high prevalence of diabetes mellitus in this population is a contributing factor for the higher in-hospital mortality.

Even though most of the patients in this study received the recommended evidence-based medical therapies, only a small percentage of patients had inpatient coronary angiogram (10.5% versus 49.1%) and revascularisation (PCI 1.3% versus 26.6%) compared to those in the GRACE registry. Multiple registries in developed countries have shown the reduction of in-hospital mortality with the use of early invasive strategies as recommended by the current guidelines (12). Many small developing countries such as Trinidad and Tobago have difficulties in implementing an early invasive strategy for ACS patients due to the lack of sufficient facilities and personnel to meet the growing number of ACS patients seen. It is therefore vital that available resources be used in a more cost-effective manner where high-risk patients are accurately identified and treated with an early invasive strategy.

The major limitations in this study were that the study was carried out in a single centre and a small sample size was used compared to other similar studies. There was also a disparity in the proportion of the various ethnic groups, with a greater number of Indo-Trinidadians compared to Afro-Trinidadians; this is not reflective of the population distribution in Trinidad and Tobago and as such, an adequate comparison of in-hospital mortality between the ethnic groups could not be made. A larger, multicentre study is required to identify any differences in these ethnic groups.

In conclusion, the GRACE risk score was found to be a reliable predictor of in-hospital mortality in this cohort of ACS patients. The GRACE risk score can be recommended for use in Trinidad and Tobago as another vital tool to assist physicians in identifying high-risk ACS patients who would benefit the most from an early invasive treatment strategy and low-risk patients who would be best managed conservatively.

ACKNOWLEDGEMENT

This research would not have been possible without the cooperation of the patients and relatives; doctors of the internal medicine department of the Eric Williams Medical Sciences Complex who assisted in data collection and Dr George Legall of the University of the West Indies who assisted in statistical analysis.

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