

TIMI Risk Score for Acute Myocardial Infarction according to Prognostic Stratification

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Summary

Background: The TIMI (Thrombolysis in Myocardial Infarction) risk score is derived from clinical trial involving patients who are eligible for fibrinolysis. As the risk profiles of these cases differ from those found in non-selected populations, it is important to review the applicability of the score in usual clinical conditions.

Objective: To evaluate the management and clinical evolution of hospital inpatients with acute myocardial infarction, according to risk stratification by the TIMI score.

Methods: We evaluated, retrospectively, 103 cases of acute myocardial infarction with ST-segment elevation admitted to the Hospital Nossa Senhora da Conceição – Tubarão, in 2004 and 2005. The cases were analyzed in three risk groups according to the TIMI score.

Results: The hospital mortality after infarction was 17.5%. In the low-risk group there was no death. The mortality was 8.1% in the medium risk group and 55.6% in the high-risk group. The risk of death in cases of high risk was 14.1 times higher than in the cases of medium and low risk (95% CI = 4.4 to 44.1 and $p < 0.001$). The chance of receiving fibrinolytic was 50% lower in the high-risk group in relation to the low risk group (95% CI = 0.27 to 0.85, $p = 0.004$).

Conclusion: There was a progressive increase in mortality and incidence of in-hospital complications according to the stratification by the TIMI score. High risk patients received thrombolytic less frequently than the patients at low risk. (Arq Bras Cardiol 2009; 93(2):100-106)

Key Words: Clinical - dynamic prognosis; myocardial infarction; hospital mortality.

Introduction

Acute myocardial infarction (AMI) is a major public health problem in industrialized countries¹. In the United States, coronary heart disease is responsible for 53% of deaths from cardiovascular disease, and approximately 782 thousand cases of myocardial infarction occur each year, in Americans aged over 65². Although the number of heart attacks that occur each year in Brazil is unknown, it is estimated to be around 300 to 400 thousand; therefore, IAM is the leading isolated cause of death in the country^{1,3}.

In recent decades, the establishment of coronary units, the widespread use of fibrinolytic, beta blockers, aspirin and the development of transluminal coronary angioplasty contributed to reduce the rate of hospital mortality after AMI, from 30% in the 50's to the current 6 to 10%³⁻⁵. However, the variability in mortality is considerable and it is related to differences in the seriousness of the conditions and the quality of medical care³⁻⁶.

In this context, the use of prognostic scores for risk stratification of post-infarction becomes an important tool in the management of these patients³. The determination of

the patient's prognosis allows an early indication of complex procedures such as coronary angiography, angioplasty and surgical revascularization for high risk cases and less in-hospital time for low-risk individuals^{7,8}.

The TIMI score⁹ for acute myocardial infarction with ST-segment elevation was originally described based on eight variables⁹. This score has been described as simple, easily applicable at the bedside and with good discriminatory power for clinical complications and early mortality^{9,10}.

Some researchers have emphasized the need to test the applicability of the clinical risk scores in other populations, different from that of the original study¹¹, arguing that the inclusion and exclusion criteria of each study can select different risk profiles that may influence the prognostic factors retained in the final score and the clinical validity of the study in different populations^{11,12}.

Considering all these aspects, the application of the TIMI score allows us to assess the performance of the score in predicting the risk of death and post-infarction complications in usual clinical conditions. Also, it allows us to identify possible differences in the management of patients as determined by the prognosis score.

Methods

This was a cross-sectional, observational and retrospective study, conducted at the Hospital Nossa

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Senhora da Conceição - Tubarão - SC, from January 1st, 2004 to December 31st, 2005, of 103 patients with a diagnosis of acute myocardial infarction with ST-segment elevation. Data collection was performed by consulting the medical records and completing a protocol developed by the researchers.

The criteria for the diagnosis of acute myocardial infarction with ST-segment elevation were: presence of chest pain or other symptoms suggestive of AMI, ST-segment elevation on admission or during hospital evolution in two or more contiguous leads (greater than 0.2 mV in V1, V2 and V3 leads or greater than 0.1 mV in other leads), new or presumably new left bundle branch block and typical curve of creatine kinase enzyme and its MB fraction³. The patients were divided into groups according to TIMI risk scores (Appendix 1). The minimum score for the TIMI is zero, and the maximum score is fourteen. All 103 cases received a score between zero and thirteen, because the variable weight was not recorded in the medical records. Therefore, low-risk cases had a score between 0 and 2; average risk cases had a score ranging from 3 to 5; and high risk cases had a score greater than 5¹³.

The study variables included age, gender, origin, time of admission, heart rate, blood pressure, cardiorespiratory arrest on admission, elapsed time between pain and first care, Killip-Kimball class on admission, electrocardiographic location of the infarction, maximum values of cardiac enzymes, complications, and use of thrombolytic.

Patients who had fasting blood glucose levels compatible with the diagnosis in previous exams or during hospitalization were considered diabetic. Hypertension and angina were diagnosed prior to the AMI.

The primary outcome analyzed was post-infarction mortality. The following complications during hospitalization were taken into consideration: sustained ventricular tachycardia, ventricular fibrillation, asystolia and high degree atrioventricular block were considered positive when documented in medical records or when present in any electrocardiograms performed during hospitalization. The diagnosis of cardiogenic shock took into account the need for vasoactive drugs and/or its documentation in the medical records. Recurrent chest pain was taken into account only if documented in medical records. Patients with Killip class II were those with crackles at lung bases or S₃ gallop, and patients with Killip class III were those with audible crackles up to the middle lung fields³.

Data analysis was done by the SPSS™ 8.0 software. The data were presented as frequencies or averages with the associated standard deviation. The chi-square, or the Fisher exact test, when appropriate, was used to test the statistical significance of the difference in proportions for the study categorical variables. A two-tailed p-value <0.05 was considered statistically significant. Confidence intervals were calculated at 95% (95% CI) for the estimated relative risk (RR) in the sample.

The study was approved by the Research Ethics Committee of the University of Southern Santa Catarina - UNISUL.

Results

The average age was 60 ± 12 years, 58.3 ± 10.9 years for males and 63.6 ± 13.5 years for females. The city of origin was Tubarão in 39.8% of cases.

The average elapsed time between the onset of symptoms and first medical care was 6.7 ± 8.6 hours. For patients from Tubarão the average time was 4.5 ± 4.6 hours, while for those coming from neighboring municipalities it was 8.2 ± 10.2 hours. The average time between the onset of the symptoms and the demand for medical care was 6.8 ± 10 hours for males and 6.5 ± 4.8 hours for females.

The location of the infarction pointed to a more frequent involvement of the inferior wall (51.5% of cases) and a higher mortality when the infarction affected the extensive anterior wall (33.3%). There was no case of left bundle branch block (Table 1).

Hospital mortality after AMI was 17.5%. Of the total deaths, 66.7% occurred within 48 hours.

There was a progressive increase in mortality as the TIMI risk score increased. The risk of death in the high-risk group, when compared to that of the medium and the low risk groups, was almost 14.1 times higher (95% CI: 4.4 to 44.9, p <0.001) (Table 2).

In the sample, 58.3% of the patients received thrombolytic, and the mortality rate in this group was 10%. Among patients aged 75 years or over, only 2.9% were treated with streptokinase. Fibrinolytic was used in 45.7% of the female patients, and in 64.7% of the male patients. The use of fibrinolytic was almost 50% lower in the high-risk group in comparison to the low risk group (RR = 0.48, 95%CI :0.27 to 0.85, p = 0.004).

The maximum values of cardiac markers were related to in-hospital mortality. The peak creatine kinase (CK) level was less than ten times the normal value in 52.9% of cases, with a mortality rate of 6.5%. Among the 32.2% of patients with intermediate values of CK (peak CK levels of 10 to 20 times the normal value), 14.3% of them died. The mortality rate in the group with a peak CK level of more than 20 times the normal value was 30.8%. As to the CK-MB isoforms, 33.3% of the patients had peak levels of less than 5 times the normal value, with a mortality rate of 6.9%. In the group that reached peak CK-MB levels of less than 5 times the normal value, 18.2% of the patients died.

The mortality rate for women was more than triple the rate for men. The female group was associated with a 2.1 times greater risk of belonging to the group at high risk (95% CI: 1.23 to 3.75, p = 0.008). The risk of presenting Killip class II to IV on admission was 2.1 times higher among women (95% CI = 1.17 to 3.68, p = 0.013). Moreover, 25.7% of women were aged 75 years or over, compared to only 7.4% of men (Table 3).

Among patients with Killip class IV on admission, 100% of them belonged to the group at high risk by the TIMI score. Moreover, 70% of the patients who developed cardiogenic shock during hospitalization were in the category of high risk (Table 4).

Among high risk patients who were hospitalized for 48 hours or less, 8.3% were transferred and the remaining died.

Cardiorespiratory arrest was associated with a mortality rate of 66.7% (58.3% when associated with ventricular fibrillation, and 75% when associated with asystolia). Patients with cardiogenic shock died in 90% of cases. There were no cases of sustained ventricular tachycardia (Table 5).

The average length of hospitalization was 9.1 ± 8.8 days. Low-risk patients remained in hospital for 7.9 ± 3.0 days, on average. For patients with medium risk, the hospitalization time was 10.7 ± 9.6 days, while for those with high-risk it was 8.5 ± 12.4 days.

Discussion

In this sample, the distribution by gender and age groups was similar to that observed in other studies^{4-6, 9,14}.

The average elapsed time of 6.7 hours between the onset of symptoms and the first evaluation in the emergency room was less than that described by Zornoff et al¹⁴ (10.6 hours).

As this is a reference hospital in the region, there were significant discrepancies in the elapsed time between the onset of symptoms and the medical care, depending on where the patient came from. For patients living in Tubarão, the average

Table 1 - Patient profiles and in-hospital post-AMI mortality. Tubarão-SC, 2004 to 2005

Variables	Number / (%)	Mortality (%)
Demographic Characteristics		
Male	68 (66.0)	10.3
Female	35 (34.0)	31.4
Age 18 to 74 years	89 (86.4)	9.0
Age 75 years or over	14 (13.6)	71.4
Risk Factors of the TIMI Score		
Diabetes Mellitus	45 (43.7)	26.7
Elevated Blood Pressure	63 (61.2)	19.0
Angina	18 (17.5)	22.2
Clinical Condition		
SBP ¹ < 100 mmHg	25 (24.3)	40.0
HR ² > 100 bpm	16 (15.5)	50.0
Cardiorespiratory Arrest	4 (3.9)	75
Killip I	72 (69.9)	1.4
Killip II – IV	31 (30.1)	54.8
$\Delta T^3 \leq 4$ hours	51 (49.5)	9.8
$\Delta T > 4$ hours	52 (50.5)	25.0
Anterior wall AMI ⁴	51 (49.5)	21.6
Extensive anterior wall AMI	6 (5.8)	33.3
Inferior wall AMI	53 (51.5)	17.0

¹ Systolic blood pressure; ² Heart rate; ³ Elapsed time between pain and initial care; ⁴ Acute Myocardial Infarction.

Table 2 – In-Hospital Post-AMI mortality according to risk groups by the TIMI score. Tubarão-SC, 2004 to 2005

Risk Group	TIMI score points	Number of cases	Mortality (%)
Low Risk	0 to 2	39	0
Medium Risk	3 to 5	37	8.1
High Risk	Above 5	27	55.6

Table 3 - Variables associated with in-hospital mortality from AMI. Tubarão-SC, 2004 to 2005

Variable	RR	95% CI	P value
Age 75 years or over	7.9	3.8 a 16.6	0.000
Female gender	3.1	1.3 a 7.2	0.007
Diabetes mellitus	3.7	1.3 a 10.8	0.008
Killip II –IV on admission	2.2	1.5 a 3.2	0.000
Heart rate above 100bpm	4.3	2.0 a 9.0	0.000
Systolic blood pressure of less than 100mmHg	3.9	1.7 a 8.8	0.002
Non-use of thrombolytics	2.8	1.2 a 6.9	0.033
Presence of one or more in-hospital complications*	4.5	1.4 a 14.7	0.004

* Killip II/III on clinical evolution, recurrent chest pain, ventricular fibrillation, asystolia, high degree atrioventricular block, and cardiogenic shock.

Table 4 - Characteristics of the patients with acute myocardial infarction in the first evaluation and in the clinical evolution, according to risk groups. Tubarão-SC, 2004 to 2005

Variable	Low Risk (%)	Medium Risk (%)	High Risk (%)
Previous Medical History			
Elevated blood pressure	46.2	73	66.7
Angina	12.8	24.3	14.8
Diabetes Mellitus	20.5	56.8	59.3
Clinical Condition			
Killip II – IV	0	25.8	74.2
SBP ¹ < 100 mmHg	0	8.1	48.1
HR ² > 100 bpm	15.4	13.5	51.9
ΔT ³ > 4 hours	38.2	56.8	70.4
Extensive anterior wall AM ⁴	10.3	16.2	25.9
Thrombolytic treatment	69.2	64.9	33.3
Hospitalization time ≤ 48hs	0	5.4	44.4
Transfer to other hospital	17.9	13.5	11.1
Presence of one ore more in-hospital complications ⁵	30.8	62.2	70.4

¹systolic blood pressure; ²Heart rate; ³Elapsed time between pain and initial care; ⁴Acute myocardial infarction; ⁵Killip II/III on clinical evolution, recurrent chest pain, ventricular fibrillation, high degree atrioventricular block, and cardiogenic shock.

Table 5 – Mortality related to in-hospital post-AMI complications. Tubarão-SC, 2004 to 2005

Complication	Frequency(%)	Mortality(%)
Killip II/III	32	27.3
Recurrent chest pain	22.3	13
Ventricular fibrillation	11.7	58.3
High degree atrioventricular block	10.7	45.5
Cardiogenic shock	9.7	90
Asystolia	7.8	75

time between pain and medical care was 4.5 hours, and for patients from neighboring municipalities, it was 8.2 hours. Another fact that stands out is that 70.4% of high risk patients had to wait more than 4 hours before receiving initial care.

The prevalence of elevated blood pressure (61.2%) was similar to that found in Brazilian studies^{4,6,15} and higher than that found in international studies (21.6%⁹ and 54%¹⁰).

Two recent studies reported a prevalence of angina before the infarction of 46%⁶ and 65%¹⁶, which are quite high values when compared to the rate of 17.5% found in this sample. Other international studies have reported a prevalence of angina before the infarction of 11.5%¹⁰ and 21.6%⁹.

The hemodynamic status of patients on admission was more severe compared to that described in the literature. In this sample, the frequency of Killip classes II-IV was 30.1%, compared to 25.1%¹⁰, 17.3%¹⁶ and 12.2%⁹ found in other studies. A systolic blood pressure of less than 100mmHg on admission was present in 24.3% of the cases. In other studies this frequency was 2.5%⁹ to 8.7%¹⁰.

Refuting the literature⁴, in this study the most affected wall in AMI was the inferior wall, instead of the anterior wall. However, in the group classified as high risk, the anterior wall was affected in 25.9% of the cases.

Whatever the technique, myocardial reperfusion is the most important intervention in the management of AMI patients³. A Brazilian study estimated that the percentage of indicated thrombolysis in Brazil is 40%¹⁷. National and international studies reported that in 36.8%¹⁷, 39%¹⁴, 48%¹⁰ and 35.1%⁴ of cases, reperfusion therapy was used. In this study, 58.3% of patients used Streptokinase. However, in the group stratified as high risk, this therapy was used in only 33.3% of the cases. An international study also stressed that patients who were not submitted to reperfusion therapy had a higher prevalence of high-risk characteristics and higher TIMI scores¹⁰.

The average length of hospitalization was similar to that reported in another study (9 days)⁶. No patients at low risk remained less than 48 hours in hospital however, 44.4% of high risk patients were discharged during that period. Approximately 67% of patients who were hospitalized for less than 48 hours died.

In the *TIMI* study⁹, 50% of patients were considered to be at low risk, and only 12% at high risk⁹. In this study, 26.2% of the cases were at high risk, and 37.9% at low risk.

In this sample, recurrent chest pain, ventricular fibrillation, a high-degree atrioventricular block and cardiogenic shock occurred in a frequency similar to that described by other authors^{3,4,14,15}.

The in-hospital mortality rate among unselected patients with AMI ranged from 10 to 20%¹⁸. The mortality rate of 17.5% found in this sample was similar to that found in other Brazilian^{4,6,19} and international studies (12.6%¹⁰). These values are quite different from the value of 6.1% found in randomized clinical trials, such as the *TIMI* study⁹.

The identification of predictors of higher mortality after AMI has been described by many authors^{4,6,14,19}. Several studies have proposed prognostic scores based on the variables with the greatest impact on mortality in multivariate analysis.

In this sense, the *TIMI* score was strongly associated with mortality, and the risk of death for patients with a score greater than or equal to 8 was 40 times higher when compared with the score 0⁹. In addition, scores higher than 5 identified, in the *TIMI* study⁹, 12% of patients who had a risk of death that was more than twice that reported in the average population.

Bassam et al¹⁹ considered as low-risk the groups with mortality rates below 10%, and as high-risk the groups with mortality rates above 40%¹⁹. In order to evaluate the infarction mortality rate six months after the acute event, Ketzner et al¹³ divided the patients into risk groups by *TIMI* scores¹³ with the following results: a mortality rate of 4.1% in the low-risk group, 10% in the medium risk group, and 52% in the high-risk group.⁽¹³⁾ In this study, the mortality rate was 55.6% in the high-risk group, 8.1% in the medium risk group and 0% in the low risk group.

The mortality after AMI increases dramatically with age, rising from 2.1% in patients under 55 years to 26.3% in patients aged 85 years or over²⁰. The elderly have reduced myocardial and coronary reserve^{19,21}, because they have higher incidence of diabetes, elevated blood pressure, prior heart attack and heart failure²². In this study, the mortality increased from 8.1% in patients younger than 65 to 71.4% in patients aged 75 or over. Part of this increase can be attributed to the more serious risk profile of the elderly. In this sample, 48.1% of patients in the high-risk group had more than 75 years, compared to no patients over 64 years in the group of low risk. There were no significant differences in age as to the elapsed time between the onset of symptoms and medical care.

In multivariate analysis, the Killip-Kimball class is the most powerful predictor of prognosis, with an increase of twice the risk of death for each worsening of class¹⁶. Other authors also emphasize the Killip class as the independent variable which is most related to mortality^{4,9,19,22}. In this study, 54.8% of patients with Killip classes II to IV died.

Although there is no unanimity in the literature in considering female gender as an independent variable associated with mortality from AMI, several authors^{4,22-24} observed this association, which is intrinsically linked to the severity of coronary disease in women, the age range involved, the greater number of comorbidities²² and underuse of effective therapeutic interventions²⁵.

In this sample, female gender corresponded to 3.1 times greater risk of death. Part of the higher mortality in women could be attributed to older age. However, the higher risk profile of these patients also contributed to the higher mortality rate. In this study, the risk of not belonging to Killip class I on admission and of being included in the category of high risk was higher for women. Vacarino et al²⁶ pointed out that women are more likely to present a more severe clinical condition; however, they emphasized that this applies only to young women²⁶. There was no significant difference in the mean elapsed time between pain and medical care for both genders.

Diabetes has remained an independent variable associated with mortality in multivariate analysis of several studies^{4,9,16,22}. Ribeiro et al²² described a chance of death 2.3 times greater in diabetics²². In this study, the risk of death was 3.7 times

higher in diabetic patients. Moreover, in this sample, the high risk group had a higher frequency of diabetes (60%) when compared to the low risk group (20%).

In conformity to what is found in the literature³, the elapsed time between the onset of symptoms and the first medical care is associated with higher mortality. Patients who took more than 4 hours to seek medical assistance had a mortality rate of 25%. Those who took 4 hours or less had a mortality rate of 9.8%.

A history of elevated blood pressure and angina also increased the risk of post-infarction death in this study^{9,10}.

In the GRACE study¹⁶, for each increase of 30 beats in the heart rate, the risk of death increased by 20%. Similarly, a 20 mmHg reduction in the systolic blood pressure increased by 1.3 times the mortality in that study. In the TIMI study⁹, a systolic blood pressure of less than 100 mmHg corresponded to a 2.7 times greater chance of death. In the same study, a heart rate higher than 100bpm was associated with a risk of death 2.3 times greater. In this sample, patients with hypotension and tachycardia also tended to have higher mortality.

Ribeiro et al²² reported a mortality rate of 16.7% in the group of patients in which thrombolytic was used, and of 28.7% in the group in which this therapy was not used. In this study, the non-use of Streptokinase corresponded to a risk of death 2.8 times greater. Groups with higher risk of death were

less subjected to reperfusion therapy^{3,10,16}. In this sample, the risk of receiving fibrinolytic was 50% lower in high risk cases. A recent study shows that 46.2% of patients aged under 55 years are treated with thrombolytic, as opposed to only 9.5% of those with 85 years or over¹⁹. In this population, only 2.9% of cases over 75 years received fibrinolytic. Prevalence of the use of Streptokinase was lower among women (45.7%) when compared to men (64.7%).

The presence of in-hospital post-infarction complications corresponds to a poorer prognosis for the patients^{3,4,8}. In this population, the risk of death for cases with one or more post-infarction complications was 4.5 times greater. Higher TIMI scores were associated, as expected, to higher rates of complications. Among the cases that have evolved with cardiogenic shock, 70% of them were characterized as high risk on admission, and 90% of the patients with cardiogenic shock died.

Conclusion

In the study sample, eight variables (age over 75 years; diabetes; Killip class; heart rate above 100 bpm; systolic blood pressure below 100 mmHg; no use of thrombolytic; and complications) were significantly associated with higher risk of in-hospital post-infarction death, and the most important were: age over 75 years, complications and heart rate above 100 bpm.

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Appendix 1 – Timi risk score⁹

History	Points
Age ≥ 75 years	3
65 to 74 years	2
DM or High blood pressure or Angina	1
Clinical Examination	
SPB < 100mmHg	3
HR > 100 bpm	2
Killip II - IV	2
Weight < 67 kg	1
Clinical Condition	
ST elevation in anterior wall or left bundle branch block	1
Elapsed time > 4h	1

Risk score	In-Hospital Mortality (%)
0	0.7
1	1.3
2	1.9
3	3.9
4	6.5
5	11.6
6	14.7
7	21.5
8	24.4
>8	31.7