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# Behavior of cardiovascular diseases and coronary risk factors in sudden cardiac death

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ARTICLE INFORMATION

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The authors declare no competing interests.

**Abbreviations**
**AMI:** acute myocardial infarction
**CAD:** coronary artery disease
**SCD:** sudden cardiac death

## ABSTRACT

*Introduction:* Half of the patients suffering from sudden cardiac death (SCD) have no history of known heart disease. However, most suffer from asymptomatic ischemic heart disease. The most effective approach to prevent SCD in the general population is the accurate quantification of individual risk for ischemic heart disease, followed by control of risk factors.
*Objectives:* To determine the association between some cardiovascular diseases and coronary risk factors with the occurrence of SCD.
*Methods:* An analytical, longitudinal and retrospective study was carried out with 261 patients who died from SCD at the Hospital Enrique Cabrera (Cuba), between January 2014 and March 2018. The possible association between history of cardiovascular disease and coronary risk factors with the occurrence of SCD was sought.
*Results:* History of coronary artery disease (CAD) (p=0.01) was associated with the appearance of SCD. Age over 70, family history of CAD, and high blood pressure were found to be risk factors associated with the occurrence of SCD. Smoking was a risk factor in the group of patients with no known history of CAD.
*Conclusions:* Coronary artery disease was the cardiovascular condition most associated with the appearance of SCD. There were both modifiable and non-modifiable coronary risk factors that were associated with the occurrence of *SCD.*
*Keywords:* Sudden cardiac death, Risk factors, Coronary artery disease, Myocardial ischemia, Ischemic heart disease

## *Comportamiento de enfermedades cardiovasculares y factores de riesgo coronario en la muerte súbita cardíaca*

## RESUMEN

*Introducción: La mitad de los pacientes que sufren muerte súbita cardíaca (MSC) no tienen antecedentes de enfermedad cardíaca conocida; sin embargo, la mayoría padecen de cardiopatía isquémica asintomática. El enfoque más eficaz para prevenir la MSC en la población general reside en la cuantificación del riesgo individual de sufrir cardiopatía isquémica, seguida del control de factores de riesgo.*
*Objetivo: Determinar la asociación entre algunas enfermedades cardiovasculares y los factores de riesgo coronario con la ocurrencia de MSC.*
*Método: Se realizó un estudio analítico, longitudinal y retrospectivo con 261 pacientes fallecidos por MSC en el Hospital Enrique Cabrera (Cuba), entre enero de 2014 y marzo de 2018. Se buscó asociación entre el antecedente de enfermedades cardiovasculares y los factores de riesgo coronario con la ocurrencia de MSC.*

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**Authors' contribution**
LDCS and RMMP: Conception and design of the research; data collection, analysis and interpretation and writing of the manuscript.
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All authors critically reviewed the manuscript and approved the final report.

*Resultados: El antecedente de enfermedad arterial coronaria (EAC) (p=0,01) se asoció con la aparición de MSC. La edad mayor de 70 años, el antecedente familiar de EAC y la hipertensión arterial resultaron ser factores de riesgo que se asociaron con la ocurrencia de MSC. El hábito de fumar se comportó como factor de riesgo en el grupo de pacientes que no tenían antecedentes conocidos de EAC.*
*Conclusiones: La enfermedad arterial coronaria fue la afección cardiovascular que mayor asociación tuvo con la aparición de MSC. Existieron factores de riesgo coronarios, tanto modificables como no modificables, que tuvieron asociación con la ocurrencia de MSC.*
*Palabras clave: Muerte súbita cardíaca, Factores de riesgo, Enfermedad arterial coronaria, Isquemia miocárdica, Cardiopatía isquémica*

## INTRODUCTION

Sudden cardiac death (SCD) continues to be a challenge for physicians and a major public health issue[1]. Although cardiovascular mortality has decreased in more developed countries over the past 20 years as a result of the implementation of preventive measures to reduce the burden of ischemic heart disease and heart failure, cardiovascular diseases are responsible for roughly 17 million deaths a year worldwide, and of these, about 25% are attributable to SCD[2]. Survival after sudden cardiac arrest remains low and has not improved significantly in recent decades, although huge efforts have been made. Hence, efforts have recently been focused on SCD prevention[3].

Sudden cardiac death is defined as death due to any potentially fatal congenital or acquired heart condition, known in life or not, where the time and mode of death are unexpected[1,2]. Furthermore, death must occur within one hour of the onset of symptoms and may be due to ventricular tachycardia/fibrillation, asystole, or non-arrhythmic causes[1,2,4]. The term is also used when there are obvious extracardiac causes not identified by post-mortem examination, so that the probable cause of death is an arrhythmic event[2].

The heart diseases associated with this event differ in age groups. While in the youngest people the main causes are channelopathies, cardiomyopathies, myocarditis and abuse of toxic substances; chronic degenerative diseases predominate in older people, such as ischemic heart disease, heart failure and heart valve disease[5,6].

Coronary artery disease is the clinical disease most related to SCD in the general population as it is attributed to 80-85% of these deaths[1]. To add insult to injury, half of cardiac arrest occurs in people who are unaware of their heart condition; yet most suffer from asymptomatic coronary artery disease (CAD)[7-9].

The importance of avoiding SCD is highly dependent on perfecting risk stratification techniques. The occurrence of this fatal event in patients with previously asymptomatic ischemic heart disease constitutes, at present, the largest hidden portion of the iceberg[1]. Therefore, the most effective approach to prevent SCD in the general population lies in the quantification of individual risk of CAD according to risk score charts, followed by control of risk factors such as: hypercholesterolemia, diabetes mellitus, high blood pressure, tobacco use and obesity; that determine the rupture of the vulnerable plaque, which have been and are the object of intense research and will probably offer even better results in the search for the determinants of SCD[3,10,11].

The aim of this research has been to determine the association between some cardiovascular diseases and modifiable and non-modifiable coronary risk factors, with the occurrence of SCD, in patients with and without a personal history of CAD.

## METHOD

An analytical, longitudinal and retrospective study was carried out with 261 deceased patients who met the SCD diagnostic criteria at the Hospital General Docente Enrique Cabrera, in Havana, Cuba, within the period from January 2014 to March 2018. The sample was divided into two groups, according to the presence or not of a personal history of CAD.

### Variables

The variables studied were: age, sex, family history of CAD, and personal history of heart disease, high blood pressure, diabetes mellitus, smoking, hyperlipidemia, obesity (body mass index greater than or

equal to 30), and ST-segment elevation myocardial infarction (AMI).

Sudden cardiac death was defined as an unexpected natural death of cardiac origin occurring within the first hour after the onset of premonitory symptoms.

### Data collection and processing

The data were obtained by reviewing the medical records and death certificates of the patients who arrived dead or died in the Emergency Department Units, and were then recorded in a data collection sheet.

An automated database was created in Microsoft Excel, and the statistical package SPSS 15.0 for Windows was used to perform the analysis and summary of the data. It was verified that for each variable recorded there were no extreme, inconsistent or missing values.

The Chi-square statistical test was applied to make the statistically correct decision regarding the behavior of the analyzed variables. The existence of association between the variables with the occurrence of SCD in each one of the groups was verified. The corresponding significance levels ($p<0.05$) were established and once the information had been processed, the results were presented in tables and graphs.

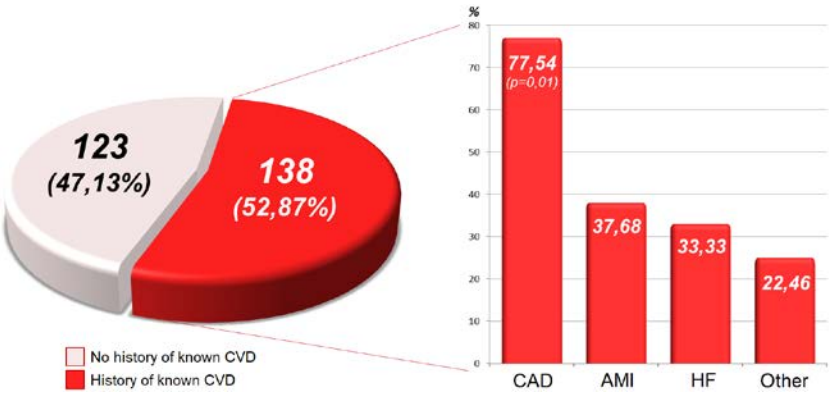


**Figure.** Prevalence of cardiovascular diseases in patients with sudden cardiac death.
CAD, coronary artery disease; CVD, cardiovascular diseases: AMI, acute myocardial infarction; HF, heart failure.

## RESULTS

Most of the patients had a history of some known cardiovascular disease (138; 52.87%); within these, CAD was associated with the appearance of SCD (p=0.01) (**Figure**).

The mean age was 70.8 years. From 60 years on, age was significantly associated with the occurrence of SCD in the group of patients with a history of CAD (**Table 1**): p=0.04 in the 61-70 age group; p=0.01 in the 71-80 age group and p<0.001 in the 81 and older age group. Conversely, in patients with no history of CAD, only the 71-80 year-old group was associated with SCD (p=0.04).

There was no statistically significant association between sex and the appearance of SCD (**Table 2**). With a history of CAD (men p=0.08 and women p=0.41) and without this history (men p=0.79 and women p=0.21).

**Table 3** shows that there was an association between the family history of CAD and SCD in the

**Table 1.** Relationship between age groups and sudden cardiac death, according to personal pathological history of coronary artery disease.

| Age groups (years) | Personal history of coronary artery disease | | | | | | Total | |
|---|---|---|---|---|---|---|---|---|
| | Yes | | | No | | | | |
| | Nº | % | p | Nº | % | p | Nº | % |
| 18-40 | 0 | 0 | 0 | 6 | 2.29 | 3.00 | 6 | 2.30 |
| 41-50 | 2 | 0.76 | 2.13 | 12 | 4.59 | 1.07 | 14 | 5.37 |
| 51-60 | 16 | 6.13 | 1.73 | 21 | 8.04 | 0.85 | 37 | 14.17 |
| 61-70 | 22 | 8.43 | 0.04 | 36 | 13.79 | 0.12 | 58 | 22.22 |
| 71-80 | 32 | 12.26 | 0.01 | 43 | 16.47 | 0.04 | 75 | 28.74 |
| 81 and older | 35 | 13.40 | <0.001 | 36 | 13.79 | 0.12 | 71 | 27.20 |
| **Total** | 107 | 40.99 | -- | 154 | 59.01 | -- | 261 | 100.00 |

**Table 2.** Relationship between sex and sudden cardiac death, according to personal pathological history of coronary artery disease.

| Sex | Personal history of coronary artery disease | | | | | | Total | |
|---|---|---|---|---|---|---|---|---|
| | Yes | | | No | | | | |
| | Nº | % | p | Nº | % | p | Nº | % |
| Male | 57 | 21.83 | 0.08 | 84 | 32.18 | 0.79 | 141 | 54.02 |
| Female | 50 | 19.16 | 0.41 | 70 | 26.82 | 0.21 | 120 | 45.98 |
| Total | 107 | 40.99 | -- | 154 | 59.01 | -- | 261 | 100.00 |

**Table 3.** Relationship between family history of ischemic heart disease and sudden cardiac death, according to personal pathological history of coronary artery disease.

| Family pathological history | Personal history of coronary artery disease | | | | | | Total | |
|---|---|---|---|---|---|---|---|---|
| | Yes | | | No | | | | |
| | Nº | % | p | Nº | % | p | Nº | % |
| Yes | 66 | 25.28 | 0.04 | 105 | 40.23 | 0.01 | 171 | 65.51 |
| No | 41 | 15.71 | | 49 | 18.78 | | 90 | 34.49 |
| Total | 107 | 40.99 | -- | 154 | 59.01 | -- | 261 | 100.00 |

**Table 4.** Relationship between modifiable coronary risk factors and sudden cardiac death, according to personal pathological history of coronary artery disease.

| Modifiable risk factors | History of coronary artery disease | | | | | | Total | |
|---|---|---|---|---|---|---|---|---|
| | Yes | | | No | | | | |
| | Nº | % | p | Nº | % | p | Nº | % |
| High blood pressure | 67 | 25.67 | 0.03 | 69 | 26.43 | 0.04 | 136 | 52.10 |
| Diabetes mellitus | 34 | 13.02 | 0.11 | 28 | 10.72 | 2.03 | 62 | 23.75 |
| Smoking | 13 | 4.98 | 3.31 | 61 | 23.37 | 0.03 | 74 | 28.35 |
| Hyperlipidemia | 26 | 9.96 | 2.15 | 22 | 8.42 | 2.91 | 48 | 18.39 |
| Obesity | 19 | 7.27 | 3.25 | 27 | 10.34 | 2.15 | 46 | 17.62 |

group of those with CAD (p = 0.04) and those without it (p=0.01).

High blood pressure was associated with the appearance of SCD in the two groups of patients (p= 0.03 and 0.04) and smoking in the group of patients with a history of CAD (p=0.03). The rest of the modifiable coronary risk factors had no statistical association with the onset of the event (**Table 4**).

**Table 5** reveals that in the group of patients with a history of CAD there was no association between having suffered an ST-segment elevation myocardial infarction and the appearance of SCD (p=0.13).

**Table 5.** Relationship between ST-segment elevation myocardial infarction and sudden cardiac death in patients with a history of coronary artery disease.

| PPH of AMI | Nº | % |
|---|---|---|
| Yes | 52 | 48.59 |
| No | 55 | 51.40 |
| **Total** | 107 | 100.0 |

p=0.13
AMI, acute myocardial infarction; PPH, personal pathological history

## DISCUSSION

Sudden cardiac death accounts for 13 18.5% of all deaths from natural causes and the geographical incidence varies based on the prevalence of CAD in different regions, since it is the disease most associated with this fatal event[3]; this is consistent with the results of our research. In the current study, age over 70 years was strongly associated with the occurrence of SCD. It is described that in adults the risk of SCD increases with age, corresponding to the behavior of ischemic heart disease[1,6,12,13].

In patients with a history of CAD, the association began at the age of 60, that is, approximately 10 years earlier than those without it. These results could be explained by the following: the onset of ischemia produces immediate electrical, mechanical and biochemical dysfunction at the level of the heart muscle and the conduction tissue is more resistant to acute ischemia than the contractile myocardium; therefore, the electrical and physiological consequences of its condition are less intense and delayed. However, acute ischemia and acute myocardial infarction (AMI), in patients with previous infarction and scar tissue, are more arrhythmogenic than in previously normal tissue, because the scar has electrophysiological alterations, including regional changes in transmembrane action potential and refractory periods[14].

Being of either sex was not related to the occurrence of SCD in this study. Ochoa *et al*[15] obtained a ratio of 1.02:1 in the behavior of SCD in males compared to females (p=0.057), while Adabag *et al*[9] found that the risk was four times higher in men than in middle-aged women, but the differences narrowed as age progressed. From the Framingham cohort, it is known that the delay in the incidence rates of AMI and SCD in women is around 20 years compared to men, but the margin decreases at older ages. The overall incidence of CAD at ages 65 to 94 doubles for males and triples for females compared to ages 35 to 64. After menopause, the incidence and severity of CAD increase rapidly, reaching rates three times higher than in the premenopausal stage[16].

The results of this work are consistent with the literature reviewed where having a family history of CAD is associated with the occurrence of coronary events and SCD[1 3,9,12,17]. Two population-based studies have described the clustering of SCD cases as the first symptom of CAD in some families. This observation indicates that genetic factors modulate the risk of SCD in the context of ischemic heart disease[3,12,17]. Recently, new advances in genomic medicine have provided other novel approaches to identify probable genes and relatively common polymorphisms, which may predispose patients to an increased risk of SCD.

Current and future studies may allow the identification of some common gene variants associated with an increased risk of SCD in the context of coronary artery disease.

Two recent studies, carried out in Cuba, found that high blood pressure significantly influenced the appearance of SCD[18,19]. Meanwhile, Morentin *et al*[20] in its study on out-of-hospital SCDs in Spain, identified it as the most important risk factor. This work coincides with what these authors have raised, as high blood pressure acts in two ways on the increased risk of SCD: one indirectly by being an important risk factor for the occurrence of diseases such as ischemic heart disease and heart failure, which are in turn causes of SCD, and another directly because it is able to produce left ventricular hypertrophy, which, by various hemodynamic, myocardial and neuroendocrine mechanisms, can increase the predisposition to ventricular arrhythmias. Furthermore, in hypertensive patients there is excessive activity of the sympathetic nervous system, which exerts a pro-arrhythmogenic effect, as does angiotensin II, which is also increased by increased activity of the renin-angiotensin system[21].

In an investigation on SCD victims, 23.1% of the cases suffered from diabetes mellitus[22]. López *et al*[18] found 39.2% (p=0.83) and in another study they reported 25.5% (p=0.05)[12]. Our study found similar figures (23.7%), but this was not enough to demonstrate an association between the presence of diabetes mellitus and SCD in this series, despite the fact that the damage this disease produces in the cardiovascular system is well described and that it constitutes one of the most important risk factors in the development of coronary artery disease. Something similar happened with a history of hyperlipidemia, which was not related to SCD, that could be justified by an under-reporting in the medical records of these patients, taking into account that we did not have at hand the previous blood chemistry laboratory results, only what the family members referred to in this regard.

This research found no association between obesity, based on body mass index, and the presence of SCD. This index is the most popular measure among health professionals to measure obesity, but several

limitations have been noted. One is that, at the individual level, it is not a good indicator of body composition because it does not distinguish in terms of the contribution of lean and fat masses to weight[23].

Waist circumference for the diagnosis of central obesity has been on the rise for several years. The preferential fat accumulation in the thoracoabdominal area has been associated with an increased risk of cardiovascular disease[23]. A number of studies[24-26] have shown an association between an increase in the waist-to-hip ratio and an increased risk of cardiovascular disease, independent of the body mass index. Adabag *et al*[27] found an association between general obesity and increased SCD but mediated by all other traditional risk factors; however, central obesity had an independent association. A significant number of obese people by abdominal circumference do not meet obesity criteria according to body mass index[25]; therefore, given the greater association between central obesity and the risk of cardiovascular disease, it would be advisable to introduce the measurement of abdominal girth in future studies.

A meta-analysis conducted by Aune and his group[28] that included 20 prospective studies reported that smoking increases the risk of SCD and that it is proportional to the number of cigarettes smoked per day. For their part, Vilches *et al*[29] found that smoking was strongly associated with the presence of lesions in the coronary artery tree and SCD. This study also found an association between smoking and SCD in the group of patients who had no history of CAD, but not in those who did, perhaps because these people gave up smoking when they learned about their cardiovascular condition. Quitting smoking after a heart attack reduces the risk of another and also the risk of death in general, as well as other benefits that could have a more immediate effect on daily life[30].

Our research also analyzed −within the group with a history of CAD− whether having suffered an ST-segment elevation myocardial infarction (AMI) was associated with the appearance of SCD, which was not statistically significant. Several studies have shown that the appearance of adverse cardiac events such as new AMI, malignant ventricular arrhythmias and SCD is initially higher in patients who suffered ST-segment elevation acute coronary syndrome, compared to those who suffered Non ST-segment elevation acute coronary syndrome; such differences begin to even out in the first 6 months and are then reversed[31-33]. This occurs firstly because generally the patients who suffer non ST-segment elevation myocardial infarction are elderly people and women, with a greater number of associated comorbidities, who often do not receive the benefits of an early invasive treatment strategy, unlike those with ST-segment elevation myocardial infarction. Secondly, these patients have recurrent ischemic events that worsen their prognosis and increase mortality[33].

## CONCLUSIONS

Older ages were at greater risk for sudden cardiac death, regardless of gender. The association between age and sudden cardiac death was advanced by approximately 10 years in patients with a history of coronary artery disease. Among cardiovascular diseases, coronary artery disease was the one associated with the appearance of sudden cardiac death; and so was its family history, even in patients who had no personal history of the disease. High blood pressure was the modifiable risk factor most associated with sudden cardiac death.

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