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In-hospital sudden cardiac death and ST-segment elevation myocardial infarction: Results from RESCUE

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ARTICLE INFORMATION

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Acronyms
GRACE: Global Registry of Acute Coronary Events
SCD: sudden cardiovascular death
SD: sudden death
STEMI: ST-segment elevation myocardial infarction

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ABSTRACT

Introduction: The sudden cardiovascular death (SCD) is one of the main challenges of modern cardiology. After a ST-segment elevation myocardial infarction (STEMI), the characteristics of the vulnerable myocardium can lead to the final arrhythmia in the in-hospital stage of the treatment of these patients.
Objective: To identify the association between parameters at admission of patients with STEMI and the emergence of the in-hospital SCD.
Method: A retrospective analysis of 251 consecutive patients from the registry of acute coronary syndromes (RESCUE, by its acronym in Spanish) was performed, who were admitted with STEMI between June 2014 and February 2016. The SCD was defined as secondary to cardiac rupture, malignant ventricular arrhythmias or acute heart failure. Two groups were established according to the presence or absence of SCD and morphometric characteristics, health history, performance times of patients and system, and clinical findings were collected.
Results: Patients with SCD were older (76.6±7.72 vs. 65.1±14.2 years, p=0.001), they came later to the doctor (469.4±295.8 vs. 344.1±262.1 minutes), they had a lower frequency of reperfusion (0 vs. 22%, p=0.02) and a higher score on the GRACE scale (129.2±12.58 vs. 101±27.07, p=0.001). Women presented worse prognosis (55% vs. 30.3% p=0.023), although this difference may be due to older age in that subgroup (78.45±7.92 vs. 70.23±11.98; p=0.031). The history of smoking was paradoxically related to the SCD (30% vs. 55.84%, p=0.028).
Conclusions: The SCD was associated with characteristics that can be determined at the admission of patients with STEMI.
Key words: Coronary artery disease, Sudden death, Myocardial infarction

Muerte súbita cardiovascular intrahospitralaria e infarto agudo de miocardio con elevación de ST: Resultados de RESCUE

RESUMEN

Introducción: La muerte súbita cardiovascular (MSC) constituye uno de los principales desafíos de la cardiología moderna. Luego de un infarto agudo de miocardio con elevación del segmento ST (IAMCEST), las características del miocardio vulnerable pueden conducir a la arritmia final en la etapa intrahospitalaria del tratamiento de estos pacientes.
Objetivo: Identificar asociación entre parámetros al ingreso de los pacientes con IAMCEST y la aparición de MSC intrahospitalaria.
Método: Se realizó un análisis retrospectivo de 251 pacientes consecutivos del re-

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gistro de síndromes coronarios agudos (RESCUE), que ingresaron con IAMCEST entre junio/2014 y febrero/2016. Se definió como MSC aquella secundaria a rotura cardíaca, arritmias ventriculares malignas o insuficiencia cardíaca aguda. Se establecieron dos grupos de acuerdo a la presencia o no de MSC y fueron recogidas las características morfométricas, los antecedentes de salud, tiempos de actuación de los pacientes y del sistema, y hallazgos clínicos.

Resultados: Los pacientes con MSC fueron mayores (76,6±7,72 vs. 65,1±14,2 años; p=0,001), acudieron más tardíamente al médico (469,4±295,8 vs. 344,1± 262,1 minutos), presentaron menor frecuencia de reperfusión (0 vs. 22%; p=0,02) y mayor puntuación en la escala GRACE (129,2±12,58 vs. 101±27,07; p=0,001). Las mujeres presentaron peor pronóstico (55% vs. 30,3% p=0,023), aunque esta diferencia puede ser debido a mayor edad en ese subgrupo (78,45±7,92 vs. 70,23±11,98; p=0,031). El antecedente de tabaquismo se relacionó paradójicamente con la MSC (30% vs. 55,84%; p=0,028).

Conclusiones: La MSC se asoció a características determinables al ingreso del paciente con IAMCEST.

Palabras clave: Enfermedad de arterias coronarias, Muerte súbita, Infarto de miocardio

INTRODUCTION

Sudden cardiac death (SCD) is one of the main challenges of modern cardiology; typically defined as death occurring unexpectedly within one hour of unwitnessed symptom onset or occurring within less than 24 hours since last the patient had been seen in good condition[1].

In Western countries, half a million deaths occur each year. In Cuba, the Sudden Death Research Group (GIMUS) estimated, in 2010, one death every 48 minutes[2].

Generally, SD occurs at the stage when man is most useful to society, perfectly able, often in the absence of apparent disease. It is the main cause of potential years lost in the world (up to 50%)[3], most episodes occur outside of medical institutions, and only 50% are eyewitnessed, which complicates early detection and attention[4].

Coronary Artery Disease is the leading cause of SD in the U.S. (up to 75% deaths). This has brought about an increased frequency of non-defibrillable rhythms, which basically disables the use of implantable defibrillators as primary or secondary therapy. Another of the described causes of this phenomenon is the increase in population ageing[3].

After an ST-segment elevation acute myocardial infarction (STEMI), the characteristics of the vulnerable myocardium can lead to the final arrhythmia in the in-hospital stage during the treatment of these patients. Several studies have associated the extension of the injury with heart failure and the appearance of arrhythmias. These are common in patients with STEMI and constitute a marker for electrical instability that increases the risk of mortality[5].

The objective of this study was to identify the association of in-hospital SD in patients discharged with a diagnosis of STEMI, and characteristics that can be determined at admission.

METHOD

A descriptive observational study of case series was carried out, using data from the Registry of Acute Coronary Syndromes (RESCUE by its acronym in Spanish) of 251 patients admitted to the Camilo Cienfuegos Provincial General Hospital in Sancti Spíritus, Cuba, from June 2014 to February 2016, with the diagnosis of STEMI (a typical-greater than 30 minutes-pain with ST segment changes). Imaging or laboratory techniques support was required in some cases.

Two groups were set up: patients who died of SCD secondary to cardiac rupture, malignant ventricular arrhythmias or acute heart failure, after initial STEMI episode stabilization; and patients discharged alive or deceased owing to other non-sudden causes (cardiogenic shock, respiratory insufficiency associated with mechanical ventilation, among others).

Data collection

In the case of patients without complications from the start, data input was carried out in three moments:

- On admission: personal data, background and aspects related to prehospital care.
- 24-48 hours after admission: hospital care data and laboratory results.
- At discharge: closing of the hospital care form, treatment and instructions on follow-up of primary care patients.

When the patient's condition made data input difficult, the process was performed at discharge. (deceased or with complications on hospital stay).

Data processing was carried out by a qualified staff with access to electronic records. They detected within the clinical history every parameter erroneously determined on any data collection stage.

Demographic and anthropometric characteristics were included among the variables: weight, height, sex and age, and clinical variables:

- Classic cardiovascular risk factors and history: diabetes mellitus, obesity, high blood pressure, smoking, coronary artery disease, previous myocardial infarction, chronic kidney disease, percutaneous transluminal coronary angioplasty, cerebrovascular and chronic obstructive pulmonary diseases, and anemia.
- Aspects of clinical presentation (heart rate [HR], systolic and diastolic blood pressure, and clinical signs of reperfusion).
- Hemodynamic state on admission (Killip-Kimball).
- GRACE risk score.
- Electrocardiographic data: alteration of the ST segment, arrhythmias, signs of reperfusion.
- Left ventricle ejection fraction by echocardiogram (Simpson method).
- Reperfusion strategy: thrombolysis (Cuban recombinant streptokinase) or percutaneous coronary intervention.
- Signs of reperfusion: clinical, electrical and –in their case– hemodynamic.
- Treatment: pharmacological or non-pharmacological administered at admission and discharge.
- Complications.
- Performance time of health personnel and patient.
- Place of first medical attention.
- State at discharge: alive or deceased.

Statistical analysis

The statistical analysis was performed with the SPSS 15.0 program. Fisher's exact test and Student's t test were used to compare the quantitative and qualitative variables in both groups.

Ethical considerations

Approval of the Ethics Committee of the institution and of the patients or relatives was procured if required. The study adheres to the Helsinki declaration.

RESULTS

There were 34 deaths (13.54%), 20 due to SCD (7.96%) (**Table 1**). Overall average age was 66.07± 13.9 years, though it was 10 years older in the SCD group (76.6±7.72 years, p=0.001), where patients older than 75 years prevailed. (80%, p>0.01). Female sex was more frequent in the SCD group; their average age was also higher (78.45±7.92 vs. 70.23±11.98, p=0.031).

Regarding the distribution of risk factors, there were no differences between both groups except in two of them. Diabetic patients predominated in the SCD group (65.0 vs. 29.44%, p=0.001), while smoking was more frequent in the other group of patients (30.0 vs. 55.84%; p=0.028).

The 80% of SCD patients were initially treated outside the provincial capital (**Table 2**). One hundred and forty-four patients (57.37%) were applied some reperfusion strategy. Clinical-electrical evidence of resuscitated myocardium showed a low overall index (15.22%), none of them in the SCD group (p=0.02).

Although the difference of average system performance time (46 minutes) does not provide significant difference (p=0.09), whether it had the difference of ischemic time (469.4±295.8 vs. 344.1±262.1 [125 minutes], p=0.047). Demonstrating that this mainly occurs due to delay in seeking medical care.

Patients with SCD had higher HR on admission (98.9±20.6 vs. 82.7±14.6 [16 beats per minute difference], p=0.001), but none of the two tension parameters was clinically different (**Table 3**). The GRACE risk score, which includes HR, was higher in patients with SCD (129.2±12.58 vs. 101±27.07, p=0.001), unlike

Table 1. Clinical and demographic characteristics of the patients.

Demographic characteristics		Total (251)	SCD (n=20)	No SCD (n=231)	p
Age	Global (years)	66.07±13.9	76.6±7.72	65.1±14.2	0.001
	> 75	82 (32.66)	13 (65.0)	69 (29.87)	0.01
	> 85	20 (7.96)	3 (15.0)	17 (7.35)	0.38
Female Sex	Frequency	81 (32.27)	11 (55.0)	70 (30.30)	0.023
	Age (years)	71.35±8.2	78.45±7.92	70.23±11.98	0.031
Body mass index		25.8±3.74	26.8±3.4	25.72±3.76	0.21
White skin color		228 (90.83)	20 (100)	208 (90.04)	0.13
Hyperlipoproteinemia		20 (7.96)	3 (15.0)	17 (7.35)	0.26
Diabetes mellitus		81 (32.27)	13 (65.0)	68 (29.44)	0.001
Obesity		138 (54.98)	14 (70.0)	124 (53.67)	0.16
High Blood Pressure		200 (79.68)	19 (95.0)	181 (78.35)	0.07
Smoking		135 (49.8)	6 (30.0)	129 (55.84)	0.028
Ischemic heart disease		89 (35.45)	10 (50.0)	79 (34.19)	0.176
Previous myocardial infarction		36 (14.34)	2 (10.0)	34 (14.71)	0.56
Chronic kidney failure		13 (5.17)	0	13 (5.62)	0.276
Glomerular filtration rate		62.88±27.16	46.11±11.92	64.20±27.44	0.001
PTCA		11 (4.38)	0	11 (4.76)	0.318
Cerebrovascular disease		9 (3.58)	0	9 (3.89)	0.369
Anemia		7 (2.78)	2 (10.0)	7 (3.03)	0.108
Peripheral venous disease		13 (5.17)	1 (5.0)	12 (5.19)	0.97
Mortality		34 (13.54)			

PTCA, percutaneous transluminal coronary angioplasty; SCD, sudden cardiac death.
The values denote n (%) and mean ± standard deviation ($\bar{\chi}$+SD).

the decreased left ventricle ejection fraction (36.81± 7.85 vs. 46.87±7.54, p=0.001), all of which was associated with a higher frequency of heart failure signs in this subgroup (Killip-Kimball functional class > I: 50.0 vs. 31.2%).

DISCUSSION

The main predictive models of SD occurrence include advanced age (over 70 years old)[6-8]. One of them, the MUSTT (Multicenter UnSustained Tachycardia Trial)[8], gives a score to ages over 50 years.

A report of nearly 1000 patients (where SCD accounted for half of total deaths after STEMI), revealed a difference in the average age between deceased due to SD and 10-year-old alive, although the average age in their subgroups was lower than that found in this investigation[9].

In the APEX-AMI[6] study, 6% of PCI-treated patients died with ventricular arrhythmias. Advanced age and the presence of multiple comorbidities were associated factors; and a recent meta-analysis[1] of 80.382 patients with advanced kidney disease concluded that SD was a critical problem in this subgroup of patients. They pointed out the need for further studies, as current data remained contradictory due to the wide range of criteria to identify a death as "sudden" in patients with end-stage chronic

Table 2. Therapeutic strategies.

Therapeutic strategy		Total (251)	SCD (n=20)	No SCD (n=231)	p
Initial Attention	Provincial Capital	108 (43)	4 (20)	104 (45)	0.03
	Other place	143 (57)	16 (80)	127 (55)	
Reperfusion Strategy	Administered	144 (57.37)	9 (45)	133 (57.6)	0.27
	Salvage of the injured myocardium*	22 (15.27)	0 (0)	22 (9.5)	0.02
	SD (min) ($\bar{\chi}$+SD)	112.7±77.8	155.6±60.4	109.5±78.17	0.09
	IT (min) ($\bar{\chi}$+SD)	354.5±266.4	469.4±295.8	344.1±262.1	0.047
PTCA	Primary	15 (5.97)	0	15 (6.49)	0.24
	Resuscitation	11 (4.38)	0	11 (4.76)	0.34
	Treatment for CL	12 (4.78)	0	12 (5.2)	0.29
	Treatment for OL	6 (2.39)	0	6 (2.59)	0.51
Drugs	Beta-Blockers	92 (42.8)	13 (65)	79 (34.19)	0.03
	DAPT	247 (98.40)	20 (100)	227 (98.26)	0.884
	Statins	238 (94.82)	18 (90)	220 (95.23)	0.764
	ACEI	239 (95.21)	18 (90)	221 (95.67)	0.784

* Refers to clinical and electrical characteristics
ACEI, angiotensin-converting enzyme inhibitors; CL, culprit lesion; DAPT, dual antiplatelet therapy; IT, ischemic time; OL, other lesions; PTCA, percutaneous transluminal coronary angioplasty; SD, system delay; SCD, sudden cardiac death.

Table 3. Hemodynamic parameters.

Hemodynamic parameters		Total (251)	SCD (n=20)	No SCD (n=231)	p
Heart rate ($\bar{\chi}$+SD)		84,4±15,6	98,9±20,6	82,7±14,6	0,001
Systolic pressure ($\bar{\chi}$+SD)		126,1±22,8	125,28±28,37	126,15±22,45	0,8
Diastolic pressure ($\bar{\chi}$+SD)		73,82±14,24	71,5±16,31	74,03±14,07	0,448
GRACE ($\bar{\chi}$+SD)		103,9±270,2	129,2±12,58	101±27,07	0,001
LVEF (%)		46,44±7,79	36,81±7,85	46,87±7,54	0,001
Killip-Kimball Classification [n (%)]	I	169 (67,3)	10 (50)	159 (68,8)	0,08
	> I	82 (32,7)	10 (50)	72 (31,2)	

GRACE: Global Registry of Acute Coronary Events; LVEF, left ventricle ejection fraction; SD, standard deviation; SCD, sudden cardiac death.

kidney disease.

The Paris Prospective Study I[10], recognizes diabetes mellitus as a risk factor per se, which increases the possibility of SD in risk subgroups, and is considered an aggravating factor associated with poor prognosis and intractable arrhythmia, apart from the presence or absence of other coronary risk factors.

The GIMUS reports[2] describe an increase in the prevalence of cardiovascular risk factors in patients who died due to SD, although the difference described is not significant at all, even in the case of multiple comorbidities. It concludes that, although

frequent in SD patients, lipid profile alterations should not be taken into account to define a subpopulation at increased risk.

The Smoker's paradox' is an observational phenomenon of favorable outcome in patients with acute coronary syndrome. Many theories have been proposed, including the presence of a greater thrombogenic component -non atherogenic- allowing a better reperfusion response[11].

However, a meta-analysis[12] showed that such effect was only evident in studies with short-term follow-up and that, in fact, medium and long term mortality is higher in smokers than in non-smokers.

More effective reperfusion techniques have significantly reduced the frequency of SD in post-STEMI patients.

Arrhythmia reentry mechanism is considered one of the triggers for SD after reperfusion in patients with acute myocardial ischemia[5] although this study found no patients with SD after effective reperfusion with resuscitated myocardium. The opposite favors the appearance of a larger area of reentry, because of a wider injury.

Patients with ventricular arrhythmias after STEMI can be classified into one of these three groups: late presenters, unsuccessful reperfusion strategy, and previous arrhythmogenic substrate[5]. In this study, patients from the first two groups predominated.

In the APEX-AMI[13], the proportion of electrical complications was higher in patients without intervention than in those who proceeded to treat the culprit artery. Our results regarding "system delay" differ from those of this same study[13] because they included the door-to-needle time; However, the relationship between mortality and longer waiting time for medical care does coincide.

The fraction of patients administered thrombolysis depends on the time of ischemia, since those with more than 300 minutes elapsed since the onset of symptoms will practically have no heart muscle to save; This corresponds to the findings of Rao et al.[9] who, after the multivariate analysis, concluded that non-application of a reperfusion strategy was one of the variables associated with the onset of SD.

Our patients are administered beta-blockers more frequently due to the increase in the mean of this parameter in the group, consistent with what was stated in the meta-analysis of Al-Gobari et al.[14]: long-term administration of beta-blockers in patients with decreased left ventricle ejection fraction was associated with a reduction in the risk of sudden death. However, the ACC/AHA guidelines of 2013[15] suggest that it should be included as usual therapy in patients with STEMI, except in cases with signs of heart failure, evidence of low output, risk of cardiogenic shock, or other contraindications.

Heart rate above 80 bpm at admission was associated with a highest risk of in-hospital mortality[16]. Although the mean of both groups in our study exceeds this figure, the difference between them ($p = 0.001$) substantially increased the risk of SD.

On the other hand, although in our study its relation to the left ventricle ejection fraction was determinant ($p = 0.001$), many other investigations consider that this should not be the only parameter to determine the risk of SD in patients with STEMI, since in large prospective follow-up multicenter studies, data remain contradictory. No relationship was found in the MUSTT[8], and in the ARIC[17], in addition to the ejection fraction itself, other echocardiographic variables were related such as mitral calcification, left atrial enlargement, left ventricular mass, as well as the presence of an E/A ratio (transmitral flow)> 1.5 or <0.7.

Limitations

Our study has some limitations which have to be pointed out. First, it is a unicentric study, without longitudinal follow-up of patients in consultations, hence the data only comprises the in-hospital period, while in literature, follow-ups of at least one year after the acute coronary syndrome are achieved.

Second, the previous characteristic only permitted a small sample (251 patients in about two years [21 months]). Although when establishing the average of patients per months of study, this center reaches 12 patients/center/month, higher than some large multicenter records of acute coronary syndromes. Besides, the statistical differences found in a small sample could be increased when analyzing larger cohorts. It could also happen with non-significant differences.

Third, the therapeutic possibilities of the Camilo Cienfuegos General Hospital and the regional care system only allow the results to be extrapolated to centers with similar characteristics.

Fewer centers will be able to use the results presented, mainly due to the widespread use of percutaneous coronary intervention; although in the third world there are still networks with little access to this type of treatment.

CONCLUSIONS

Deaths due to avoidable causes are frequent in coronary care units with adequate and early reperfusion strategies. Those units with limited access to coronary intervention should properly stratify their patients to provide it to those who may benefit most. This stratification, which is based on characteristics that can be determined upon admission of the patient with ST-segment elevation acute myocardial infarction, is feasible.

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