ORIGINAL ARTICLE

Validation of TIMI risk score for STEMI

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Abstract

Background: TIMI risk score for ST elevation myocardial infarction (STEMI) is an important tool to assess mortality risk; however, it has not yet been validated in Brazil.

Objectives: To validate the TIMI risk score for STEMI patients as a predictor of in-hospital mortality and to identify new independent predictors of in-hospital mortality not described by this score. A new risk score called "Modified TIMI Risk Score" was created in an attempt to increase its discriminatory power.

Methods: Retrospective cohort study evaluating 983 patients with STEMI, obtained from a database of two leading cardiology institutions in Rio Grande do Sul. Clinical variables described for the TIMI risk score were tested using univariate analysis and multivariate analysis by logistic regression. Area under curve (AUC) was used to define sensitivity, specificity and discriminatory power of the score. Non-significant variables on multivariate analysis were excluded, and the discriminatory power of the modified TIMI risk score was calculated.

Results: In-hospital mortality was 8.6%. The TIMI risk score for STEMI showed a discriminatory power of 0.82, with no identification of new predictors of mortality. In the multivariate analysis, weight < 67 Kg, previous infarction, left bundle branch block and hypertension did not show statistical significance. A modified TIMI score that excluded these variables had discriminatory power of 0.84.

Conclusion: TIMI risk score for STEMI presented good discriminatory power as a predictor of in-hospital mortality. No new predictors of in-hospital mortality were found. The modified TIMI score did not present a discriminatory power that was superior to the TIMI score. (Int J Cardiovasc Sci. 2016;29(3):189-197)

Keywords: Cardiovascular Diseases/mortality; Myocardial Infarction/mortality; Hospital Mortality; Risk Assessment; Validation Studies.

Introduction

Cardiovascular diseases constitute the main cause of death in western populations, accounting for approximately 16% of all deaths in developed countries.[1-3] According to the National Registry of Myocardial Infarction (NRMI-2),[4] 13.7 million North-Americans present coronary artery disease (CAD). Its prevalence increases with age, reaching 7% of individuals between 40 and 49 years of age, and 22% of those between 70 and 79. In Brazil, in 2015, according to data from the Information Technology Department of the Public Health Care System (DATASUS), cardiovascular diseases accounted for 1,047,953 hospital admissions, of which 92,522 resulted in death by acute myocardial infarction (AMI).[5]

Clinically, AMI has a strong impact on patients' quality of life and prognosis, and it is the subject of numerous clinical studies seeking new diagnostic and therapeutic strategies. Risk stratification pROCess of AMI patients has two components: early identification of patients at

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high risk for recurring events at the time of admission, and determination of which patients, after AMI, have a high risk of major cardiac events. Those at high risk are generally candidates for a more aggressive treatment. Individuals at a lower risk can receive conservative treatment.[6,7]

Shah et al.[8] have recently demonstrated that the use of risk scores in chest pain units may be cost-effective tools. The most well known risk stratification scores are the TIMI index, GRACE risk model, and TIMI risk score.[9-12]

Among them, TIMI risk score has been the most utilized in clinical practice. It was elaborated from data of 15,000 patients who were eligible for fibrinolytic therapy, and corresponds to the sum of eight variables predictors of mortality (Table 1).[9]

In Brazil, TIMI risk score is the most widely used, even though there are few studies done with our population. For that reason, and because we believe it to be a tool of easy application, we aim to validate the TIMI risk score for STEMI in our environment.

Methods

This was a retrospective cohort study, where we evaluated 938 patients of both genders, between 20 and 95 years old, admitted for STEMI, between January 1st of 2005 and December 31st of 2007, in the Intensive Care Unit of the Institute of Cardiology of Rio Grande do Sul / University Foundation of Cardiology and at Hospital São Lucas from PUCRS.

We included patients who presented with chest pains and ECG showing ST-segment elevation in at least two contiguous leads, and new, or presumably new, left bundle branch block. Blood sample collection for the analysis of cardiac enzymes was done with all the patients.

Data were obtained through the data bank of one of the involved hospitals and a list of the names of all AMI patients from another hospital. TIMI risk score points were attributed as defined in Table 1. With this information, charts were reviewed and all pertinent data were registered. A single data bank was generated.

Table 1
TIMI risk score[9]

Age between 65-74 years old	2 points
Age ≥ 75 years old	3 points
History of diabetes, hypertension or angina	1 point
Systolic blood pressure < 100 mmHg	3 points
Heart rate > 100 bpm	2 points
Killip classification II to IV	2 points
Weight < 67 Kg	1 point
ST segment elevation in anterior wall or left bundle branch block	1 point
Reperfusion time > 4 hours	1 point

Statistical Analysis

The analysis was done using the software SPSS 20.0, with descriptive analysis of general data, univariate analysis through chi-square test for categorical variables, and Student's T test for continuous variables. Multivariate analysis by logistic regression was done for variables that presented $p < 0.05$ in the univariate analysis. Statistical significance was established at $p < 0.05$ for the multivariate analysis.

To estimate a sensitivity of 75%-90% with absolute error margin of 10% and confidence level of 95%, the sample had to contain at least 73 deaths, equivalent to approximately 9% of the total sample, according to the analysis by the software SPSS 22.0. In total, 811 patients were necessary. Multivariate analysis and risk score performances were based on the data of patients who had the complete necessary information for the score

application. The relation between the characteristics of the population and in-hospital mortality was done through univariate analysis. Independent mortality predictors were identified and submitted to multivariate analysis though logistic regression when $p < 0.2$.

The selection of independent predictor variables for TIMI risk score was based on their contribution to the prognosis relative to in-hospital mortality, defined by logistic regression. For each patient, TIMI score was calculated by the arithmetic sum of the points determined for each risk criterion through the following relation: one point for OR 1-2, two points for OR 2-2.5, and three points if OR > 2.5. Variable presentation of AMI was compared to the sum of all other presentations.

Discriminatory ability of the risk score was evaluated through ROC curve and through AUC. For the risk score, categories were unified when ≥ 8 points, due to the small prevalence of patients were higher scores.

The study was submitted to the analysis and approval of the Research Ethics Committee of the hospitals involved, according to the resolution of the National Health Council. Free consent forms were not presented because this was a retrospective analysis study of charts from patients who are difficult to be located due to outdated addresses or who are deceased. However, the researchers were committed to abiding by the norms of resolution 196/96 of the National Health Council, ensuring confidentiality with regards to privacy of confidential data involved.

This study was financed with private resources and was done as part of a Masters dissertation in the Program of Post-Graduation in Health Sciences, Cardiology Concentration Area of the Cardiology University Foundation/Institute of Cardiology of Rio Grande do Sul.

Results

A total of 34% percent of the sample was female; mean age was 59.9 +/- 12.6 years. There were 602 individuals (64.2%) who were under 65 years old and were used as reference category. In regards to coronary risk factors referred at admission, 24.2% presented with diabetes mellitus type 2 (DM2); 65.8% had arterial hypertension; 36.2% had dyslipidemia; 51.8% were smokers; 22.3% presented sedentarism; and 16.7% were obese. Family history of coronary disease was found in 27.8% of the sample.

In-hospital mortality was 8.6% (81 patients). Cardiogenic shock occurred in 10.3%, reinfarction in 3%, and stroke in 1.1%.

Reperfusion through thrombolysis was realized in 17.9% (168 patients), and through percutaneous coronary angioplasty (PTCA) in 58% (544 patients). Rescue PTCA was done in 4.9%, and facilitated PTCA in 0.85%. Population characteristics and in-hospital mortality, by univariate analysis, are summarized in Table 2.

Predictors of In-Hospital Mortality and Application of TIMI Score

Each clinical variable of relevance was submitted to univariate analysis, amounting to a total 22 variables (Table 2). Age was divided into three intervals: ≥ 75 years old, between 65 and 74 years old and < 65 years old.

Weight < 67 Kg, hypertension, previous AMI, peripheral vascular disease, previous PTCA, previous MRS, DM, SAH, angina and previous AMI did not present statistical significance in the univariate analysis. Variable presentation of AMI was compared to the sum of all other presentations.

Smoking and inferior AMI showed statistical significance, but were protectors.

The 12 variables that present statistical significance in the univariate analysis (age ≥ 75 years old and between 65 – 74 years old, diabetes mellitus/angina, smoking, cerebrovascular disease, previous angina, inferior wall infarction, left bundle branch block and other location in AMI presentation, Killip II-IV, HR > 100 bpm, SBP < 100 mmHg and time to treatment > 4 hours) were submitted to multivariate analysis.

Of the variables above, age 65-74 years old (OR 1.98, CI 1.03-3.8), ≥ 75 years old (OR 5.62, CI 2.89-10.91), SBP < 100 mmHg (OR 7.38, CI 3.86–14.09), HR over 100 bpm (OR 3.43, CI 1.43-8.19), Killip II-IV (OR 2.83 CI 1.54-5.20), reperfusion time over 4 hours (OR 2.09, CI 1.54-5.20) , diabetes (OR 2.43, CI 1.41–4.20) and history of previous angina (OR 2.24, CI – 1.10–4.66) remained statistically significant after multivariate analysis. For each patient, the TIMI score was calculated as the simple arithmetic

Table 2
Univariate analysis of risk of in-hospital death

Variables	Total =938 n (%)	Death n (%)	OR (CI 95%)	p
Demographic Data				
Age				
75 years	124 (13.2%)	31 (25%)	7.1 (3.9-12.9)	< 0.001
65 – 74 years	212 (22.6%)	23 (10.8%)	2.59 (1.4-4.8)	< 0.001
Gender				
Male	625 (66.6%)	47 (7.5%)	0.66 (0.4-1.1)	0.108
Female	313 (33.4%)	34 (10.9%)		
Anthropometry				
Weigh < 67 Kg (referred)	09 (1%)	01 (11.1%)	1.32(0.1–10.7)	0.558
Risk Factors				
Diabete Mellitus	227 (24.2%)	33 (14.5%)	2.35 (1.4-3.7)	0.001
Arterial Hypertension	617 (65.8%)	50 (8.1%)	0.85 (0.5-1.3)	0.463
Smoking	486 (51.8%)	30 (6.2%)	0.52 (0.3–0.8)	0.007
Cardiovascular History Previous				
AMI	162 (17.3%)	16 (9.9%)	1.19(0.6–2.1)	0.539
Peripheral Vascular Disease	34 (3.6%)	04 (11.8%)	1.4 (0.5-4.2)	0.726
Cerebrovascular Disease	38 (4.1%)	11(28.9%)	4.8 (2.2–10.1)	< 0.001
Previous Angina	84 (9%)	13 (15.5%)	2.11 (1.1-4)	0.025
Previous PTCA	86 (9.2%)	06 (7%)	0.77 (0.3-1.8)	0.689
Previous MRS	62 (6.6%)	05 (8.1%)	0.92 (0.3–2.3)	0.550
DM/SAH/Previous Angina	687 (73.2%)	57 (8.3%)	0.85 (0.5-1.4)	0.599
AMI Presentation (Localization /	366 (39%)	33 (9%)	1.02(0.6-1.7)	0.812
Characteristics)	24 (2.6%)	08 (33.3%)	5.8 (2.4-13.9)	< 0.001
LBBB	505 (53.8%)	35 (6.9%)	0.62 (0.3-0.9)	0.040
Others	75 (8%)	14(18.7%)	2.7 (1.4-5.1)	< 0.003
Killip II – IV	108 (11.5%)	28 (25.9%)	5.13 (3.0-8.5)	< 0.001
HR > 100 bpm	55 (5.9%)	12 (28.6%)	4.7 (2.3-9.7)	< 0.001
SBP (mmHg) < 100	69 (7.4%)	26 (37.7%)	8.9 (5.1-15.6)	< 0.001
Time to treatment > 4h	607 (64.7%)	66 (10.9%)	2.57 (1.4-4.5)	0.001

OR: odds ratio; CI: confidence interval; AMI: acute myocardial infarction; PTCA: percutaneous coronary angioplasty; MRS: myocardial revascularization surgery; DM: diabete mellitus; SAH: systemic arterial hypertension; LBBB: left bundle branch block; HR: heart rate; SBP: systolic blood pressure.

sum of he obtained points for each variable, according to the OR. Graph 1 shows the TIMI risk score and its relation to in-hospital mortality.

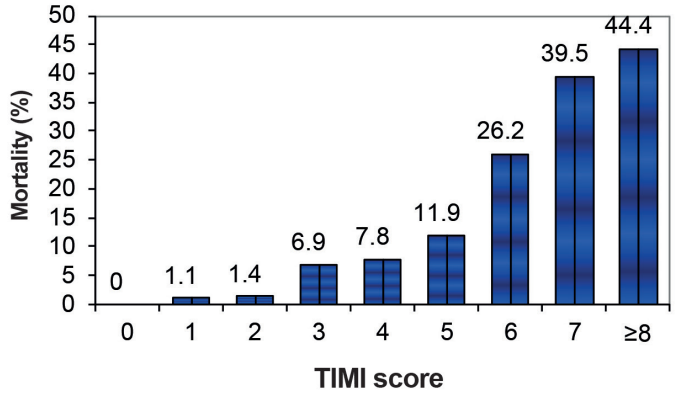
TIMI risk score for STEMI applied in this population proved to be a predictor of in-hospital mortality. Patients with 1 point showed mortality of 1.1%, and those with a score ≥ 8 presented 44.4% mortality in the sample. In patients with a score of zero (33 patients) no deaths occurred.

Discriminatory power of TIMI risk score was 0.82, with 70% sensitivity and 79% specificity, in its best index (Graph 2).

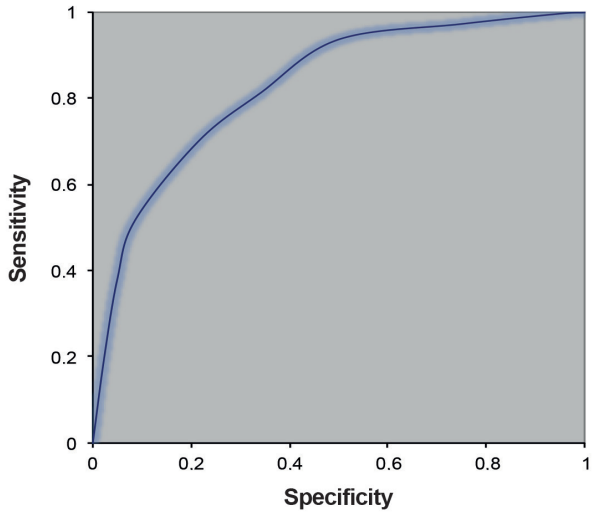
With base on in-hospital mortality predictors of AMI, in our population, we elaborated a new risk score – the Modified TIMI score. Table 3 shows the variables that were not significant after multivariate analysis and that were excluded for the creation of a new score.

For the variables that remained significant after multivariate analysis, new scores were attributed according to the OR (Table 4).

The score was limited between 0 and ≥ 8 points, due to the low number of individuals with higher scores (46 patients).



Graph 1
In-hospital mortality and TIMI risk score.



Graph 2
ROC curve of the TIMI score for in-hospital mortality.

Table 3
Variables submitted to the multivariate analysis excluded from the modified TIMI score

Variable	OR (CI)	p
LBBB	1.38 (1.03 – 1.83)	0.01
Inferior AMI	0.76 (0.45 – 1.29)	0.32
ECG others	1.13 (1.01 – 1.26)	0.04
Smoking	0.94 (0.58-1.79)	0.94
Cerebrovascular disease	2.24 (0.89 – 5.5)	0.84

LBBB: left bundle branch block; AMI: acute myocardial infarction; ECG: electROCardiogram

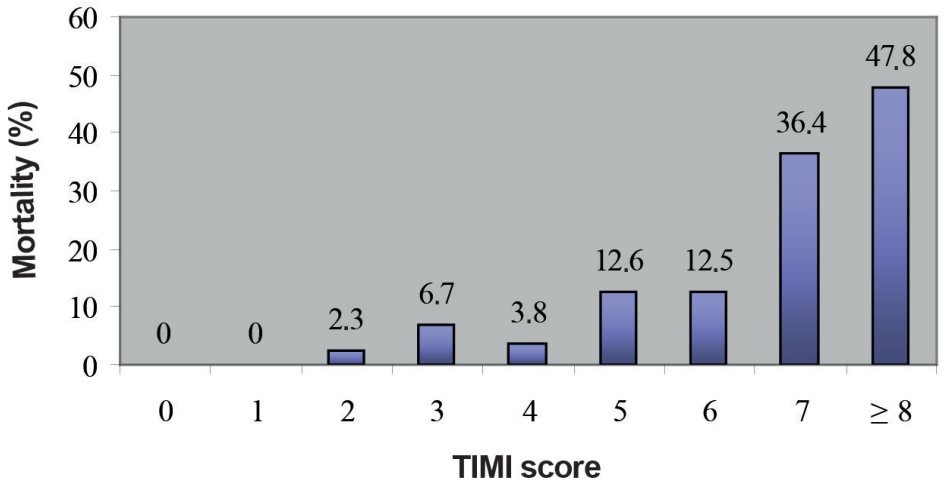
Table 4
Modified risk score according to OR

Variable	OR (CI)	Score
Age 65-75 years old	2.0 (1.03-3.83)	2
Age ≥ 75 years old	5.62 (2.89-10.91)	3
SBP <100 mmHg	7.38 (3.86 - 14.09)	3
HR > 100 bpm	3.43 (1.43-8.19)	3
Killip II-IV	2.83 (1.10-3.99)	3
Reperfusion time > 4 h	2.09 (1.54-5.20)	2
Diabetes	2.43 (1.41-4.2)	2
PH stable angina	2.24 (1.10 – 4.66)	2

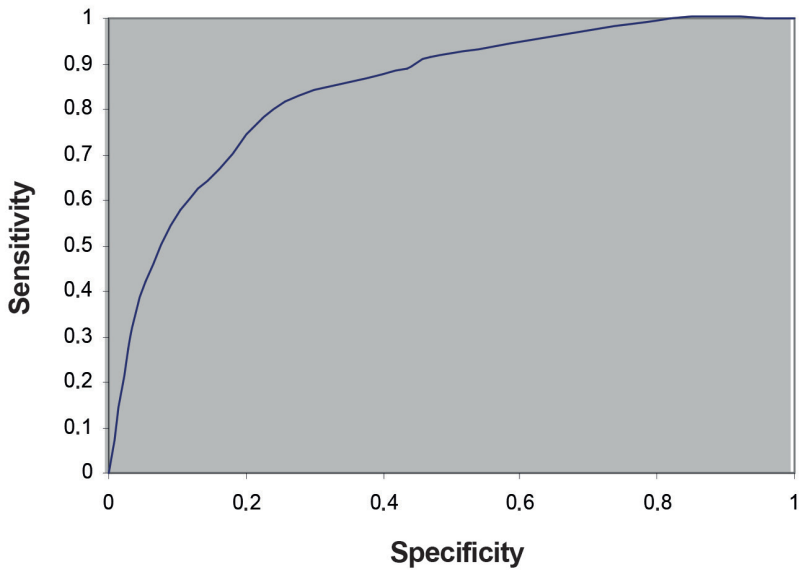
CI: confidence interval; PH: previous history

In-hospital mortality, evaluated by the new model, presented a variation between 2.3% in patients with a score of 2 points, and 47.8% for scores ≥ 8 points (Graph 3).

While assessing the AUC of the modified TIMI score, we observed a discriminatory power of 0.84 with 81% sensitivity and 75% specificity in its best index (Graph 4).



Graph 3
In-hospital mortality and modified TIMI score.



Graph 4
ROC curve of the modified TIMI score.

Discussion

TIMI risk score for STEMI proved to be fully applicable as a robust method with a good ability to predict in-hospital mortality. In our population, composed of patients undergoing chemical and/or mechanical thrombolysis and individuals who did not receive thrombolysis, mortality of 1.4% appeared for those with a score of 2, 11.9% in patients with a score of 5, and 44.8% in patients with a score ≥ 8.

Morrow et al. applied the TIMI risk score in 84,029 patients from the 3° American Registry of AMI, which demonstrated a gradual increase of mortality as the calculated score increased. Patients with a score of 2 presented mortality within 30 days of 6.8% (not submitted to reperfusion therapy) and 2.2% (submitted to reperfusion), while those with a score of 5 had 19% mortality within 30 days (not submitted to reperfusion therapy) and 10% (with reperfusion therapy). Scores > 8 points in this population presented mortality rates of 35% in those with reperfusion therapy, and 29% without.[12]

Score application in the population of the InTIME II study also showed mortality indices that were very similar to those found in our population. Of the patients with a score of 2 points, 1.3% died, while at a score of 5, mortality reached 12% in 30 days. Patients with scores > 8 points presented 32% mortality in the same period.[9]

Antmann et al. evaluated the score in 20,479 patients from the Extract-TIMI 25 study, observing a mortality of 2.7% and 8.9% in patients with AMI with scores of 2 and 5 points, respectively, while those with 8 points at admission presented a 29.6% mortality.[13]

The data obtained from a cohort of 2,022 patients ≥ 65 years old with AMI revealed superior mortality indices. Patients with a TIMI score of 2 points presented mortality of 4.4%, while scores ≥ 8 points showed indices of 35.6% of mortality in 30 days, though with a lower discriminatory power (0.67).[14]

In the Brazilian population, Pereira et al. demonstrated a progressive increase in mortality and in the occurrence of in-hospital complications, according risk stratification by the TIMI score.[15]

Results from the application of tools elaborated for risk stratification in AMI patients usually cannot be generalized. The population in which risk scores were developed invariable belong to clinical studies, and may not correspond to local reality.

Data obtained with the elaboration of the modified TIMI score show that patients with a score of 2 points had 2.3% of deaths during hospital stay, while patients with a score of 5 points presented in-hospital mortality of 12.6%. In our population, the discriminatory power of the TIMI risk score was superior to indices found in

literature (0.82), and the creation of a modified TIMI score slightly increased this value (0.84).[16]

The application of the score in the population of a study called Gusto I, including 41,021 patients submitted to thrombolytic therapy, demonstrated good discriminatory power (0.80).[12] Morrow et al.[12], in turn, found different indices in patients submitted to thrombolysis (0.79), when compared to those without reperfusion (0.65), where the latter has low discriminatory power, elevating the risk of underestimating deaths.[10] When applying the score to the population from the InTime II study, the same author found good discriminatory power (0.746). When evaluating the TIMI risk score for STEMI, Antmann et al.[13] obtained similar discriminatory power (0.73).

Correia et al.[17] have recently evaluated the discriminatory power of the TIMI risk score in comparison to the GRACE risk score in 152 STEACS patients, showing a similarity between the scores, but better calibration for the TIMI risk score.[17]

The comparison between the TIMI risk score and other scores (PAMI, CADILLAC, and GRACE), also done by Méndez-Eirin et al.[18], did not show superiority for any of them, and confirmed the high accuracy of mortality prediction in all the evaluated scores.[18]

Abelin et al.[19] have recently concluded that TIMI, GRACE and Zwolle scores presented adequate performance as mortality predictors in patients submitted to primary angioplasty in the current practice. Results suggest that such risk scores are the appropriate options for assessment in the real world.[19]

This study presents limitations such as the fact of it being retrospective and based on previously formulated data banks; some variables were not available in all cases. Moreover, we do not have access to 30-day follow up data, and the score was validated for in-hospital mortality only.

Conclusion

TIMI risk score proved to be a fully applicable bedside tool in our population as an in-hospital mortality predictor, providing important prognostic information. We did not find any independent variables that were not referred to in the TIMI score. The modified TIMI risk score did not show better power in the prediction of in-hospital mortality.

Author contributions

Conception and design of the research:Silveira DS, Jaeger CP, Hatschbach L, Manenti ERF. Acquisition of data: Silveira DS, Jaeger CP, Hatschbach L, Manenti ERF. Analysis and interpretation of the data: Silveira DS, Jaeger CP. Statistical analysis: Silveira DS. Writing of the manuscript: Silveira DS, Jaeger CP, Hatschbach L, Manenti ERF. Critical revision of the manuscript for intellectual content: Silveira DS, Jaeger CP, Hatschbach L, Manenti ERF.

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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