Prognostic Score for Acute Coronary Syndrome in a Private Terciary Hospital

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Abstract

Background: Available predictive models for acute coronary syndromes (ACS) have limitations as they have been elaborated some years ago or limitations with applicability.

Objectives: To develop scores for predicting adverse events in 30 days and 6 months in ST-segment elevation and non-ST-segment elevation ACS patients admitted to private tertiary hospital.

Methods: Prospective cohort of ACS patients admitted between August, 2009 and June, 2012. Our primary composite outcome for both the 30-day and 6-month models was death from any cause, myocardial infarction or re-infarction, cerebrovascular accident (CVA), cardiac arrest and major bleeding. Predicting variables were selected for clinical, laboratory, electrocardiographic and therapeutic data. The final model was obtained with multiple logistic regression and submitted to internal validation with bootstrap analysis.

Results: We considered 760 patients for the development sample, of which 132 had ST-segment elevation ACS and 628 non-ST-segment elevation ACS. The mean age was 63.2 ± 11.7 years, and 583 were men (76.7%). The final model to predict 30-day events is comprised by five independent variables: age ≥ 70 years, history of cancer, left ventricular ejection fraction (LVEF) < 40%, troponin I > 12.4 ng /ml and chemical thrombolysis. In the internal validation, the model showed good discrimination with C-statistic of 0.71. The predictors in the 6-month event final model are: history of cancer, LVEF < 40%, chemical thrombolysis, troponin I >14.3 ng/ml, serum creatinine>1.2 mg/dl, history of chronic obstructive pulmonary disease and hemoglobin < 13.5 g/dl. In the internal validation, the model had good performance with C-statistic of 0.69.

Conclusion: We have developed easy to apply scores for predicting 30-day and 6-month adverse events in patients with ST-elevation and non-ST-elevation ACS. (Arq Bras Cardiol. 2014; 102(3):226-236)

Keywords: Acute Coronary Syndrome; Prognosis; Probability; Hospitals, Private; Risk Factors.

Introduction

The epidemiological relevance of cardiovascular disease (CVD), particularly coronary artery disease (CAD), is widely recognized. CAD is one of the main causes of death in the country, [Remark 2] particularly in patients with acute coronary syndrome (ACS)[1,2]. Despite optimized treatment with potent anti-ischemic and anti-thrombotic drugs and the array of technologies available for the diagnosis and treatment of ACS, there is still a high incidence of death and recurrent acute myocardial infarction (AMI) after hospital discharge. The estimated rates vary between 5% and 10% within a month after the acute event, and the long-term risk is high[3].

Patients with ACS are a heterogeneous population with distinct clinical conditions and variable prognosis both in the short and long term; the latter is particularly observed in individuals affected by ACS without ST elevation. Therefore, the probability of complications, particularly death and cardiovascular events during disease progression, led to the development of risk prediction models. These models have become essential for decision-making about the best therapeutic strategy and transfer of serious cases to more resourceful facilities and to avoid unnecessary tests and prolonged hospitalizations of low-risk cases, which is relevant for the adequate management of hospital beds[4-6].

There are several prognostic models for patients with ACS; however, these can present with limitations in terms of calibration or discrimination, either because they were designed several years ago[7-10] or because they were developed using samples selected from clinical trials[7-9]. One model was

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developed for the Brazilian population; however, it only involved patients with ACS and no ST elevation who were treated at a public hospital[11]. This study aimed to develop scores for the prediction of adverse events at 30 days and 6 months in a nonselected population of patients with ST-elevation ACS (STE-ACS) or non-ST-elevation ACS (NSTE-ACS) treated at a private tertiary hospital.

Methods

Design

This prospective study reviewed patients admitted to the Coronary Unit of the Hospital do Coração (HCor), São Paulo, SP between August 1, 2009 and June 20, 2012. HCor is a tertiary philanthropic hospital that admits private patients and patients with insurance protocols. The study protocol was approved by the Hcor Research Ethics Committee, and all patients provided written informed consent before participation.

Patients

Male and female patients with STE-ACS or NSTE-ACS who were aged ≥18 years and hospitalized in the Coronary Unit of the HCor hospital during the abovementioned period were included. Patients who did not provide written informed consent document and those with serious cognitive impairments (which could limit the study) were excluded.

Creatinine phosphokinase-MB (CK-MB) and troponin I levels were used as biomarkers of myocardial necrosis. The criteria recommended by the "Universal Definition of Myocardial Infarction" of 2007[12] were used for the diagnosis of acute myocardial infarction (AMI), clinical reinfarction, or infarction following percutaneous coronary intervention (PCI) or myocardial revascularization surgery. The definition of unstable angina was based on the Braunwald classification[13].

Predictor variables

The predictor variables were selected from clinical, laboratory, electrocardiography, and echocardiography data obtained within the first 48 hours. In addition, the therapy administered in the first 12 hours after admission was selected as a variable. The clinical variables included age; gender; history of angina, AMI, PCI, myocardial revascularization surgery, stroke, diabetes mellitus, heart failure, chronic renal failure renal, sedentarism, smoking, chronic obstructive pulmonary disease (COPD), arterial coronary disease with stenosis ≥ 50%, peripheral arterial disease, dyslipidemia, systemic arterial hypertension, cancer, and cardiac arrhythmia; family history of CAD; use of medications prior to hospitalization (aspirin, beta blockers, calcium channel blockers, angiotensin II receptor blockers, clopidogrel, ticlopidine, statins, angiotensin II converting enzyme inhibitors, digitalis, nitrate, diuretic, oral hypoglycemic drugs, and oral anticoagulant drugs); and initial clinical data (systolic arterial pressure, heart rate, dyspnea, syncope, Killip class).

Among the laboratory variables, we analyzed the poorest values observed within the first 48 hours after hospitalization. The laboratory variables evaluated as predictors included leucocyte count, hemoglobin levels, hematocrit, glucose levels, creatinine levels, creatinine clearance, total cholesterol and cholesterol fractions, C-reactive protein (CRP) ultrasensitive levels, triglyceride levels, and troponin levels.

The electrocardiography findings considered to be potential predictors included an elevated ST segment (≥1 mm), ST depression (≥0.5 mm), or a combined finding characterized by the presence of one of the abovementioned alterations. The left ventricular ejection fraction was measured using the Simpson method within the first 48 hours of admission using transthoracic echocardiography. With regard to therapeutic interventions, we considered the use of chemical thrombolysis as a potential predictor.

Clinical outcome and follow-up

The composite primary outcome was defined as the occurrence of death from any cause, AMI, or nonfatal reinfarction, nonfatal stroke, major bleeding, or cardiorespiratory arrest that could be reversed in a period of 30 days or 6 months, depending on the model under study. Major bleeding was defined as the loss of blood accompanied by a decrease in Hb levels by > 3.0 g/dL or > 4.0 g/dL; intracranial, intraocular, or retroperitoneal bleeding; and/or transfusion of 2 or more units of red blood cells[14]. The 30-day and 6-month follow-up was conducted via telephone interview with the patient or family.

Statistical analysis

Continuous variables of skewed and normal distribution are expressed as medians (interquartile ranges) and means ± standard deviations, respectively. Normality was assessed through visual inspection of histograms. Categorical variables are expressed using absolute and relative frequencies. All significance probabilities (p-values) were two-sided, and values of ≤ 0.05 were considered statistically significant. SAS software, version 9.3, was used for the statistical analysis of data.

Multivariate analysis via binary multiple logistic regression was used to identify covariables associated with the occurrence of the binary outcome. Initially, univariate binary logistic regression analyses were performed to test the association between each covariable and the binary response variable. In these analyses, when the phenomenon of data separation was observed[15], p-values and 95% confidence intervals (CIs) were estimated using the method of restricted maximum likelihood[16]. Covariables with a p-value of < 0.10 as per univariate regression analyses were included in the multiple logistic regression analysis using the method (conventional) of maximum likelihood and variable selection using backward elimination. A p-value of < 0.10 was used as a criterion for retaining variables in the final model[17]. The assumption of linearity in the logit scale (log-odds) between each quantitative covariable and the binary response variable in binary logistic regression analysis was assessed by examination of smoothed scatter plots[17]. When the assumption was not met, continuous covariables were dichotomized for logistic regression using a cutt-off point described in the literature or established by receiver operating characteristic (ROC) curve analysis. The cut-off that maximized the sum of sensitivity and specificity minus one (Youden index) was determined[18,19]. Multicolinearity

was assessed in the covariables that exhibited a p-value of < 0.10 in univariate regression analysis via estimation of variance inflation factor (VIF). VIF values of > 2.5 were used as indicators of considerable multicollinearity[20].

Overall performance, calibration, and the discriminatory power of the final multiple logistic regression model were assessed using the Brier score, the Hosmer–Lemeshow test, and the area under the ROC (AROC) curve, respectively. The Brier score for a model can vary between 0 (perfect model) and 0.25 (noninformative model)[21]. A p value of > 0.05 as per the Hosmer–Lemeshow test indicates that the model is calibrated, i.e., the probabilities predicted by the model adequately reflect event occurrence. In general, the following interpretation for AROC was considered: AROC = 0.5, absence of discrimination; 0.5 ≤ AROC < 0.7, discrimination of little relevance; 0.7 ≤ AROC < 0.8, acceptable discrimination; 0.8 ≤ AROC < 0.9, excellent discrimination; AROC ≥ 0.9, near perfect discrimination[17].

Internal validation of the multiple logistic regression model was performed via bootstrap analysis based on 200 replications[21-23]. This method has shown better performance than other methods of internal validation[21]. The performance of the internal validation model was assessed using the Brier score and AROC curve.

Next, a weighted risk score was calculated using the coefficients of the multiple logistic regression model. These coefficients were converted into scores by multiplying them by 10 and rounding them to the nearest whole number, which were sequentially added to produce a total aggregate score of[24].

Risk groups were defined on the basis of the score frequency distribution, and the proportion of events was compared among groups according to the Cochran–Armitage linear trend test[25].

Results

Background Characteristics

The study included 760 patients, of which 278 (36.5%) had non-ST-elevation AMI, 350 (46.0%) had unstable angina, and 132 (17.3%) had ST-elevation AMI. The mean age was 63.2 ± 11.7 years, and the majority of patients were male (76.7%). The remaining background characteristics are described in Table 1.

Outcomes

Death, AMI or nonfatal reinfarction, nonfatal stroke, major bleeding, or reversible cardiorespiratory arrest was observed in 52 patients at the 30-day follow-up and 79 patients at the 6-month follow-up. The incidence of each outcome is shown in Table 2.

Score at 30 days

The results of univariate logistic regression analyses are shown in Table 3. The variables associated with the primary outcome (p < 0.10) at 30 days were age ≥ 70 years, history of cancer, history of diuretic use, history of angiotensin II converting enzyme inhibitor use, Killip class II or more, leukocytes > 11,200/mm^3, hematocrit < 41.9%, hemoglobin < 14 g/dL, creatinine > 1.2 mg/dL, ultrasensitive CRP > 11 mg/dL, troponin > 12.4 ng/mL, left ventricular ejection fraction < 40%, and use of chemical thrombolysis.

Table 4 shows the results of multiple logistic regression analyses for the 30-day follow-up, associated with the scoring system. The variables in the final model included age ≥ 70 years, troponin > 12.4 ng/dL, history of cancer, left ventricular ejection fraction < 40%, and use of chemical thrombolysis.

In the development sample, the overall performance of the final model was adequate (Brier score = 0.06). The discriminatory power of this model, i.e., the model's capacity to discriminate between event and nonevent, was acceptable, with an AROC curve of 0.71 [95% confidence interval (95%CI): 0.63–0.79]. The model's calibration was adequate (Hosmer–Lemeshow of p = 0.72), i.e., the probabilities predicted by the model adequately reflected event occurrence.

A good performance was observed in the internal validation sample (Brier score = 0.06), similar to the performance observed in the development model. In addition, a good power of discrimination was observed (AROC curve = 0.71).

Patients were classified into low-, intermediate-, and high-risk groups according to 30-day scores of 0, 8, or >8, respectively. Totally, 352 (46.3%) patients were at low risk, 262 (34.5%) at intermediate risk, and 146 (19.2%) at high risk. The probability of primary outcome at 30 days was 2.8%, 6.5%, and 17.1% in the low-, intermediate-, and high-risk groups, respectively (p < 0.0001).

Score at 6 months

The variables associated with the primary outcome at 6 months as per the univariate analysis are presented in Table 5. Variables with p < 0.10 included age > 65 years; history of chronic renal failure, cancer, and/or chronic obstructive pulmonary disease; history of angiotensin II converting enzyme inhibitor use; heart rate ≥ 100 bpm; Killip class ≥ 2; leukocytes > 9,750/mm^3; hemoglobin < 14.5 g/dL; creatinine > 1.2 mg/dL; creatinine clearance < 30 mL/min; troponin I > 14.3 ng/mL; left ventricular ejection fraction < 40%; and use of chemical thrombolysis.

The final multivariate model comprised the following predictors: troponin I > 14.3 ng/mL, history of COPD and/or cancer, left ventricle ejection fraction < 40%, creatinine > 1.2 mg/dL, hemoglobin < 13.5 g/dL, and use of chemical thrombolysis (Table 6).

We observed adequate overall performance in the development sample (Brier score = 0.09). Moreover, we observed good discriminatory power (AROC curve = 0.69, 95% CI: 0.62–0.76) and adequate calibration (Hosmer–Lemeshow of p = 0.38).

The internal validation sample showed good performance (Brier score = 0.08) and reasonable discriminatory power (AROC curve = 0.69).

Table 1 – Background characteristics of the study sample (n = 760)

Electrocardiogram findings, n (%)	
ST-segment depression ≥ 0.5 mm	94 (12.8)
ST-segment elevation ≥ 1 mm in other leads	115 (15.6)
Any ST-segment shift	209 (28.4)
Laboratory tests	
Total leukocyte count (mm^3): mean ± SD	8.974 ± 4.554
Platelets (mm^3), mean ± SD	217.407 ± 78.076
Hematocrit (%), mean ± SD	41.8 ± 5.4
Hemoglobin (g/dL), mean ± SD	14.1 ± 2.2
Glucose (mg/dL), mean ± SD	118 ± 42.8
Potassium (mEq/L), mean ± SD	4.3 ± 1.9
Creatinine (mg/dL), mean ± SD	1.1 ± 0.9
Creatinine clearance (mL/m), mean ± SD	91.0 ± 39.5
Total cholesterol (mg/dL), mean ± SD	166.9 ± 44.7
LDL cholesterol (mg/dL), mean ± SD	98.1 ± 39.9
HDL cholesterol (mg/dL), mean ± SD	38.1 ± 10.9
CRPus (mg/dL), median (interquartile range)	6.6 (2.5–21.6)
Uric acid (mEq/L), mean ± SD	5.7 ± 2.0
Tryglicerides (mg/dL), mean ± SD	175.1 ± 152.2
Troponin (ng/mL), median (interquartile range)	1.7 (0.19–16.2)
Left ventricular ejection fraction < 40%, n (%)	49 (6.5)
Chemical thrombolysis, n (%)	16 (2.1)

AMI: acute myocardial infarction; CAD: coronary arterial disease; LDL: low-density lipoprotein; HDL: high-density lipoprotein; CRPus: ultrasensitive C-reactive protein.

Table 2 – Incidence of the primary outcome variables

Events	30 days n (%)	6 months n (%)
Combined outcome	52 (6.8)	79 (10.4)
Death from any cause	7 (0.9)	25 (3.2)
AMI or nonfatal reinfarction	08 (1.1)	16 (2.1)
Nonfatal stroke	08 (1.1)	12 (1.5)
Major bleeding	22 (2.9)	22 (2.9)
Reversible cardiorespiratory arrest	10 (1.3)	10 (1.3)

AMI: acute myocardial infarction.

The patients were considered to be at low risk if their score was 0, intermediate risk if their score was 5–7, and high risk if their score was ≥8. Among all patients, 316 (46.3%) were at low risk, 262 (34.5%) were at intermediate risk, and 146 (19.2%) were at high risk. The probability of observing a primary outcome at 6 months was 6.0%, 7.3%, and 19.6% in the low-, intermediate-, and high-risk groups, respectively ($p < 0.0001$).

Discussion

Main results

In this study of ACS patients consecutively recruited in a private tertiary hospital, we developed scores for the prediction of adverse events at 30 days and 6 months (Hcor score). The 30-day score was based on the following predictor

Table 3 – Results of the univariate logistic regression models for the prediction of the combined outcome at 30 days

Variable	Events at 30 days number of events/total number in the group (%)	Univariate model	
		Odds ratio (95% CI)	p value
Age > 70 years	25/240 (10.4)	2.12 (1.20 to 3.74)	0.009
Women	12/177 (6.8)	0.99 (0.51 to 1.93)	0.97
Medical history, n (%)			
SAH	39/571 (6.8)	0.99 (0.52 to 1.90)	0.98
Dyslipidemia	32/488 (6.6)	0,88 (0.50 to 1.58)	0.68
Sedentarism	35/449 (7.8)	1,46 (0.80 to 2.66)	0.21
Family history of CAD	28/396 (7.1)	1.08 (0.61 to 1.90)	0.79
Diabetes mellitus	12/228 (5.3)	0.68 (0.35 to 1.33)	0.26
Smoking	14/169 (8.3)	1.32 (0.70 to 2.49)	0.40
Previous AMI	16/167 (9.6)	1.63 (0.88 to 3.03)	0.11
Previous MRS	13/170 (7.6)	1.17 (0.61 to 2.25)	0.64
Previous PCI	13/201 (6.5)	0.92 (0.48 to 1.77)	0.81
Previous CRF	6/58 (10.3)	1.65 (0.67 to 4.03)	0.28
Cancer	8/42 (19.0)	3.60 (1.57 to 8.25)	0.002
Previous stroke	1/18 (5.6)	0.80 (0.10 to 6.11)	0.83
CCF	2/17 (11.8)	1.85 (0.41 to 8.31)	0.42
PAD	1/15 (6.7)	0.97 (0.12 to 7.54)	0.97
COPD	5/40 (12.5)	2.04 (0.76 to 5.46)	0.15
CAD with stenosis ≥ 50%	0/32 (0.0)	0.20 (0.00 to 1.43)	0.26
Arrhythmia	2/47 (4.3)	0.59 (0.14 to 2.50)	0.47
Previous medications			
Statin	26/399 (6.5)	0.89 (0.51 to 1.57)	0.70
ASA	26/365 (7.1)	1.08 (0.62 to 1.91)	0.76
Beta blocker	20/295 (6.8)	0.98 (0.55 to 1.75)	0.95
ARB	18/265 (6.8)	0.98 (0.55 to 1.78)	0.96
Oral hypoglycemic	11/185 (5.9)	0.82 (0.41 to 1.63)	0.57
Diuretic	16/164 (9.8)	1.68 (0.90 to 3.11)	0.09
Nitrate	11/118 (9.3)	1.50 (0.75 to 3.02)	0.24
CCB	9/118 (7.6)	1.15 (0.54 to 2.42)	0.71
ACEI	13/117 (11.1)	1.93 (0.99 to 3.75)	0.05
Clopidogrel	7/107 (6.5)	0.94 (0.41 to 2.15)	0.89
Anticoagulant	1/17 (5.9)	0.84 (0.11 to 6.52)	0.87
Insulin	3/34 (8.8)	1.33 (0.39 to 4.53)	0.64
Initial clinical data			
Systolic arterial pressure < 90 mmHg	0/7 (0)	0.89 (0.00 to 7.48)	0.94
Heart rate ≥ 100 bpm	6/66 (9.1)	1.40 (0.57 to 3.43)	0.45
Dyspnea	5/59 (8.5)	1.28 (0.49 to 3.37)	0.60
Killip class ≥ 2	7/35 (17.9)	3.28 (1.37 to 7.85)	0.007
Electrocardiogram findings			
ST depression ≥ 0.5 mm	9/94 (9.6)	1.47 (0.69 to 3.12)	0.31
ST elevation ≥ 1 mm	8/115 (7.0)	0.97 (0.44 to 2.13)	0.95
Any ST shift	17/209 (8.1)	1.24 (0.68 to 2.27)	0.48

Continuation

Laboratory tests			
Leukocytes > 11,200/mm^3	17/131 (13.0)	2.51 (1.26 to 4.64)	0.003
Glucose ≥ 100 mg/dL	34/456 (7.5)	1.30 (0.71 to 2.38)	0.38
Hematocrit < 41.9%	30/348 (8.6)	1.66 (0.94 to 2.94)	0.07
Hemoglobin < 14.5 g/dL	36/419 (8.6)	1.89 (1.03 to 3.48)	0.03
Creatinine > 1.2 mg/dL	17/141 (12.1)	2.28 (1.24 to 4.20)	0.008
Creatinine clearance ≤ 30 mL/min	3/23 (13.0)	2.10 (0.60 to 7.32)	0.24
Total cholesterol ≥ 200 mg/dL	8/123 (6.5)	1.03 (0.46 to 2.29)	0.93
LDL cholesterol > 100 mg/dL	18/252 (7.1)	1.23 (0.65 to 2.31)	0.51
HDL cholesterol < 40 mg/dL	26/418 (6.2)	0.94 (0.49 to 1.79)	0.85
CRPus > 11 mg/dL	27/254 (10.6)	2.47 (1.33 to 4.60)	0.04
Tryglicerides > 150 mg/dL	20/314 (6.4)	1.01 (0.54 to 1.89)	0.97
Troponin > 12.4 ng/mL	25/209 (12.0)	2.66 (1.49 to 4.72)	0.0008
LVEF < 40%	11/49 (22.4)	4.70 (2.24 to 9.87)	< 0.001
Chemical thrombolysis	5/16 (31.3)	6.74 (2.25 to 20.20)	< 0.001

SAH: systemic arterial hypertension; CAD: coronary arterial disease; AMI: acute myocardial infarction; MRS: myocardial revascularization surgery; PCI: percutaneous coronary intervention; CRF: chronic renal failure; CCF: congestive cardiac failure; PAD: peripheral arterial disease; COPD: chronic obstructive pulmonary disease; ASA: acetylsalicylic acid; ARB: angiotensin II receptor blocker; ACEI: angiotensin converting enzyme inhibitor; CCB: calcium channel blocker; LVEF: left ventricular ejection fraction.

Table 4 – Results of multivariate logistic regression analysis associated with the scoring system (score) for the final 30-day model

Variable	Regression coefficient	OR 95% CI	p value	Score
Age ≥ 70	0.7653	2.15 (1.16 to 3.99)	0.02	8
Troponin I > 12.4 ng/mL	0.7875	2.20 (1.19 to 4.05)	0.01	8
Cancer	1.0327	2.81 (1.17 to 6.75)	0.02	10
LVEF < 40%	1.0817	2.95 (1.33 to 6.52)	0.008	11
Use of chemical thrombolysis	1.7752	5.90 (1.76 to 19.83)	0.004	18

LVEF: Left ventricular ejection fraction.

variables: age ≥ 70 years, troponin I > 12.4 ng/mL, history of cancer, left ventricular ejection fraction < 40%, and use of chemical thrombolysis. The 6-month score was based on the following predictor variables: troponin I > 14.3 ng/mL, history of COPD, history of cancer, left ventricular ejection fraction < 40%, creatinine > 1.2 mg/dL, hemoglobin < 13.5 g/dL, and use of chemical thrombolysis. The final models for the prediction of events at 30 days and 6 months exhibited good overall performance, good discriminatory power, and adequate calibration. Overall performance and discrimination remained good in the validation samples.

Significance of the study findings

Our model identified variables common to other previous prognostic models[7-11], such as advanced age, elevated troponin I, and, in the 6-month model, elevated creatinine. Moreover, in our 30-day model, we identified independent predictors that were not included in the previous models, such as history of neoplasia, left ventricular ejection fraction < 40%, and use of chemical thrombolysis. In the 6-month model, the variables were history of COPD, history of cancer, left ventricular ejection fraction < 40%, hemoglobin < 13.5 g/dL, and use of chemical thrombolysis; these were also not included in the previous models.

History of cancer was identified as an independent predictor of adverse events for various reasons. First, cancer treatment has resulted in increased survival rates, which has led to increased occurrence of acute decompensations such as ACS[26]. Second, cancer induces a prothrombotic state that can increase the risk of ACS[26,27]. Third, a variety of chemotherapeutic drugs and radiotherapy are cardiotoxic and cause manifestations such as myocarditis, pericardits, ACS, and arrhythmias[28,29]. Fourth, cancer is associated with a higher incidence of thrombocytopenia, predisposing to bleeding and affecting the major bleeding component of the combined primary outcome[30]. Fifth, mortality within 30 days or 6 months among cancer patients can be affected by ACS as well as cancer progression itself.

Table 5 – Results of univariate logistic regression models for the prediction of combined outcome at 6 months

Variable	Events at 6 months number of events/total number in the group (%)	Univariate model	
		Odds ratio (95% CI)	p value
Age > 65 years	45/38 (13.3)	1.75 (1.09 to 2.80)	0.02
Women	18/177 (10.2)	0.97 (0.55 to 1.68)	0.91
Medical history			
SAH	62/571 (10.9)	1.23 (0.70 to 2.16)	0.46
Dyslipidemia	52/488 (10.7)	1.08 (0.66 to 1.76)	0.75
Sedentarism	49/449 (10.9)	1.14 (0.71 to 1.85)	0.57
Family history of CAD	42/396 (10.6)	1.49 (0.65 to 1.67)	0.84
Diabetes Mellitus	20/228 (8.2)	0.77 (0.45 to 1.31)	0.33
Smoking	23/169 (3.6)	1.50 (0.89 to 2.52)	0.12
Previous AMI	20/167 (12.0)	1.22 (0.71 to 2.11)	0.44
Previous MRS	19/170 (11.2)	1.11 (0.64 to 1.92)	0.70
Previous PCI	22/201 (10.8)	1.08 (0.64 to 1.82)	0.76
Previous CRF	10/58 (17.2)	1.91 (0.92 to 3.94)	0.08
Cancer	12/42 (28.6)	3.88 (1.90 to 7.94)	<0.001
Previous stroke	3/18 (16.7)	1.75 (0.49 to 6.19)	0.38
CCF	2/17 (11.8)	1.15 (0.25 to 5.13)	0.85
PAD	1/15 (6.7)	0.61 (0.07 to 4.70)	0.63
COPD	10/40 (25)	3.14 (1.47 to 6.71)	0.003
CAD with stenosis ≥ 50%	0/32 (0.0)	0.13 (0.01 to 0.90)	0.15
Arrhythmia	2/47 (4.3)	0.36 (0.08 to 1.54)	0.17
Previous medications			
Statin	40/399 (10.0)	0.95 (0.57 to 1.46)	0.72
ASA	36/365 (9.9)	0.89 (0.56 to 1.43)	0.64
Beta blocker	33/295 (11.2)	1.14 (0.71 to 1.84)	0.56
ARB	29/265 (10.9)	1.09 (0.67 to 1.77)	0.71
Oral hypoglycemic	18/185 (9.7)	0.90 (0.52 to 1.58)	0.73
Diuretic	22/164 (13.4)	1.46 (0.86 to 2.47)	0.15
Nitrate	14/118 (11.9)	1.19 (0.64 to 2.20)	0.56
CCB	12/118 (10.2)	0.97 (0.50 to 1.85)	0.93
ACEI	18/117 (15.4)	1.73 (0.98 to 3.05)	0.06
Clopidogrel	9/107 (8.4)	0.76 (0.37 to 1.58)	0.46
Anticoagulant	2/17 (11.8)	1.15 (0.25 to 5.13)	0.85
Insulin	4/34 (11.8)	1.15 (0.39 to 3.37)	0.78
Initial clinical data			
Systolic arterial pressure < 90 mmHg	2/7 (28.6)	3.51 (0.67 to 18.4)	0.13
Heart rate ≥ 100 bpm	12/66 (18.2)	2.08 (1.06 to 4.08)	0.03
Dyspnea	9/59 (15.3)	1.62 (0.76 to 3.44)	0.20
Killip class ≥ 2	10/39 (25.6)	3.26 (1.52 to 6.97)	0.002
Electrocardiogram findings			
ST depression ≥ 0.5mm	12/94 (12.8)	1.25 (0.65 to 2.41)	0.49
ST elevation ≥ 1mm	14/115 (12.2)	1.18 (0.64 to 2.19)	0.59
Any ST shift	26/209 (12.4)	1.26 (0.77 to 2.08)	0.35

Continuation

Laboratory variables			
Leukocytes > 9.750/mm^3	32/226 (14.2)	1.69 (1.05 to 2.73)	0.03
Glucose ≥100 mg/dL	53/454 (11.7)	1.42 (0.86 to 2.35)	0.16
Hematocrit < 39.0%	27/182 (14.8)	1.50 (0.88 to 2.51)	0.11
Hemoglobin <14.5 g/dL	38/235 (16.2)	2.26 (1.41 to 3.63)	< 0.001
Creatinine > 1.2 mg/dL	25/142 (17.6)	2.22 (1.33 to 3.72)	0.002
Creatinine clearance ≤ 30mL/min	5/23 (21.7)	2,48 (0.89 to 6.88)	0.08
Total cholesterol ≥ 200 mg/dL	13/123 (10.6)	1.10 (0.58 to 2.10)	0.75
LDL cholesterol > 100 mg/dL	26/252 (10.6)	1.08 (0.64 to 1.83)	0.75
HDL cholesterol < 40mg/dL	42/420 (10.0)	1.06 (0.62 to 1.82)	0.81
Triglycerides > 150 mg/dL	29/314 (9.2)	0.88 (0.52 to 1.48)	0.64
Troponin > 14,3 ng/mL	32/197 (16.2)	2.10 (1.36 to 3.61)	0.001
LVEF < 40%	13/49 (26.5)	3.51 (1.62 to 7.17)	<0.001
Chemical thrombolysis	6/16 (37.5)	5.51 (1.94 to 15.61)	0.001

SAH: systemic arterial hypertension; CAD: coronary arterial disease; AMI: acute myocardial infartion; MRS: myocardial revascularization surgery; PCI: percutaneous coronary intervention; CRF: chronic renal failure; CCF: congestive cardiac failure; PAD: peripheral arterial disease; COPD: chronic obstructive pulmonary disease; ASA: acetylsalicylic acid; ARB: angiotensin II receptor blockers; ACEI: angiotensin converting enzyme inhibitor; CCB: calcium channel blocker; LVEF: left ventricular ejection fraction.

Table 6 – Results of multivariate logistic regression analysis associated with the scoring system (score) for the final 6-month model

Variable	Regression coefficient	OR 95% CI	p value	Score
Troponin I > 14.3 ng/mL	0.47	1.62 (0.95 to 2.73)	0.07	5
COPD	0.89	2.44 (1.10 to 5.44)	0.03	9
Cancer	1.00	2.73 (1.27 to 5.85)	0.01	10
LVEF < 40%	090	2.46 (1.18 to 5.12)	0.01	9
Creatinine > 1.2 mg/dL	0.50	1.65 (0.95 to 2.85)	0.07	5
Hemoglobin < 13.5 g/dL	0.69	2.00 (1.21 to 3.32)	0.007	7
Chemical thrombolysis	1.52	4.59 (1.47 to 14,34)	0.008	15

COPD: chronic obstructive pulmonary disease; LVEF: left ventricle ejection fraction

Our study identified a left ventricular ejection fraction of <40% as an independent predictor in the 30-day and 60-month models. Left ventricular ejection fraction was not considered in other prognostic models, probably because this variable was not available within the initial few hours for most patients[7-11]. However, in our routine, all patients underwent echocardiography within the initial few hours.

In our unit, the majority of patients with ST-elevation AMI are treated with primary PCI; few undergo chemical thrombolysis. Chemical thrombolysis is associated with a higher incidence of death, reinfarction, or stroke when compared with primary PCI in patients with ST-elevation AMI[31]. This is probably the main reason why the use of chemical thrombolysis was an independent predictor of events at 30 days and 6 months.

Previous history of COPD was an independent predictor of the primary outcome at 6 months. Various studies have shown that although COPD does not affect hospital mortality in patients with ACS, it increases mid- and long-term mortality[32,33].

Anemia (hemoglobin < 13.5 g/dL) was an independent predictor of the primary outcome at 6 months. This condition is highly prevalent in elderly patients[34] and is usually associated with other serious comorbidities such as neoplasia, chronic renal failure, diabetes mellitus, and bleeding diathesis, which can adversely affect mortality risk[35]. In addition, low hemoglobin levels increase the risk of ischemic coronary events[36]. Finally, blood transfusions contain prothrombotic and proinflammatory factors that favor arterial thrombosis[37].

Results from the literature

The Hcor score was developed on the basis of a consecutive sample of patients with ACS who were routinely admitted to the unit. On the other hand, the PURSUIT and TIMI models were derived from samples of patients selected to participate in randomized clinical studies; therefore, their applicability to patients is limited in actual clinical practice[7-9]. In addition, the PURSUIT and Dante scores are

specific for patients with STE-ACS, whereas the Hcor model is more versatile and applicable to patients with or without ST elevation[8,11].

Our score is easy to use; it includes only five dichotomous variables in the 30-day model and 7 dichotomous variables in the 6-month model. The GRACE model shows the best discrimination among the most used scores; however, its application without the help of an electronic device is more complex[10].

The Dante score was developed in a study of Brazilian patients with NESTE-ACS treated at a public hospital. Therefore, in Brazil, it has greater applicability compared with models developed in studies of patients from other countries[11]. The Hcor model can also be a good option for Brazilian patients, particularly those treated at private hospitals who present with distinct characteristics.

Limitations

This study has some limitations. It was conducted in a single center, and this may limit its external validity. However, it can be specifically applied to patients with ACS treated in other Brazilian private hospitals. Another limitation was the occurrence of a limited number of events, thus decreasing the precision of the estimates of effects; the occurrence of a larger number of events would enable us to include more variables in the 30-day and 6-month models, thus increasing its performance. In our study, the use of chemical thrombolysis was a predictor of worst prognosis, possibly in comparison with the prognosis of primary PCI in most patients with ST-elevation AMI. It is possible that the effect is neutral or protective in hospitals that use chemical thrombolysis for primary reperfusion in patients with ACS. Lastly, external validation is needed, i.e., the validity and reliability of the Hcor scores at 30 days and 6 months need to be assessed in other populations.

This study also has several strengths. In addition to ease of use and good discriminatory power and calibration of the models as mentioned previously, we emphasize the methodological rigor of the research. We derived the models from a prospective cohort and collected the data using standardized medical records with predictor variables and well-defined outcomes. All patients with ACS hospitalized during the study period were included, with the exception of those who did not give consent, thus minimizing selection bias. Finally, we performed internal validation with bootstrap analysis, which confirmed the good discriminatory power and calibration of the models.

Conclusions

The Hcor score to predict death, AMI or nonfatal reinfarction, nonfatal stroke, reversible cardiorespiratory arrest, or major bleeding at 30 days or 6 months is easy to use and exhibits good discriminatory power and performance. The score may be useful for prognostic stratification of patients with ACS (with or without ST elevation) treated at Brazilian hospitals, particularly in private hospitals. Further studies are necessary to validate the model in independent samples of patients such as Brazilian patients treated at private and public hospitals.

Author contributions

Conception and design of the research: Romano ER, Liguori IM, Piegas LS; Acquisition of data: Romano ER, Liguori IM, FarranJA, Egito RMP, Romano MLP, WerneckVA, Barbosa MAO, Egito EST; Analysis and interpretation of the data and Critical revision of the manuscript for intellectual content: Romano ER, Piegas LS; Statistical analysis: Romano ER; Writing of the manuscript: Romano ER, Cavalcanti AB, Piegas LS.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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