ORIGINAL ARTICLE

Validation and Comparison of Two Risk Stratification Models in ST-Segment Elevation Myocardial Infarction

Validación y comparación de dos modelos de estratificación de riesgo en infarto de miocardio con elevación del segmento ST

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ABSTRACT

Background: Risk scores are recommended to stratify and predict mortality in ST-segment elevation acute myocardial infarction (STEMI). The ProACS and Simple Risk Index (SRI) models are simple scores that have demonstrated adequate predictive capacity of in-hospital mortality in other countries.
Objective: The aim of this study was to validate and compare the ProACS and SRI scores as predictors of in-hospital mortality in patients with STEMI.
Methods: This was a retrospective analysis of a cohort composed of consecutive patients from the CONAREC XVII registry hospitalized with STEMI diagnosis. The predictive value for in-hospital mortality was estimated and validity was assessed by discrimination and calibration.
Results: The study analyzed 694 patients. In-hospital mortality was 8.78%. The median ProACS score was 4 (IQR 25-75, 2.5-5) in patients who presented the event, and 2 (IQR 25-75 1-3) in those without the event ($p < 0.001$) and the median SRI score was 41.3 (IQR 25-75, 29.8-62.5) and 20.8 (IQR 25-75 15.4-30) in those who died and those who did not, respectively ($p < 0.001$). The SRI score showed excellent discrimination (AUC 0.83, 95% CI 0.78-0.88, $p=0.001$) and the ProACS score evidenced good discrimination (AUC 0.78, 95% CI 0.71-0.86, $p = 0.001$) for the outcome. The HL test applied to the ProACS score presented $\chi 2=8.6$ ($p=0.3$), and the SRI score $\chi 2=5.4$ ($p=0.7$).
Conclusions: The ProACS and SRI risk scores for the prediction of in-hospital mortality were adequately validated in patients with STEMI in Argentina. This suggests their suitability for clinical use in this population.

Keywords: Myocardial infarction – ST elevation myocardial infarction - Acute coronary syndrome – Prognosis

RESUMEN

Introducción: Los scores de riesgo se encuentran recomendados para estratificar y predecir mortalidad en el infarto agudo de miocardio con elevación del segmento ST (IAMCEST). Los modelos ProACS y Simple Risk Index (SRI) son scores simples que demostraron una buena capacidad predictiva de mortalidad intrahospitalaria en otros países.
Objetivo: Validar y comparar los scores ProACS y SRI como predictores de mortalidad intrahospitalaria en pacientes con IAMCEST.
Material y métodos: Análisis retrospectivo de una cohorte compuesta por pacientes ingresados de forma consecutiva con diagnóstico de IAMCEST, en el que se utilizaron datos del registro CONAREC XVII. Se estimó el valor predictivo para muerte intrahospitalaria y se evaluó la validez mediante la discriminación y la calibración.
Resultados: Se analizaron 694 pacientes. La mortalidad intrahospitalaria fue del 8,78%. En aquellos que presentaron el evento, la mediana del score ProACS fue de 4 (Pc 25-75, 2,5-5); y una mediana de 2 (Pc 25-75 1-3) en aquellos que no presentaron ($p < 0,001$). La mediana del score SRI fue de 41,3 (Pc 25-75, 29,8-62,5) y de 20,8 (Pc 25-75 15,4-30) en aquellos que fallecieron y los que no, respectivamente ($p < 0,001$), y demostró una excelente discriminación (AUC 0,83, IC95% 0,78-0,88, $p = 0,001$) y el score ProACS presentó una buena discriminación del desenlace (AUC 0,78, IC95% 0,71-0,86, $p = 0.001$). La prueba de HL aplicada al score Proacs presentó $\chi 2 = 8,6$ ($p = 0,3$), y el score SRi $\chi 2 = 5,4$ ($p = 0,7$).
Conclusiones: Los puntajes de riesgo de ProACS y SRI para la predicción de mortalidad intrahospitalaria fueron validados adecuadamente en pacientes con IAMCEST en Argentina. Esto sugiere su idoneidad para el uso clínico en esta población.

Palabras clave: Infarto del miocardio - Infarto del miocardio con elevación del ST - Síndrome coronario agudo – Pronóstico

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Abbreviations

ACS	Acute coronary syndrome	GRACE	Global Registry of Acute Coronary Events
PAMIA	Post-acute myocardial infarction angina	HL	Hosmer-Lemeshow test
AUC	Area under the receiver operating characteristic (ROC) curve	SRI	Simple Risk Index
E/O	Expected to observed events ratio	STEMI	ST-segment elevation acute myocardial infarction

INTRODUCTION

Risk stratification is defined as a statistical process to determine the identifiable characteristics associated with a higher probability of experiencing undesired outcomes. (1) When risk is stratified in acute coronary syndromes (ACS), it helps to guide healthcare resources and lead physicians in the patient's approach, the choice of revascularization strategy and other treatments. (2) All patients with ST-segment elevation acute myocardial infarction (STEMI) should undergo early risk stratification in order to identify patients at high risk of new events, such as death. (3) Higher risk scores guide the use of more aggressive treatments and the close monitoring for complications. (4)

Multiple risk scores have been developed based on identifiable parameters in the acute phase of infarction. These differ in predictive accuracy, as well as in the number, type and complexity of included variables. The first score developed was the TIMI risk score, (5, 6) but its predictive accuracy is usually lower than that of scores developed later, and the most recent and most utilized is the Global Registry of Acute Coronary Events (GRACE) score. (7, 8) This has high predictive accuracy, but includes multiple variables of significant complexity. On the other hand, the model derived from the Portuguese registry of acute coronary syndromes, called ProACS, (9, 10) and the Simple Risk Index (SRI) (11) are simple scoring systems with a low number of clinical variables, which have demonstrated good predictive capacity of in-hospital mortality in patients with STEMI in other countries.

Despite risk scores are recommended by clinical practice guidelines to stratify and predict mortality in STEMI, (4, 11-13) no validations have been performed in Argentina and there are barriers to their implementation given the complexity of the most widespread risk scores. Taking into account the variability of the clinical, ethnic, sociodemographic, cultural or idiosyncratic characteristics of the patients and the healthcare patterns of the different health systems of each country, before using and applying a probabilistic model of prediction outside the environment where it was created, (9-11) it is necessary to perform validations to ensure that it does not provide erroneous probabilities, thus enabling right decisions.

Objective

The aim of this study was to validate and compare the SRI and ProACS scores as predictors of in-hospital mortality in a cohort of patients diagnosed with STEMI in Argentina.

METHODS

A validation study of ProACS and SRI prognostic scores was conducted through the retrospective analysis of a cohort consisting of 694 consecutive patients with STEMI diagnosis, admitted to 45 centers (26.67% public, 73.3% private) from all over the country between December 2009 and July 2010, using data from the CONAREC XVII registry. (14) The score on admission was calculated and the predictive value of the score for in-hospital death was estimated.

All patients over 18 years of age admitted with presumptive STEMI diagnosis, interpreted as primary thrombotic event, were included in the study. To be cataloged within this condition required increased myocardial damage markers (preferably troponin, although CPK MB could also be used, depending on the availability of the center) with at least one of the following signs of ischemia: symptoms, changes in the electrocardiogram (ST-segment elevation or new left bundle branch block, or new Q waves) or new motility disorder on the echocardiogram.

Demographic data, educational attainment, stressful situations associated with the event, cardiovascular risk factors, comorbidities, patient's symptoms, hemodynamic status on admission, treatments adopted, times in which these were implemented, in-hospital complications and medication at discharge were collected.

Statistical analysis

Discrete variables were expressed as percentages, and continuous variables as mean or median, with their corresponding standard deviation and interquartile range, according to their distribution. Discrete variables were compared using the chi-square test or Fisher's exact test when appropriate, and, Student's t test or the Mann-Whitney test was used for continuous variables, according to sample distribution. A two-tailed p value <0.05 was defined as statistically significant.

The validity of the models was evaluated through its two components: discrimination through the area under the receiver operating characteristic (ROC) curve (AUC), and calibration using the Hosmer-Lemeshow goodness-of fit test (HL). Model calibration was evaluated using the HL test, which compares the difference between observed and model-predicted mortality –p >0.05 indicates that the model fits the data well and therefore accurately predicts the patients' probability of death-, and by means of calibration plots, comparing observed and expected mortality by risk deciles and the expected to observed events ratio (E/O) and its 95% confidence interval. Discrimination of scoring systems was determined based on their ability to identify patients who will die during hospitalization, and was analyzed by calculating the AUC.

All data were analyzed using SPSS 23 IBM software.

Variable definition

- ST-segment elevation infarction: Presence of ST-segment elevation measured at point J in two contiguous leads: ≥0.25 mV in men <40 years, ≥0.2 mV in men ≥40 years, or ≥0.15 mV in women in leads V2-V3 and/or ≥0.1 mV in other leads. (15) On the other hand, ST-segment elevation was interpreted as a presumably new complete left bundle branch block or with positive criteria. (16)

- Dyslipidemia: Total cholesterol values >200 mg/dL and/or triglycerides >150 mg/dL, in patients under treatment with lipid-lowering agents or self-referential.
- Diabetes: Fasting blood glucose >126 mg/dL, oral glucose tolerance test (OGTT) >200 mg/dL at 2 h, or random blood glucose >200 mg/dL before the event, in patients under treatment with hypoglycemic agents or insulin, or self-referential.
- Smoking: Regular or occasional tobacco consumption within the year prior to the event.
- Ex-smoker: Presenting at least one year of tobacco abstinence.
- Hypertension: Blood pressure ≥140/90 mmHg (130/80 mmHg in diabetic patients) and chronic kidney failure in baseline conditions in patients under antihypertensive treatment or self-referential.
- Post-acute myocardial infarction angina (PAMIA): Angina after 24 hours and within 30 days post infarction, in the case of STEMI.
- Re-AMI: 24 hours to 7 days after the event, angina lasting more than 20 minutes or new or recurrent changes in the electrocardiogram (supra-ST or infra-ST >1 mm in two or more contiguous leads) and CK-MB × 2 or 50% increase from the previous value.
- Stroke: New neurological focus, lasting more than 24 hours or compatible image in computed tomography or magnetic resonance imaging of the brain.
- Kidney failure: Creatinine clearance <60 mL/min estimated by the Cocroft Gault formula.

Risk scoring systems

The PROACS score (9, 10) is estimated from the following variables: age ≥72 years: 2 points, systolic blood pressure ≤116 mmHg, Killip and Kimball class 2 or 3 on admission and ST-segment elevation: 1 point each and Killip and Kimball class 4: 3 points. (9, 10) The result is classified into three risk categories: 0, with 0% mortality; 1-2, from 1% to 4% mortality; and ≥3 points, a probability of in-hospital death >4% (Table 1).

The SRI score or TIMI Risk Index (11) is derived from the following formula: heart rate in beats/min × ([age/10] 2)/systolic blood pressure. According to the assigned score, it is classified into 5 risk categories according to quintiles, with each of probability of 24-hour, in-hospital and 30-day death (11) (Table 2).

Ethical considerations

The studys was approved by the institutional Ethics Committee.

RESULTS

A total of 694 patients were analyzed. Mean age was 63.35±13.1 years and 78.3% were men; 63.4% were hypertensive; 21.9%, diabetics; and 51.6%, dyslipidemic. The rest of the baseline clinical characteristics are summarized in Table 3.

Overall in-hospital mortality was 8.78%. In patients who presented the event, the median ProACS score was 4 with IQR 2.5-5, which was significantly different from that of patients who did not present the event (median: 2, IQR 25%-75%: 1-3; p<0.001). Median SRI score was 41.3 (25%-75% IQR: 29.8-62.5) and 20.8 (25%-75% IQR: 15.4-30) in those who died and those who did not, respectively, with p <0.001 (Table 4).

The SRI score showed excellent discrimination for in-hospital mortality (AUC 0.83, 95% CI 0.78-0.88, p=0.001), and the ProACS score presented good discrimination for the outcome (AUC 0.78, 95% CI 0.71-0.86, P=0.001) (Figure 1 and Table 5).

The HL test applied to the ProACS score showed $\chi2$ of 8.6 (p=0.36), and the SRI score $\chi2$ of 5.4 (p=0.71). Both scores showed good calibration (Table 5 and Figure 2), with an E/O ratio of 1.02 (95% CI 0.72-1.39) and 0.99 (95% CI 0.72-1.48) in the SRI and ProACS scores, respectively (Table 5).

DISCUSSION

In the present study, we validated and compared two simple clinical models, ProACS and SRI scores as predictors of in-hospital mortality in a cohort of patients diagnosed with STEMI in Argentina. We found that

Table 1. ProACS risk score

Variable	Cut-off points	Points
Age	< 72 years	0
	≥ 72 years	2
SBP	< 116 mmHg	1
	≥ 116 mmHg	0
Killip and Kimball	1	0
	2	1
	3	1
	4	3
ST-segment elevation	No	0
	Yes	1

SBP: Systolic blood pressure.

Table 2. SRI risk score

Points	Risk group	Risk of death		
		24 hours	24 hours	p value
≤12.5	1	0.2%	0.6%	0.8%
>12.5-17.5	2	0.4%	1.5%	1.9%
>17.5-22.5	3	1%	3.1%	3.3%
>22.5-30	4	2.4%	6.5%	7.3%
>30	5	6.9%	15.8%	17.4%

both scoring systems have good calibration and discrimination, and that the SRI score is superior to the ProACS score to predict in-hospital mortality.

Stratification of ACS risk is fundamental in decision making. It is so important that in the clinical practice guidelines of the main cardiological societies some risk scores are listed as a tool, even to guide invasive vs. conservative treatment in the case of non-ST-segment elevation ACS. (17-19) In the case of patients with STEMI, this decision is not usually adopted using scores, since emergency reperfusion is the first-line of treatment for all cases. However, global risk assessment provides the opportunity to integrate several patient characteristics into a semiquantitative score that can convey a general estimate of a patient's prognosis; it can dictate the acumen, intensity and location of care; and can provide the patient and his family with a more informed sense of the possible outcomes. Higher risk scores generally imply that more intense treatments may be appropriate in the context of the patient's health status. (4)

Table 3. Baseline population characteristics

Variables	n = 694
Age (mean±SD)	63.35±13.1
Male gender (n; %)	544 (78,4%)
Hypertension (n; %)	440 (63.4%)
Diabetes (n; %)	152 (21.9%)
Dyslipidemia (n; %)	358 (51.6%)
Ex-smoker/smoker (n; %)	459 (66.1%)
Peripheral vascular disease (n; %)	34 (4.9%)
Stroke (n; %)	20 (2.9%)
History of coronary artery disease	
Acute Myocardial infarction	92 (13.3%)
CABG	16 (2.3%)
PCI	64 (9.2%)

CABG: Coronary artery bypass grafting. PCI: Percutaneous coronary intervention.

Table 4. Comparison of scores according to mortality

Score	Death	No death	p
ProACS (median; IQR)	4 (2.5-5)	2 (1-3)	<0.001
SRI (median; IQR)	41.3 (29.8-62.5)	20.8 (15.4-30)	<0.001

On the other hand, taking into account the healthcare reality of our country, with asymmetries in the availability of resources, it would be possible to select the patients who would derive the greatest benefit from a transfer to high complexity centers. A good example as an analogy of the value of an early triage strategy using scores can be seen in patients with multiple injuries, in whom the use of the Revised Trauma Score, which assembles simple easy accessible variables, allows the identification of more critical patients and at greater risk of complications for their transfer to specialized trauma centers. (20) This rapid initial triage was reflected in better outcomes for these patients and in the development of trauma networks in many countries. (21) However, for this to be applicable, risk scores must use simple and easily available variables.

As indicated by the STEMI clinical practice guide-

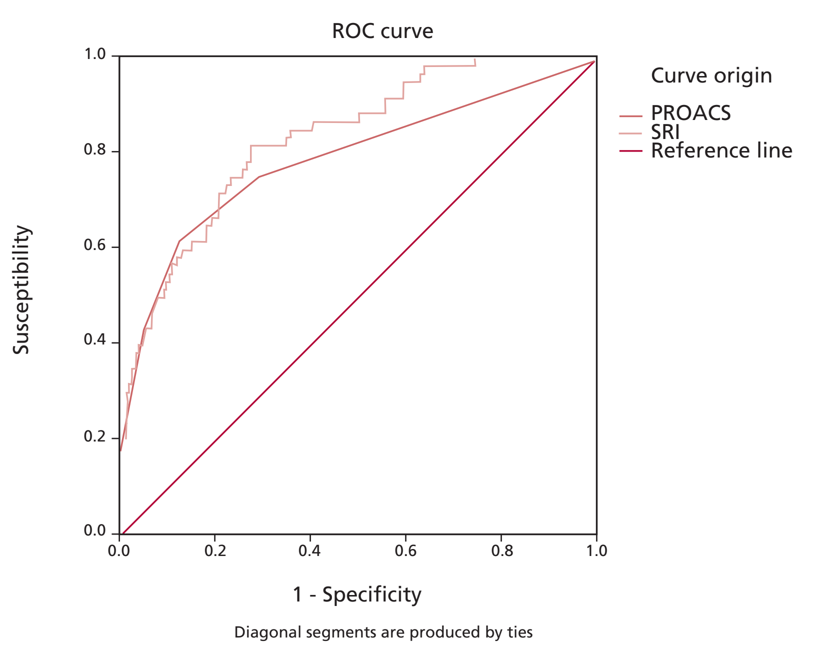

Fig. 1. ProACS and SRI score ROC curves to predict in-hospital mortality.

Table 5. Comparison of discrimination power and calibration degree of ProACS and SRI risk models to predict in-hospital death

Points	Discrimination			Calibration			
	AUC	95% CI	p	HL χ2	DF	p	E/O ratio 95% CI
SRI	0.83	0.78-0.88	0.001	5.43	8	0.71	1.02 (0.72-1.39)
ProACS	0.78	0.71-0.86	0.001	8.69	8	0.36	0.99 (0.72-1.48)

AUC: Area under the Roc curve. CI: Confidence interval. HL: Hosmer-Lemeshow test. DF: Degrees of freedom. E/O: Expected to observed ratio.

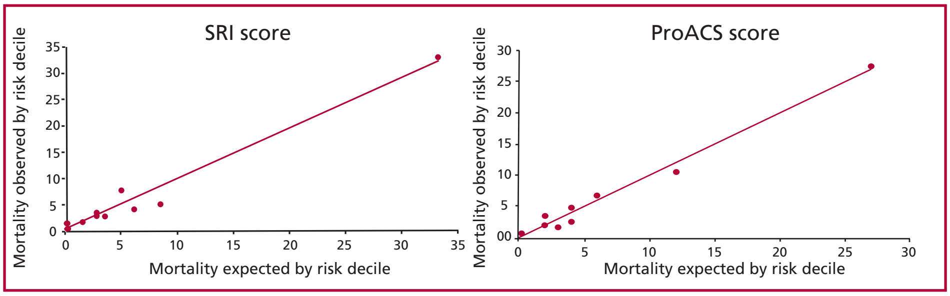

Fig. 2. Calibration of ProACS and SRI scores to predict in-hospital mortality.

line of the Argentine Society of Cardiology, (13) the optimal treatment of STEMI from a community perspective should be based on the use of networks between hospitals, with various levels of complexity connected by an efficient ambulance service, employing protocols based on risk stratification and transport in adequately equipped ambulances or other transfer systems for highly complex cases.

There are scores of high predictive value, but they require complex elements, including laboratory test values, such as the GRACE score, which would not be useful in the early stages of ACS. Other stratification systems seldom used in our practice and not validated in our setting are the CADILLAC score, (22) which is the most complex since it includes angiographic and echocardiographic variables, and the Primary Angioplasty in Myocardial Infarction (PAMI) Score. (23) In this context, the ProACS and SRI risk scores are attractive due to their simplicity and great predictive value.

The ProACS score showed an excellent discrimination capacity in the external validation cohort, allowing a simple risk stratification for in-hospital mortality in patients with ACS that may be used in the first medical contact. (9, 10) The SRI score, also called the "TIMI risk index", is a simpler model derived from the InTIME-II trial of fibrinolytic therapy and then validated in multiple populations, such as STEMI with primary angioplasty, which shows good behavior to predict in-hospital mortality. (11, 24, 25)

In our work, the ProACS score showed an AUC of 0.78, which is similar to that reported in the original work, where it presented an AUC of 0.815 (0.793-0.837) in the total ACS population and of 0.799 (0.768-0.830) in the STEMI subpopulation. This score, which uses only four variables, all of them clinical, was slightly lower than the GRACE score to predict in-hospital mortality (0.888 [0.865-0.910]). On the other hand, the SRI score presented an AUC of 0.78 in the first original validation and of 0.79 in the external validation, compared to an AUC of 0.83 in our work, demonstrating a superior predictive capacity in this validation. In general, a model with AUC >0.70 has an acceptable discrimination capacity. (26)

As limitations, we can mention that a retrospective analysis was performed with the biases inherent to this type of design and, in addition, 11 patients were excluded from the analysis (1.56%) because of incomplete data to calculate the scores. To our knowledge, this is the first work where these two predictive models were validated in our country for a STEMI population. A larger study with a prospective design should be carried out to evaluate the predictive capacity of these risk models for long-term mortality.

CONCLUSIONS

In this analysis of a multicenter study, the ProACS and SRI risk scores for the prediction of in-hospital mortality were adequately validated in patients with STEMI in Argentina, with adequate discrimination capacity and calibration, suggesting their suitability for clinical use in this population. They are simple risk models, based on characteristics easily assessed by any healthcare personnel, allowing a rapid stratification of the patient's risk without the need to use more complex scores, which are not validated in our setting and with less predictive value.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

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