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Predictive factors of in-hospital mortality in ST-segment elevation acute myocardial infarction

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Acronyms
AMI: acute myocardial infarction
AVB: atrio-ventricular block
STEMI: ST-segment elevation acute myocardial infarction

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ABSTRACT

Introduction: Many factors have been associated with high in-hospital mortality in acute myocardial infarction (AMI).
Objectives: To determine the risk factors of in-hospital death in patients with ST-segment elevation acute myocardial infarction.
Method: A case-control analytical study was carried out with the 94 patients who died due to myocardial infarction (study group) between January 2011 and December 2016. For each of them, two surviving patients were randomly chosen (control group). Descriptive statistics through percentage analysis and arithmetic mean were applied. A multiple logistic regression model was used to determine the risk factors of in-hospital mortality.
Results: The deceased had an average age of 73±11 years, 81.9% were hypertensive, 78.8% did not receive thrombolysis or was ineffective, 72.3% arrived late and had greater complications than those of the control group. Cardiogenic shock (OR 22.59), blood glucose greater than 15 mmol/L (OR 6.60) and between 7.3-15 mmol/L (OR 2.22), biventricular AMI (OR 4.27), late arrival to first medical assistance facility (OR 3.83), age over 70 years (OR 3.62), and creatinine greater than 200 µmol/L (OR 2.93) were statistically significant for in-hospital mortality.
Conclusions: Cardiogenic shock, blood glucose greater than 15 mmol/L and between 7.3-15 mmol/L, biventricular AMI, late arrival to first medical assistance facility, age over 70 years, and creatinine >200 µmol/L behaved as risk factors for in-hospital mortality.
Keywords: Myocardial infarction, Risk factors, Risk stratification, Mortality

Factores predictivos de mortalidad hospitalaria en el infarto agudo de miocardio con elevación del segmento ST

RESUMEN

Introducción: Múltiples factores se han relacionado con una elevada mortalidad hospitalaria en el infarto agudo de miocardio (IAM).
Objetivo: Determinar los factores de riesgo de muerte hospitalaria en pacientes con infarto con elevación del segmento ST.
Método: Se realizó un estudio analítico caso-control con los 94 pacientes fallecidos por infarto (grupo estudio) entre enero de 2011 y diciembre de 2016. Por cada uno de ellos se escogieron aleatoriamente 2 pacientes egresados vivos (grupo control). Se utilizó la estadística descriptiva a través del análisis porcentual y la media aritmética con desviación estándar. Para determinar los factores de riesgos de mortalidad hospitalaria se utilizó un modelo de regresión logística múltiple.

Resultados: Los fallecidos tenían edad promedio de 73±11 años, el 81,9% eran hipertensos, el 78,8% no recibió trombólisis o esta no fue efectiva, el 72,3% llegó tardíamente y tuvo mayores complicaciones que los del grupo control. El shock cardiogénico (OR 22,59), la glucemia mayor de 15 mmol/L (OR 6,60) y entre 7,3-15 mmol/L (OR 2,22), el IAM biventricular (OR 4,27), la llegada tardía al lugar de primera asistencia médica (OR 3,83), la edad mayor de 70 años (OR 3,62) y la creatinina mayor de 200 µmol/L (OR 2,93) tuvieron significación estadística con la mortalidad hospitalaria.

Conclusiones: El shock cardiogénico, la glucemia por encima de 15 mmol/L y entre 7,3-15 mmol/L, el IAM biventricular, la llegada tardía al lugar de primera asistencia médica, la edad mayor de 70 años y la creatinina >200 µmol/L se comportaron como factores de riesgos de mortalidad hospitalaria.

Palabras clave: Infarto de miocardio, Factores de riesgo, Estratificación de riesgo, Mortalidad

INTRODUCTION

Acute myocardial infarction (AMI), described in 1912, represents a serious health problem with a relevant socioeconomic impact and very high mortality and morbidity rates. Despite countless research efforts in this field, AMI remains a challenge for any physician, a crossroad for decision-making and an evident problem nowadays[1].

According to the World Health Organization, more than 8 million people die every year from AMI. In general, mortality rates substantially vary from 5-30% depending on the characteristics of the patient, type of ischemic event, characteristics of the health system in each country and type of facility where the patient is admitted, among other factors. In-hospital mortality is higher in patients with ST-segment elevation AMI (STEMI), but at 6 months the mortality rates between these and those with non-STEMI are 12% and 13% respectively, and at older ages is 20 times higher than in patients younger than 50 years[2,3].

This situation is very complex in Latin America as up to 40% of deaths occur prematurely, right at the time of higher productivity, when the economic and social impact is more devastating, and because the resulting disability rate is a too heavy burden for individuals, families and health systems[1,4].

Currently, cardiovascular diseases are the leading cause of death in Cuba, with a rate of 217.7 per 100000 inhabitants. 66% of them are caused by ischemic heart diseases, of which 44.4% are due to AMI. Despite the creation of a unified emergency medical system, coronary intensive care units in each province of the territory, municipal therapy units and of premises for thrombolysis in several health areas, you would expect a major drop in mortality due to AMI. But death rates are increasing: if 6128 people died in 2011, at late 2016 the figures grew to 7177, which is a 7.2% of the total deaths from any cause and age in our country[5].

Because of the aforementioned, AMI and acute coronary syndromes (ACS) usually remain an important research focus in the world. That is why most countries have constant national and regional records of ACS-AMI[6-8]. This serves as the basis for the analysis and conduct of clinical and epidemiological studies as well as for decision-making in health matters. This also allows carrying out studies in search of predictive factors of mortality and adverse cardiovascular events during hospitalization and immediate follow-up, in order to draw up strategies to reduce mortality in this type of patient.

Multicenter studies show the association of several factors with an increased risk of dying from AMI. Although there are differences depending on where the research is performed, the total sample, presence of diabetes mellitus, cardiogenic shock, post-MI angina, reinfarction, left ventricular ejection fraction at admission below 30%, presence of malignant ventricular arrhythmias and elevation of markers of myocardial necrosis, are some of the most associated with a gloomy prognosis, high in-hospital and short-term follow-up mortality in these patients[1,9,10].

Knowing these factors enables to create different scales for risk stratification of patients. This allows a more accurate therapeutic intervention and a more rigorous monitoring in moderate and high risk cases; which has led to decrease mortality and improve their quality of life[11,12].

The aging of the Cuban population and a high

prevalence of classic cardiovascular risk factors suggest that in the coming years we will face an increase in morbidity and mortality due to AMI. So, knowing the predictors of mortality from this condition would be extremely helpful in order to reduce in-hospital mortality in the immediate future. For this reason and through a research project, a stratification scale for in-hospital mortality was created in Las Tunas, which is why the following research is carried out to determine the predictive factors of hospital death due to STEMI.

METHOD

An analytical study was conducted in patients with STEMI, who died during hospitalization, in the Department of Cardiology of the *Hospital General Docente Dr. Ernesto Guevara de la Serna* in the province of Las Tunas, between January 2011 and December. 2016. The population consisted of patients admitted to the department with a diagnosis of AMI during the study period. The sample consisted of the 94 patients from the study group who died of STEMI, in whom all the variables were measured. For each patient in this group, we chose 2 with the same diagnosis who were discharged alive; so to control the confounding factors. They were randomly selected from a database of the Department that made up the control group.

We reviewed the data screening forms used for all patients admitted with AMI in the Department of Cardiology of the hospital. We created a database using Microsoft Excel where every study variable was collected.

Descriptive statistics was used through the percentage analysis for the descriptive variables. Arithmetic mean with standard deviation was used in the case of age, blood glucose, creatinine values and blood pressure at admission.

To determine predictive or risk factors of in-hospital mortality we used a multiple logistic regression model where the patient's state at discharge (deceased or alive) was used as a dependent variable to see the association between the rest used or independent variables. The variables were, age older than 70 years, hyperglycemia, elevated creatinine, anterior and biventricular AMI, late arrival to first medical assistance facility and the presence of cardiogenic shock (Killip-Kimball IV). Odds ratios (OR) and confidence intervals were calculated for 95% reliability and a value of $p < 0.05$ was determined as statistically significant.

One variable was considered as a risk factor for in-hospital death if $OR > 1$ and $p < 0.05$. As a protective factor if $OR < 1$ and $p < 0.05$. If the variable presented $OR = 1$, it was not considered risk or protection. In the case of $OR > 1$ with a value of $p < 0.25$, the variable with weak association to the dependent variable was considered.

The statistical program SPSS version 19.0 was used. Results were illustrated in the form of texts and tables. For their discussion, they were compared with other studies and conclusions were reached.

RESULTS

Table 1 shows male predominance in both groups, although it was more frequent in the control group, 72.8% and 52.1% in the deceased patients. High blood pressure was the most frequent associated factor in both the deceased patients and the control group with 81.9% and 73.4% cases, respectively. The average age of the deceased patients was 8 years older than in the live cases. 41.4% of those in the control group were smokers, compared to only 26.6% among the deceased, and 58.5% of them had 3 or more associated factors.

When analyzing the topography of the AMI, **table 1** also shows that inferior AMI predominated in the patients discharged alive, whereas anterior AMI was more frequent in deceased patients.

The difference between biventricular AMIs is noteworthy, since they were present in 22.3% of the deceased patients, for only 7.4% of patients in the control group.

The 44.1% of the deceased and 53.7% of the patients in the control group received thrombolysis (**Table 2**). 78.8% of the deceased did not receive thrombolytic therapy or was not effective. This is a much higher figure than the 59.6% of the control group. In addition, 72.3% of the deceased arrived late to first medical assistance facility.

Table 3 shows that the blood glucose figures at admission in deceased patients doubled those of the control group (15.1 vs. 7.2 mmol/L). These same patients had a higher heart rate, higher creatinine levels, and less average systolic blood pressure than those discharged alive.

Left ventricular dysfunction was the most fre-

Table 1. Associated factors and type of infarction in deceased patients and controls with ST-segment elevation acute myocardial infarction. Department of Cardiology, Hospital General Docente "Dr. Ernesto Guevara de la Serna", 2011-2016.

Aspects	Deceased (n=94) %	Control (n=188) %
Associated factors		
Male sex	52.1	72.8
Age	73±6	65±4
High blood pressure	81.9	73.4
Diabetes mellitus	30.9	13.8
Smoking habit	26.6	41.4
Hypercholesterolemia	5.3	6.9
Hypertriglyceridemia	12.8	17.2
Ischemic heart disease PPH	31.9	27.2
Plus 3 associated factors	58.5	56.4
Type of AMI		
Inferior	36.2	48.7
Anterior	41.5	43.9
Biventricular	22.3	7.4

PPH, pathological personal history; AMI, acute myocardial infarction

Table 2. Deceased patients and control group, according to the performance and effectiveness of thrombolysis and late arrival to the first medical assistance facility.

Aspects	Deceased (n=94) %	Control (n=188) %
Thrombolysis	44.1	53.7
- Effective	21.2	40.4
- Uneffective	22.9	13.3
No thrombolysis	55.9	46.3
Late arrival at FMA	72.3	35.7

FMA, first medical assistance

quent complication in both groups (**Table 4**). It was present in 92.1% of the deceased patients and in 43.5% of the control group. The deceased had more atrial and ventricular fibrillation, more ventricular tachycardia, more complete atrio-ventricular block (AVB) and more reinfarctions than patients from the control group.

Cardiogenic shock, with OR=22.59 and p<0.001, was the more associated factor to the onset of in-hospital death (**Table 5**). Other factors such as blood glucose values above 15 mmol/L (OR=6.60, p=0.005), biventricular AMI (OR=4.27, p<0.001), late arrival to first medical assistance facility (OR=3.83, p<0.001), age over 70 years (OR=3.62, p<0.001), blood glucose values between 7.3 and 15 mmol/L (OR=2.22, p=0.001) and those having creatinine high-

Table 3. Deceased patients and control group according to clinical and laboratory variables at admission.

Aspects	Deceased (n=94)	Control (n=188)
Heart rate (bpm)	86	76
Systolic BP (mmHg)	112	130
Blood glucose (mmol/L)	15,1	7.2
Creatinine (mmol/L)	123	94
Total CK (UI)	1114	1074

CK, creatine kinase; BP, blood pressure

Table 4. Pacientes fallecidos y grupo control según complicaciones.

Complicaciones	Deceased (n=94) %	Control (n=188) %
LV dysfunction		
- Killip-Kimball II	14.5	30.8
- Killip-Kimball III	12.8	5.3
- Killip-Kimball IV	64.8	7.4
VF-VT	30.8	9.0
Atrial fibrillation	15.9	6.9
Complete AV block	28.7	10.6
Reinfarction	14.8	5.3

AV, atrio-ventricular; VF, ventricular fibrillation; VT, ventricular tachycardia; LV, left ventricle.

Table 5. Logistic regression model. In-hospital mortality as a dependent variable.

Factores	OR (IC del 95%)	p
Age>70 years	3.62	<0.001
Blood glucose between 7.3-15 mmol/L	2.22	0.001
Blood glucose >15 mmol/L	6.60	0.005
Creatinine between 132-200 µmol/L	2.46	0.114
Creatinine>200 µmol/L	2.93	0.002
Late arrival at FMA	3.83	<0.001
Anterior AMI	0.78	0.341
Biventricular AMI	4.27	<0.001
Cardiogenic shock	22.59	<0.001

AMI, acute myocardial infarction; FMA, first medical assistance

er than 200 µmol/ L (OR=2.93, p=0.002) behaved as risk factors for in-hospital mortality in patients with STEMI.

DISCUSSION

The prevalence of associated factors in patients with AMI varies depending on the geographical area, customs, lifestyle of the population and health systems of each country. Most of the modifiable risk factors, with the exception of smoking in the early AMI phase, have been associated with a poorer prognosis. Within them, high blood pressure and diabetes mellitus are the most described[1,13].

Age is one of the factors which has a major impact on the prognosis of patients with AMI. Its increase is associated with an exponential increase in mortality in both, acute and late phases. In the study conducted by Andrés *et al*[14] in Spain, the average age of people who died due to AMI was 78 years, which is higher than what we found in this study. This may be related to the number of cases in their research, which was higher than ours.

The "paradoxical effect" of tobacco has been described with respect to the lower early mortality found in this group in relation to those who do not smoke. The main mechanisms involved seem to be its association with a more favorable clinical profile and the presence of higher values of fibrinogen and platelets. This has led to the hypothesis that such patients have a state of hypercoagulability that would cause them heart attacks in early stages, with milder coronary disease and probably with a more frequent spontaneous reperfusion process[1].

In the GRACE study cohort[15], high blood pressure (58.2%) and smoking habit (57.8%) were the most frequent classic associated factors, high blood pressure had a lower percentage than in this study, while GRACE patients had

higher percentages in smoking, dyslipidemia and diabetes mellitus.

In the case of inferior AMI, the presence of serious complications is about 25-28% and the mortality found in most studies is 6-8%. When there is right ventricular involvement during inferior AMI, serious complications exceeds 65% and mortality ranges from 25-40% during the hospital phase[1,16]. The higher mortality in patients with biventricular AMI can be explained since they are larger infarctions. More proximal occlusions of the right main coronary artery are usually present and, therefore, greater area of myocardium at risk; which is related to serum concentrations of very high biomarkers that denote the large amount of affected myocardium. We must also take into account the decrease in systolic and diastolic function of the right ventricle with decreased left ventricular preload that may lead these patients to low cardiac output, cardiogenic shock, severe left ventricular concomitant dysfunction and loss of atrial supply by a complete AVB, which is frequently associated with this type of AMI.

The greatest benefit of thrombolytic therapy is seen in those patients who receive the drug within 3 hours of the onset of symptoms. The analysis of clinical trials in which more than 6000 patients were randomly assigned to pre-hospital or in-hospital fibrinolysis, shows a significant reduction (17%) in early mortality with pre-hospital treatment, which confirms the need to perform this procedure as early as possible[11,17].

We should note that it is not only about applying thrombolysis or any other reperfusion procedure but also analyzing whether it was effective or not. The success of pharmacological or mechanical reperfusion can be evaluated with clinical, electrocardiographic, enzymatic, angiographic, echocardiographic and nuclear medicine parameters. In daily practice, it is possible to determine whether thrombolysis was effective or not using clinical, electrocardiographic and enzymatic criteria and therefore, its relationship with mortality, as evidenced in the INJECT study where three types of ST segment resolution were considered: complete >70%, partial 30-70% and without resolution <30%; the mortality found in each situation was 2.5; 4.3 and 17.5% ($p<0.0001$)[16]. When the baseline characteristics were taken into consideration, the resolution of the ST segment was the main independent factor of the 35-day mortality prognosis. Therefore, the absence of ST segment elevation resolution that occurs in up to 25-50% of patients, indicates failure in reperfusion and predicts high mortality. On the other hand, a complete resolution was associated with smaller infarctions, low mortality and greater probability of having epicardial and microvascular perfusion, without a non-reflux phenomenon[1,16].

Ventricular fibrillation after STEMI is associated with increased in-hospital mortality, but not with increased long-term mortality. Typically, it has been pointed out that primary ventricular fibrillation does not change the prognosis of patients with AMI when it can be reversed early, before causing sequelae. However, according to Mann[1] and Ruesga Zamora[16], Volpi *et al* observed that in the case of the patients included in the GISSI study, those with primary ventricular fibrillation had an in-hospital mortality that doubled that of those who did not (10.8 vs. 5.9%), although they could not distinguish whether it was a marker of poor prognosis or the direct cause of death.

AVB in the acute phase of myocardial infarction is associated with a worse short-term prognosis, both in anterior and inferior AMI. In fact, its presence has been associated with relative risks of in-hospital death between 3 and 4 times higher than those who do not, although there may be other prognostic factors. However, its influence on the prognosis in the lower AMI, where more frequently occurs, seems to depend mainly on its association with right ventricular infarction. Thus, Mann[1] states that according to the Mavric study, patients with complete AVB and right ventricular infarction have a much worse prognosis, while those with AVB without right ventricular extension are similar to those who do not develop AVB.

For a long time, thera have been attempts to stratify the different coronary diseases to optimize the urgency treatment and, at the same time, evaluate the diagnostic and therapeutic strategy to be implemented. This is a complex, heterogeneous task, with multiple factors, in constant evolution, in constant progression to achieve anticipation of events and choose the best strategy for each patient. It should be noted that in each population the predictive or risk factors for mortality can vary and that is why the predictors that are associated in each region should be looked for and subsequently studied thoroughly.

The literature includes several studies in which various predictive factors of mortality are obtained depending on the geographical area, the sample size and other aspects. A study carried out in Chile evidenced advanced age, female sex and diabetes

mellitus as independent predictors of mortality[18]. In the Argentine registry of infarction in patients undergoing angioplasty[19], cardiogenic shock was the main predictor of mortality with OR=44.1 and p= 0.0001, followed by the presence of diabetes mellitus with OR=2.64 and p=0.002, and renal failure OR=2.5 and p=0.003.

Several studies agree that left ventricular dysfunction is the strongest independent predictor of mortality after AMI[1,11,16,] which is conditioned by the severity of the heart failure, if in Killip-Kimball I pump failure mortality reaches a 6%, in cardiogenic shock (Killip-Kimball IV) it reaches close to 80%. This shock is the most serious clinical expression of left ventricular failure and is associated with large left ventricular myocardial injury, in more than 80% of STEMI cases where it occurs. The rest is related to mechanical defects, such as rupture of the interventricular septum, papillary muscle or with predominant right ventricular infarction.

Hyperglycemia at admission is common in patients with AMI and is a powerful predictor of mortality and in-hospital complications. Elevated glucose levels have been associated with an adverse prognosis, both in diabetic and non-diabetic patients. Different studies have found that glucose levels of 140 mg/dL or more in non-diabetic patients, and higher or equal to 180 mg/dl in diabetics are associated with a 3.9 times relative risk of death[1]. It has been demonstrated in patients with non-diabetic STEMI that hyperglycemia and increased glycosylated hemoglobin A1c (HbA1c) are associated with worse prognosis due to different mechanisms. Hyperglycemia is the one that best predicts the short-term prognosis of large infarcts, while the elevation of HbA1c is associated with long-term clinical effects due to an increase in baseline risk[20].

One of the aspects that has been studied in recent years and has received special attention at the international level is the relationship between chronic kidney disease and cardiovascular disease, which is patent and growing as the kidney function, cardiac function or both get worse. High creatinine levels, whatever their cause, have been associated with an increased risk and cardiovascular mortality, confirmed in large-scale studies, such as HOPE and HOT[1,16].

Four reasons may explain the poor cardiovascular prognosis in patients with renal dysfunction after AMI[1,16]:

1) An excess of simultaneous disorders associated with chronic and terminal kidney disease, in particular, the presence of diabetes mellitus and heart failure in these patients.
2) The therapeutic nihilism, which consists on the underutilization of drugs of proven cardiac mortality prevention in this type of patients, since when presenting coronary events in more advanced stages of their kidney disease, they may have more contraindications or may exist other aspects related to the presentation that encourage the doctor to use fewer treatments or to develop a more conservative approach.
3) The toxicity of the treatments, such as, the increased risk of bleeding in these patients; as well as the effect of uremia, which causes excessive thrombin production, increase in circulating thrombin-antithrombin complexes, low concentrations of antithrombin III, increase in plasminogen activator inhibitor and decrease in platelet aggregation.
4) Presence of special biological and pathophysiological factors of renal dysfunction that worsen the results, such as lipid alterations and metabolism of phosphorus and calcium.

In the early arrival to first medical assistance facility lies the importance of early diagnosis and reperfusion treatment in patients with AMI, either pharmacologically or by percutaneous coronary intervention, with the resulting improvement in the outcome of patients, with a decrease in mortality and in-hospital complications. Recent studies found that late arrival was one of the risk factors for cardiac rupture and others have shown their relationship with a higher probability of dying from AMI[11,21].

CONCLUSIONS

Cardiogenic shock, blood glucose greater than 15 mmol/L, biventricular AMI, late arrival to first medical assistance facility, age over 70 years, blood glucose values between 7.3 and 15 mmol/L and creatinine values greater than 200 μmol/L, behaved as risk factors for in-hospital mortality in patients with ST-segment elevation acute myocardial infarction.

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