Internal Medicine

Prognosis and risk of death in patients with non-ST segment elevation acute coronary syndrome: A single-center observational study, application of the GRACE scale.

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Abstract

Introduction: The GRACE score is a validated tool for predicting in-hospital and 6-month mortality in patients with acute coronary syndrome (ACS). This study aimed to measure the mortality of patients with ACS without ST-segment elevation.

Methods: The present observational study was conducted at the Teodoro Maldonado Hospital in Guayaquil, Ecuador, from January to June 2019. The variables were age, comorbidities, sex, systolic blood pressure, serum creatinine, biomarkers of myocardial damage, electrocardiographic changes in the ST segment, and Killip and Kimball classification. In-hospital mortality and mortality six months later were measured. The sample was nonprobabilistic. Noninferential and inferential statistics were used.

Results: A total of 100 patients were analyzed. According to the GRACE scale upon hospital admission, 47% (n = 47) were at high risk, 33% (n = 33) were at moderate risk, and 20% (n = 20) were at low risk. In patients evaluated at six months, mortality increased in 70 patients considered at high risk; patients at intermediate risk maintained the same probability of mortality, which was 22% (n = 22); and patients at low risk at six months represented 8% (n = 8), indicating that all patients developed HIGH RISK.

Conclusions: In this study group, there were no differences in mortality between hospital admission and six months after admission. All mortality cases were high risk.

Keywords:

MeSH: GRACE Scale, Acute Coronary Syndrome without ST-Segment Elevation, Prognosis, Validation.

Abbreviations

GRACE: Global registry of acute coronary events.
ACS: acute coronary syndrome.
TIMI: Thrombolysis in Myocardial Infarction Scale

Supplementary information

No supplementary materials are declared.

Acknowledgments

We thank the administrative staff and patients of the Teodoro Maldonado Carbo Hospital of the Ecuadorian Institute of Social Security in Guayaquil, Ecuador, where the study was conducted.

Authors' contributions

Karen Pamela García Huayamave: Conceptualization, data curation, formal analysis, acquisition of funds, research, writing - original draft.
Telmo Fernández: Acquisition of funds, Research, Methodology, Resources, Supervision, Validation, Visualization, Writing - original draft, Writing - review and edition.
All the authors have read and approved the final version of the manuscript.

Financing

The authors of this article financed the expenses of this research.

Availability of data and materials

The datasets used and analyzed during the present study are available from the corresponding author upon reasonable request.

Introduction

Cardiovascular diseases are the leading cause of death in developed countries [1]. Non-ST-segment elevation acute coronary syndrome is more common than ST-segment elevation ACS. Although mortality at six months was the same between both clinical forms, late mortality (between 6 months and four years) from ACS without ST-segment elevation was more excellent, which can be explained by the profiles of different older patients with more comorbidities. Therefore, invasive assessment should be performed early, within 24 hours for high-risk patients, may be delayed within 24 to 72 hours for intermediate-risk patients, and is not systematic for low-risk patients.

In addition to the two diagnostic elements of electrocardiographic changes and positive troponins, the European Society of Cardiology issued recommendations [2] in which the GRACE score appears as a validated tool for the prediction of in-hospital mortality and, at six months, applies to any ACS [3].

Many studies have tested different predictive scores. The GRACE score is an integral predictor, proving its value. The disadvantage of its application or use is that some doctors need computer software or a smartphone calculation application, making its routine and timely calculation difficult. This situation is reinforced when care is provided in establishments that do not have interventional cardiology.

The clinical guidelines recommend that the optimal management of ACS should include early and individualized stratification of the patient's risk by a specialist physician. In addition to informing patients of their prognosis, an accurate risk assessment can help identify high-risk patients who could benefit the most from intensive medical therapies and early invasive strategies while minimizing unnecessary treatment complications in low-risk patients [4].

The GRACE score is a multinational prospective observational registry that includes patients with the entire spectrum of ACS. It was designed to study an unbiased general population of patients from multiple locations. After the start of GRACE in 1999, an expanded version (GRACE2) was launched in 2003, allowing additional hospitals from various countries to enroll patients. Patients were eligible if they were at least 18 years old and admitted to the hospital with a presumptive diagnosis of ACS, defined as symptoms consistent with cardiac ischemia and at least one of the following: abnormal cardiac biomarkers, ECG changes consistent with ACS, and documented antecedents of coronary artery disease [5].

The following variables were used: age, creatinine, heart rate, systolic blood pressure, presence of heart failure (Killip and Kimball classification), ST segment changes, elevated troponin levels, and cardiac arrest on admission. The scale does not include lipid values or other blood biomarkers [6]. Patients were excluded if their cardiac event precipitated or was accompanied by severe comorbidities such as trauma or surgery [4].

The general objective of this research was to assess the prognosis and risk of death in patients admitted with a diagnosis of acute coronary syndrome without ST-segment elevation in a regional reference public unit for cardiovascular ischemic diseases in Guayaquil, Ecuador.

Materials and methods

Study design

The present study was observational and longitudinal. The source is retrospective.

Stage

This study was carried out at the Outpatient Service of the Teodoro Maldonado Specialty Hospital of the Ecuadorian Institute of Social Security in Guayaquil, Ecuador, from January 1, 2019, to June 30, 2019.

Participants

Adult patients with a diagnosis of non-ST segment elevation myocardial infarction were included. Patients with incomplete data were excluded from the analysis.

Variables

The variables were age, comorbidities, sex, systolic blood pressure, heart rate, serum creatinine, myocardial damage biomarkers, ST segment electrocardiographic changes, history of cardiac arrest, and Killip and Kimball classification. In-hospital mortality and mortality were measured six months later.

Data sources/measurements

The source was indirect; an electronic form was created from the institutional medical history of the patients who entered the hospitalization period. Within the diagnosis of myocardial infarction, the elevation of biomarkers of myocardial necrosis and precordial pain of cardiovascular origin was verified. The information was treated confidentially; no personal data were included to identify the study subjects.

Biases

To avoid possible interviewer, information, and memory biases, the principal investigator always maintained the data with a guide and records approved in the research protocol.

Observation and selection bias were avoided by applying the participant selection criteria. Two researchers independently analyzed each record in duplicate, and the variables were recorded in the database once their agreement was verified.

Study size

The sample was nonprobabilistic, and all the cases from the study period were included.

Quantitative variables

Descriptive statistics were used. The results are expressed as frequencies and percentages.

Statistical analysis

Noninferential statistics were used. For descriptive analysis, frequencies and percentages are presented. For the incidents, the 95% confidence intervals are presented for proportions. Statistical comparisons between proportions were made with chi-square tests. The statistical package used was IBM Corp., Released in 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.

Results

Participants

A total of 700 patients with heart attack/angina pectoris and chest pain were analyzed during this period. One hundred patients (14.29%) met the inclusion criteria.

Main characteristics of the study group

Seventy-six percent of the patients were ≥60 years old, and 24% were <60 years old; 53% were males, and 47% were females. The most frequent comorbidity was arterial hypertension (79%), followed by hyperlipidemia (44%), cardiac catheterization (44%), diabetes (35%), smoking (18%), chronic kidney disease (16%), and thyroid disease (9%). Sixty-eight percent of the patients had a blood pressure ≥120 mmHg, 69% had a heart rate ≥ 70, 70% had a blood pressure <0.80 mg/dl and 30% had a heart rate ≥0.80 mg/dl. Fifty percent of the patients had biomarkers of myocardial damage, 67% presented TS changes, and 7% had cardiac arrest. According to the Killip-Kimball classification, 80% presented functional class 1, 19% functional class 2, and 1% functional class 3. The hospital mortality rate was 9%. At six (6) months, the mortality rate was the same; no deaths were recorded after discharge (Table 1).

GRACE rating scale

The mean GRACE score was 145.86, with a standard deviation of 46.91. This scale reflects normal behavior (Figure 1). According to the GRACE score, the risk of mortality was classified as follows: for in-hospital mortality, the risk was low (≤108) 20%, intermediate (109-140) 33%, and high (> 140) 47%; for six (6) months, the risk was low (≤88) 8%, intermediate (89-118) 22% and high (> 118) 70% (Figure 2). The GRACE score for survivors was 137, and for nonsurvivors, it was 227 (P <0.0001). The proportion of deaths in the hospital period is presented in Table 2, which was exclusively in the group with the highest classification.

Table 1. Descriptive characteristics of the study group.

Variable		N=100	%
Age	<60 years old	24	24.0
	> ó = 60 years old	76	76.0
Sex	Man	53	53.0
	Female	47	47.0
Comorbidities	High blood pressure	79	79.0
	Hyperlipidemia	44	44.0
	Previous cardiac catheterization	44	44.0
	Type 2 diabetes mellitus	35	35.0
	Smoking	18	18.0
	Chronic kidney disease	16	16.0
	Thyroid disease	9	9.0
BP	>120 mmHg	68	68.0
	<120 mmHg	32	32.0
HR	>70 lpm	69	69.0
	<70 lpm	31	31.0
SC	<0.8 mg/dl	70	70.0
	>0.8 mg/dl	30	30.0

BP: systolic blood pressure. HR: Heart rate. SC: Serum creatinine.

Table 2. Relationship between mortality and GRACE score in patients with non-ST segment elevation acute coronary syndrome.

GRACE scale	Mortality	Survival	*P*
Score	227 ± 40.7	137 ± 39.4	<0.001
Hospital risk			
Low (<108)	0	20 (100%)	0.001
Medium (109-140)	0	33 (100%)	
High (>140)	9 (15.2%)	38 (80.85%)	
Risk at 6 months			
Low (<108)	0	8 (100%)	0.033
Medium (109-140)	0	22 (100%)	
High (>140)	9 (12.86%)	61 (87.14%)	

Figure 1. Histogram of the GRACE scale in the study group.

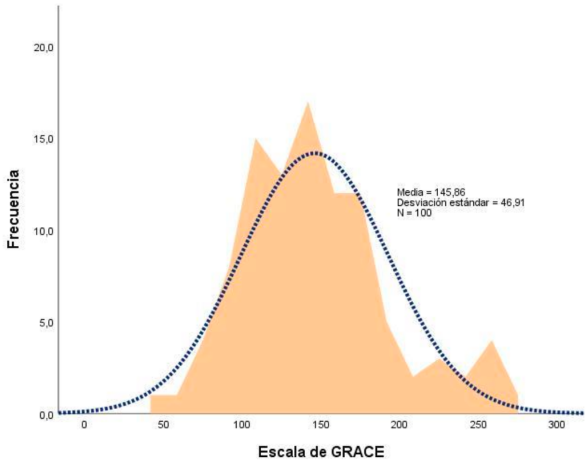
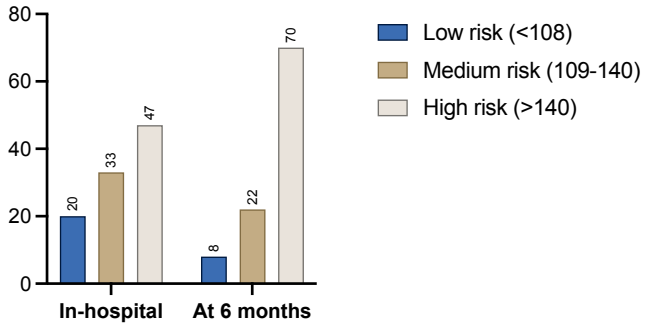


Figure 2. Distribution of patients according to in-hospital mortality risk classification at six months.



Relationships of variables according to hospital risk

During the hospital period, the following risk factors were associated with "high risk" according to the GRACE scale: age greater than 60, chronic kidney disease, systolic blood pressure greater than 120 mmHg, serum creatinine greater than 0.8 mg/dl, presence of positivity in biomarkers, functional classes 2 and 3 of the Killip-Kimball scale, and new changes in the ST segment (Table 3).

In the outpatient period at six months, the following risk factors for the outcome of "high risk" were identified on the GRACE scale: age greater than 60, the presence of chronic kidney disease, the presence of positivity in the biomarkers, class functional 2 and 3 of the Killip-Kimball scale, and a new change in the ST segment (Table 4).

Discussion

Risk stratification is one of the main objectives in the comprehensive management of acute coronary syndrome patients. Currently, the guidelines recommend stratification using risk scores, either the TIMI or GRACE [7].

The GRACE scale has been widely accepted for its ease of application, ability to assess clinical aspects and risk factors, and ability to homogenize patients. However, because its application requires laboratory parameters, many hospitals need the means to obtain these values upon admission, limiting this scale's predictive power.

The GRACE scale is a model applied to all coronary syndromes that estimate the risk of heart attack and hospital death for six months based on a multivariate analysis of a global observational registry; this scale incorporates new variables that provide considerable predictive information regarding patients' physiological situation and laboratory alterations.

In a validation study (Aragam et al. 2009), the ability to predict in-hospital mortality was compared at six months in a cohort of patients with ACS with and without ST-segment elevation, and they reported that for the non-ST syndrome, the GRACE score has a more remarkable ability to predict hospital outcomes for six months; for ST-segment elevation coronary syndrome, both the TIMI and GRACE scores had adequate discrimination for in-hospital mortality and at six months [8].

Different studies have demonstrated the usefulness of applying these scales and their predictive capacity. Many of them have demonstrated better results with GRACE than with the TIMI in relation to their discrimination capacity and predictive power.

In a study performed in Brazil [9] that included 154 patients with a diagnosis of non-ST ACS, the predictive value of the TIMI score was compared with that of the GRACE score for hospital outcomes. This revealed that both scales had good calibration power; however, in the discrimination analysis, the GRACE score was much greater than the TIMI score.

Considering the high prevalence of this disease, it is essential to determine the usefulness of these scales for the comprehensive treatment of patients with acute coronary syndrome and to determine which scale has the best mortality prediction capacity.

The present study applied the GRACE scale to a cohort of patients admitted for acute coronary syndrome without ST-segment elevation at the Teodoro Maldonado Carbo Specialty Hospital. The GRACE scale is a valid predictor of mortality. The six patients who died due to cardiovascular causes in our study all presented a high risk for coronary disease during hospitalization.

Table 3. Relationship between hospital risk and variables in patients with non-ST segment elevation acute coronary syndrome.

GRACE scale	High Risk N=47	Low/medium risk N=53	*P*	OR (IC 95%)
Age				
>60 años	45 (59.1%)	31 (40.79%)	0.001	15.97 (3.5-72.87)
<60 años	2 (8.33%)	22 (91.67%)		
Sex				
Man	29 (54.7%)	24 (45.28%)	0.101	NS
Female	18 (38.3%)	29 (61.7%)		
Comorbidities				
HT	39 (49.4%)	40 (50.63%)	0.454	NS
Hyperlipidemia	23 (52.3%)	21 (47.73%)	0.349	NS
Type 2 diabetes	19 (54.3%)	16 (45.7%)	0.316	NS
Smoking	12 (66.7%)	6 (33.33%)	0.065	NS
CKD	14 (87.5)	2 (12.5%)	0.001	10.82 (2.31-50.71)
Systolic blood pressure				
<120 mmHg	20 (65.5%)	11 (35.48%)	0.015	2.94 (1.21-7.11)
>120 mmHg	26 (38.2%)	42 (61.76%)		
Heart rate				
>70 mmHg	32 (46.4%)	37 (53.62%)	0.852	NS
<70 mmHg	15 (48.4%)	16 (51.61%)		
Serum creatinine				
>0.8 mg/dl	40 (57.1%)	30 (42.86%)	0.002	4.38 (1.66-11.55)
<0.8 mg/dl	7 (23.3%)	23 (76.67%)		
Biomarkers				
Positive	36 (72.0%)	14 (28.00%)	0.001	9.12 (3.67-22.66)
Killip-Kimball classification				
Class 2 and 3	19 (95.0%)	1 (5.00%)	0.001	35.29 (4.49-277.6)
Class 1	28 (35.0%)	52 (65.00%)		
ST shift				
Present	41 (61.2%)	26 (38.81%)	0.001	7.10 (2.58-19.52)

CKD: Chronic Kidney Disease. HT: Hypertension.

A total of 76% of the patients were aged ≥60 years, 24% were <60 years in terms of sex, 53% (n = 53) were men, and 47% (n = 47) were women. In addition, within the group of patients who died during hospitalization due to cardiovascular causes, three patients were women, and three patients were men, which indicates that there was the same risk in terms of sex. This was observed in the study population, which differs from other investigations where there was a predominance of females rather than males [10].

Diabetes mellitus is considered a significant comorbidity in patients with acute coronary syndrome.

This study observed that it was not a predominant factor in the population, occurring in 35% of the patients (P = 0.316 OR = 1.53). Arterial hypertension, which was present in 79% of patients and is a significant risk factor, was not detected. Cardiovascular disease was present in 5 (83.3%) of the six patients who died from cardiovascular causes secondary to acute myocardial infarction (P = 0.45 OR = 1.46), which coincides with studies in which arterial hypertension was also classified as a factor predominant risk present in acute coronary syndrome.

The Killip-Kimball classification continues to be an essential prognostic predictor in patients with acute coronary syndrome. It is determined that the higher the functional class is, the worse the patient's prognosis (Mello et al.). This finding was corroborated in the present study, where 80 patients presented with Killip Kimball class I 19 patients.

Table 4. Relationship between risk at six months and variables in patients with non-ST segment elevation acute coronary syndrome.

GRACE scale	High Risk N=70	Low/medium risk N=30	*P*	OR (IC 95%)
Age				
>60 years old	63 (82.89%)	13 (17.11%)	0.001	11.77 (4.06-34.09)
<60 years old	7 (29.17%)	17 (70.83%)		
Sex				
Man	39 (73.58%)	14 (26.42%)	0.406	NS
Female	31 (65.96%)	16 (34.04%)		
Comorbidities				
HT	59 (74.68%)	20 (25.32%)	0.084	NS
Hyperlipidemia	34 (77.27%)	10 (22.73%)	0.159	NS
Type 2 diabetes	26 (74.29%)	9 (25.71%)	0.563	NS
Smoking	14 (77.78%)	4 (22.22%)	0.426	NS
CKD	15 (93.75%)	1 (6.25%)	0.034	7.91 (1.01-62.9)
Systolic blood pressure				
<120 mmHg	25 (80.65%)	6 (19.35%)	0.110	NS
>120 mmHg	44 (64.71%)	24 (35.48%)		
Heart rate				
>70 mmHg	50 (72.46%)	19 (27.54%)	0.422	NS
<70 mmHg	20 (64.52%)	11 (35.48%)		
Serum creatinine				
>0.8 mg/dl	53 (75.71%)	19 (27.54%)	0.057	NS
<0.8 mg/dl	17 (56.67%)	13 (43.33%)		
Biomarkers				
Positive	44 (88.0%)	6 (12.00%)	0.001	6.77 (2.45-18.73)
Killip-Kimball classification				
Class 2 and 3	19 (95.0%)	1 (5.00%)	0.001	10.80 (1.37-84.93)
Class 1	51 (63.75%)	29 (36.25%)		
ST shift				
Present	55 (82.09%)	12 (17.91%)	0.001	5.50 (2.18-13.90)

CKD: Chronic Kidney Disease. HT: Hypertension.

Killip Kimball class II and one patient presented Killip Kimball class III. Of the group of patients who died due to cardiovascular disease, 5 of the six patients were Killip Kimball class II (P = 0.0001 OR = 35.29).

According to the GRACE scale, the proportion of in-hospital deaths was 15.15% for high-risk patients (> 140) vs. 0% for low-risk patients (≤108) and intermediate-risk patients (109-140). At six months, 12.86% of the patients were at high risk (> 118), whereas 0% were at low risk (≤88) or intermediate risk (89-118). Significant differences were observed with P values of 0.001 and 0.033, respectively.

Conclusions

The GRACE scale is widely established as the best predictor of cardiovascular risk after acute coronary syndrome without ST-segment elevation. In our patients, it was established that its assessment is essential to predict the progression of the disease according to the score obtained based on parameters that are available to the doctor and indicate the risk of death from heart attack in the long term.

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Declarations

Ethics committee approval and consent to participate

The ethics committee of the Universidad de Especialidades Espíritu Santo approved this study.

Publication consent

It is not required when images, radiographs, and specific studies of patients are not published.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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Editor's Note

The Journal Actas Médicas (Ecuador) remains neutral regarding jurisdictional claims on published maps and institutional affiliations.

Received: April 7, 2024.
Accepted: June 1, 2024.
Published: June 8, 2024.
Editor: Dra. Mayra Ordoñez Martínez.

How to cite:

García K, Fernández T. Prognosis and risk of death in patients with an acute coronary syndrome without ST-segment elevation: A single-center observational study, application of the GRACE scale. Medical Records (Ecuador) 2024; 34 (1): 10-17.

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