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# Risk factors for post-infarction heart rupture after sudden death in Las Tunas

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ARTICLE INFORMATION

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**Competing interests**
The authors declare no competing interests

**Abreviaturas**
AMI: acute myocardial infarction
CK: creatine kinase
CR: cardiac rupture
SD: sudden death

## ABSTRACT

*Introduction:* Left ventricular free wall rupture is an infrequent complication of acute myocardial infarction, and a cause of sudden death.
*Objective:* To determine risk factors for heart rupture in patients with acute myocardial infarction in the Cardiology Department of Las Tunas.
*Method:* Case-control analytical study in 25 patients who died due to heart rupture, verified by pathological anatomy between 2011 and 2015. Descriptive statistics were used through percentage analysis and arithmetic mean for the descriptive variables. Risk factors were determined using Epi Info version 6 which determined odds ratios (OR), confidence and probability intervals for a 99%.
*Results:* Sixty percent of the deceased were male, with an average age of 72±16 years. Previous infarction and less than 24 hours-hospital stay predominated. Elevation of the creatine kinase enzyme above 1200 units (OR 3.23), late arrival to the first medical contact (OR 2.92) and presence of more than 7 affected leads (OR 2.57) on the electrocardiogram, were risk factors for heart rupture.
*Conclusions:* Elevated creatine kinase values, late arrival and presence of 7 or more affected leads in the electrocardiogram are risk factors for heart rupture.
*Key words: Myocardial infarction, Heart Rupture, Sudden death*

## *Factores de riesgo de rotura cardíaca posinfarto con muerte súbita en Las Tunas*

## RESUMEN

*Introducción: La rotura de la pared libre del ventrículo izquierdo es una complicación infrecuente del infarto agudo de miocardio, y es causa de muerte súbita.*
*Objetivo: Determinar factores de riesgo de rotura cardíaca en pacientes con infarto agudo de miocardio en el Servicio de Cardiología de Las Tunas.*
*Método: Estudio analítico caso-control, en 25 pacientes fallecidos por rotura cardíaca, comprobados por anatomía patológica entre el 2011 y el 2015. Se utilizó la estadística descriptiva a través del análisis porcentual y la media aritmética para las variables descriptivas. Para determinar los factores de riesgo se utilizó el Epi Info versión 6, con el que se determinaron las razones de posibilidad (OR [odds ratio]), los intervalos de confianza y de probabilidad para un 99%.*
*Resultados: El 60% de los fallecidos era del sexo masculino, con edad promedio de 72±16 años. Predominaron el infarto anterior y la estadía hospitalaria menor de 24 horas. La elevación de la enzima creatinquinasa por encima de las 1200 unidades (OR 3,23), la llegada tardía al primer contacto médico (OR 2,92) y la presencia*

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*de más de 7 derivaciones afectadas (OR 2,57) en el electrocardiograma, constituyeron factores de riesgo de rotura cardíaca.*
*Conclusiones: Los valores elevados de creatinquinasa, la llegada tardía y la presencia de 7 o más derivaciones afectadas en el electrocardiograma constituyen factores de riesgo de rotura cardíaca.*
*Palabras clave: Infarto de miocardio, Rotura cardíaca, Muerte súbita*

## INTRODUCTION

Sudden cardiac death is probably the most important problem in modern cardiology. Its high incidence represents one of the main challenges for current health systems in the present century. This phenomenon accounts for nearly 4-5 million deaths for a total 14650 daily deaths and 10 events per minute. Sudden cardiac death presentation constitutes an additional emotional factor that affects both family and society as a consequence of the unexpected nature of the event and the enormous economic losses generated by years of useful life prematurely lost in labor-active people[1].

It becomes the first and only manifestation of cardiovascular disease in up to 40% of patients. Heart disease contributes to the causes of SD in 80% of cases, among them, ischemic heart disease accounts for 90%[2,3].

In patients with acute myocardial infarction (AMI), SD represents 25% of its presentation. Mechanical complications, among these, cardiac rupture (CR) , is the second most frequent cause of SD in patients with AMI and, in addition, the second cause of death after cardiogenic shock[4,5].

At present, risk stratification of patients has been highly appreciated. There are several studies of risk validation for hospital mortality, reinfarction and SD, but CR has been poorly assessed, a complication that despite having a decreased incidence since the post-thrombolytic stage still has a prevalence of 5-10%, with 50% of out-of-hospital cases where SD is their first manifestation[6,7].

In Las Tunas, published work on SD is scarce, as well as in relation to post-AMI CR, so we decided to carry out this work to determine the risk factors for postinfarction CR with SD in the Cardiology Department of this province.

## METHOD

A case-control analytical study was carried out in the Cardiology Department of Las Tunas with 25 AMI patients who died owing to SD, after a CR verified by pathological anatomy, between 2011 and 2015. Three controls were matched for each case, (deceased by AMI, without CR, or SD), randomly chosen from the department's database.

The variables used were: sex, age, history of high blood pressure, diabetes mellitus, type of infarction, number of ECG electrocardiogram (ECG) leads involved, thrombolysis, creatine kinase (CK), Killip-Kimball on admission, hospital stay and late arrival in search for medical attention.

Descriptive statistics was used through percentage analysis and arithmetic mean for descriptive variables. Risk factors were determined by Epi Info version 6, with which the odds ratios (OR) were determined, as well as the confidence and probability intervals for 99%.

## RESULTS

In examining the baseline characteristics of the patients with CR (**Table 1**), 60.0% were male, while in the control group only 45.6%. The mean age was 75±16 years in patients who died of CR.

Seventy-six percent had a history of hypertension, lower than the 86.7% of patients in the control group. ST-segment elevation AMI prevailed in both groups, (92.0% vs. 86.7%) and anterior topography (56% vs. 37.3%), although predominance of this location is evident in the deceased who presented CR and SD. Sixty percent of them had hospital stay of less than 24 hours. Thrombolytic therapy was given to 52% of deceased patients, not being effective in almost half of cases (**Table 2**); while 54.7% of patients in the control group did not receive this treatment.

**Table 3** shows the analysis of risk factors for CR. Presence of total CK values above 1200 units with OR 3.31 (p=0.0012), late arrival to first medical contact with OR 3.06 (p=0.0013) and the presence of more than 7 ECG leads with ST elevation and/or de-

pression, with OR 2.66 (p=0.0020), behaved as risk factors.

**Table 1.** Baseline characteristics of patients with acute myocardial infarction, cardiac rupture and sudden death. Department of Cardiology. *Hospital General Docente Dr. Ernesto Guevara*. 2011-2015.

| Aspects | Cases (n=25) | Controls (n=75) |
|---|---|---|
| | % | % |
| **Associated factors** | | |
| Male sex | 60,0 | 45,6 |
| Age (years, χ±DE) | 75±16 | 73±10 |
| High blood pressure | 76,0 | 86,7 |
| Diabetes mellitus | 16,0 | 32,0 |
| **Type of infarction** | | |
| - **Non-STEMI** | 8,0 | 13,3 |
| - **STEMI** | 92,0 | 86,7 |
| • Inferior | 32,0 | 21,3 |
| • Anterior | 56,0 | 37,3 |
| • Biventricular | 12,0 | 29,3 |
| **Killip-Kimball on admission** | | |
| - I | 20,0 | 5,3 |
| - II | 16,0 | 17,3 |
| - III | 24,0 | 6,6 |
| - IV | 40,0 | 70,6 |
| **Hospital stay** | | |
| - Less than 24 hours | 60,0 | 34,6 |
| - 1-3 days | 24,0 | 28,0 |
| - 3-5 days | 12,0 | 25,3 |
| - >5 days | 4,0 | 12.0 |

χ, mean; SD, standard deviation
STEMI, ST segment elevation myocardial infarction

**Table 2.** Patients who died with cardiac rupture and control group according to administration and effectiveness of thrombolysis.

| Aspects | Cases (n=25) | Controls (n=75) |
|---|---|---|
| | n (%) | n (%) |
| Thrombolysis | 13 (52,0) | 34 (45,3) |
| - Effective | 7 (28,0) | 14 (18,6) |
| - Inefective | 6 (24,0) | 20 (26,7) |
| No thrombolysis | 12 (48,0) | 41 (54,7) |

## DISCUSSION

Left ventricular free wall rupture during AMI is one of the most frequent causes of sudden cardiac death. Most of the ruptures (90%) occur within the first 9 days post-AMI, and show two incidence peaks, in the first 24 hours and between the sixth and ninth postinfarction days. A study led in Spain which enrolled 110 CR cases, revealed that the average stay was 3 days. In the pre-thrombolytic era, most CR cases occurred during the first week after AMI, with a peak incidence between the fifth and seventh days. A study including more than 100 autopsies of patients with CR secondary to AMI showed that in 13% it occurred during the first 24 hours, in 58% within the first 5 days and in 80% within the first 7 days[8,9].

Most studies agree that CR cases are predominant in women; however, in this study the majority of patients are men. A similar result was found by Figueras *et al.*[10], in their 30-year study, where 55.5% of patients were men, although it is noteworthy that in this case, results were divided into five-year periods, thus CR incidence increased in the female sex depending on each period.

Coronary reperfusion treatment, particularly thrombolytic therapy changed the natural history of this complication by shifting its peak incidence to the first day because of the increased number of fatal events in the first 24 hours. The relationship between the use of thrombolytics and CR has been a matter of discussion for long, probably due to the disparity of data arising from the different works or the way they are interpreted[11,12].

Initial studies have suggested an increased risk of CR with thrombolytics usage. Although the GISSI1[13] and ISIS-2[14] studies showed a significant reduction in overall mortality (20%), this was accompanied by an increase in early mortality (<24 hours). Subsequently, Bueno *et al.*[15] found similar results in terms of increased risk, although they ascribed it to late commencement of treatment (> 11 hours) and to the patient's advanced age (> 75 years).

**Table 3.** Risk factors for heart failure in infarcted patients with sudden death.

| Risk factors | Cases | | Controls | | *OR* | CI (95%) | | Probability |
|---|---|---|---|---|---|---|---|---|
| | Nº | % | Nº | % | | LL | UL | |
| Age > 70 años | 14 | 56,0 | 44 | 58,7 | 0,89 | 0,26 | 2,98 | 0,4079 |
| Female sex | 10 | 40,0 | 39 | 52,0 | 0,61 | 0,18 | 2,06 | 0,1557 |
| No thrombolysis | 12 | 48,0 | 41 | 54,7 | 0.76 | 0,23 | 2,52 | 0,2864 |
| Lower AMI | 14 | 56,0 | 28 | 37,3 | 2,13 | 0,63 | 7,13 | 0,0889 |
| Killip-Kimball IV | 10 | 40,0 | 53 | 70,7 | 0,27 | 0,08 | 0,95 | 0,4024 |
| total CK > 1200 UI | 20 | 80,0 | 41 | 54,7 | 3,31 | 0,80 | 6,65 | 0,0012 |
| > 7 ECG leads with ↑ or ↓ of ST | 16 | 64,0 | 30 | 40,0 | 2,66 | 0,78 | 6,64 | 0,0020 |
| Late arrival | 14 | 56,0 | 22 | 29,3 | 3,06 | 0,89 | 8,85 | 0,0013 |

CK, creatine quinase; ECG, electrocardiogram; AMI, acute myocardial infarction; LL, lower limit; UL, upper limit; IU, international units.

Studies on predisposing factors or those that increase the risk of CR in the context of AMI have not been frequent at present. In the past few decades they were studied extensively, and the results obtained considered female sex, advanced age (> 65 years), first infarction (typically transmural), single-vessel disease (often significant, with poor collateral circulation) and absence of history of angina, as risk factors for CR in patients with AMI. On the other hand, multivessel disease and previous infarction seem to have a relatively protective effect, probably linked to increased collateral circulation and better tolerance to traction in non-ischemic myocardial segments[16,17].

Some studies have suggested that corticosteroids and non-steroidal anti-inflammatory drugs interfere with tissue repair processes and consequently increase the risk for CR. However the meta-analysis of Giugliano *et al.*[18] which included more than 3000 patients failed to demonstrate this link.

The relationship between the rise of biomarkers and severity of ischemia, besides poor prognosis of patients with AMI has been shown in several studies, especially those related to troponins and, to a lesser extent, with the MB fraction of CK[19,20].

In our setting, where we do not have troponins and many times CK-MB either, total CK values above 1200 were risk factors for CR, which may be related to the wider area of infarction in this type of patients.

Several studies have tried to determine the correlation between electrocardiographic signs and CR. Among its alterations are: extreme bradycardia, prominent R wave in lead aVR, persistent and recurrent ST segment elevation with pseudonormalization of negative T waves (evidence of AMI expansion), as well as progressive and sustained ST segment elevation, between 0.3-1.0 mV, in the affected area. Although none of these signs is sufficiently sensitive or specific to identify this type of patients, other ECG alterations have been sought; among them are ST alterations (elevation and depression) in 7 or more affected leads, which it is related to a possible left main coronary artery subocclusion or when there is significant proximal involvement of the three main vessels (left anterior descending, circumflex and right coronary artery)[3,5].

Early arrival to the first place of medical assistance is important for early diagnosis and treatment in AMI patients with subsequent improved outcome. A typical example is the application of thrombolytic treatment, where patients who receive the drug within the first 3 hours after onset of symptoms are more benefitted. Recent studies have found that late arrival to the first medical contact is a risk factor for CR[3,7].

Currently, international studies are being conducted to identify new risk factors with a view to increase prevention of SD in patients with AMI and CR. Scientists from Belgium, the Netherlands and the United States have discovered that the calmodulin-dependent protein kinases (CaM kinases) have a decisive influence on the biochemical cascade res-

ponsible for the occurrence of CR. This study showed that the CaM kinase stimulates the heart muscle cells to generate an enzyme called MMP9 that influences the rupture of the heart wall[5].

## CONCLUSIONS

High creatine kinase levels, late arrival at the first medical contact and presence of 7 or more electrocardiogram leads involved constituted risk factors for cardiac rupture.

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