

## Sudden Cardiac Death in Brazil: A Community-Based Autopsy Series (2006-2010)

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### Abstract

**Background:** Sudden cardiac death (SCD) is a sudden unexpected event, from a cardiac cause, that occurs in less than one hour after the symptoms onset, in a person without any previous condition that would seem fatal or who was seen without any symptoms 24 hours before found dead. Although it is a relatively frequent event, there are only few reliable data in underdeveloped countries.

**Objectives:** We aimed to describe the features of SCD in Ribeirão Preto, Brazil (600,000 residents) according to Coroners' Office autopsy reports.

**Methods:** We retrospectively reviewed 4501 autopsy reports between 2006 and 2010, to identify cases of SCD. Specific cause of death as well as demographic information, date, location and time of the event, comorbidities and whether cardiopulmonary resuscitation (CPR) was attempted were collected.

**Results:** We identified 899 cases of SCD (20%); the rate was 30/100000 residents per year. The vast majority of cases of SCD involved a coronary artery disease (CAD) (64%) and occurred in men (67%), between the 6<sup>th</sup> and the 7<sup>th</sup> decades of life. Most events occurred during the morning in the home setting (53.3%) and CPR was attempted in almost half of victims (49.7%). The most prevalent comorbidity was systemic hypertension (57.3%). Chagas' disease was present in 49 cases (5.5%).

**Conclusion:** The majority of victims of SCD were men, in their sixties and seventies and the main cause of death was CAD. Chagas' disease, an important public health problem in Latin America, was found in about 5.5% of the cases. (Arq Bras Cardiol. 2015; 104(2):120-127)

**Keywords:** Death, Sudden, Cardiac / epidemiology; Brazil; Autopsy.

### Introduction

Sudden cardiac death (SCD) is an unexpected event from a cardiac cause<sup>1</sup>. According to the World Health Organization (WHO), SCD is a natural event that occurs within less than one hour of symptom onset in individuals without any potentially fatal precondition. However, 40% of cases are not witnessed and, in these situations, the victims must have been seen asymptomatic in the last 24 hours before the event<sup>2</sup>.

An incidence of SCD between 180.00-400.00 cases / year<sup>3</sup> is estimated in the United States. However, an accurate estimate is not possible for several reasons: different MSCD definitions

are used<sup>4</sup>, studies based on retrospective analysis of death certificates<sup>5</sup> or even absence of a structured system to report cases of SCD in some regions. Such difficulties are more evident in developing countries<sup>6</sup>.

The most affected individuals are men between the sixth and seventh decades of life<sup>7</sup>. The epidemiology of SCD is closely correlated with coronary artery disease (CAD) and up to 80% of the victims have CAD<sup>4</sup>. Risk factors such as systemic arterial hypertension, diabetes and smoking increase the risk of SCD<sup>8</sup>, as well as advanced left ventricular dysfunction (ejection fraction < 30%)<sup>4</sup>. In young individuals, the most common diagnoses are hypertrophic cardiomyopathy, coronary artery anomalies, arrhythmogenic dysplasia of the right ventricle and channelopathies<sup>9</sup>. In Latin America, Chagas disease is a significant cause of SCD<sup>10</sup>.

Circadian and seasonal SCD variations have been described. A marked variation in the occurrence of SCD with peaks in the morning can be observed on Mondays, in the winter months<sup>11</sup>. Stressful situations such as terrorist attacks or events such as the FIFA World Cup have been associated to increased SCD rates<sup>12,13</sup>.

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The high incidence of this event, combined with low survival rates, makes SCD a relevant health issue<sup>7</sup>. In Latin America, few studies have been performed to date, with small populations and specific heart diseases<sup>14,15</sup>.

Our objective was to describe the characteristics of SCD in the city of Ribeirão Preto, state of Sao Paulo, Brazil (approximately 600,000 inhabitants) in five years, according to the autopsy reports of the Death Verification Service of the Countryside (SVOi).

## Methods

Ribeirão Preto is a medium-sized city located in the state of São Paulo, Brazil. It has a public body linked to the School of Medicine of Ribeirão Preto, Universidade de São Paulo, the Death Verification Service of the Countryside (SVOi), responsible for the autopsies of victims of non-violent deaths referred from any health service of the city, in accordance with applicable federal laws, as requested by the health professional who assisted the victim.

In our study, we assessed the autopsy request forms and complete reports of autopsies performed by SVOi in victims from the city of Ribeirão Preto between 2006 and 2010. All cases that met SCD criteria were included, according to the most widely used definition of the WHO: unexpected death within one hour of symptom onset, or in cases of unwitnessed death, when the victim was seen in good health in the 24 hours prior to the event<sup>2</sup>.

Data related to the event were collected, such as the cause of death reported by the pathologist who performed the investigation, demographic characteristics and comorbidities of the victims, date, time and place of the event and cardiopulmonary resuscitation (CPR) maneuvers performed. The study was approved by the Research Ethics Committee of our institution.

## Exclusion criteria

Initially, deaths of newborns and children were excluded. Then, all individuals with causes of death not compatible with sudden death were excluded: infectious diseases, advanced malignancies, abdominal diseases, such as bowel obstruction or perforated gastric ulcer, cachexia and prolonged bed rest. Subsequently, cases of sudden death from noncardiac causes were also excluded: pulmonary embolism, acute aortic syndromes, asthma or hemorrhagic cerebrovascular accident (CVA). Finally, cases with no clinical history consistent with SCD, according to the WHO criteria employed in our study, or with incomplete information were also excluded.

## Statistical Analysis

The data were expressed as absolute values and percentages. ANOVA parametric test and Bonferroni post-test were used to analyze continuous variables, while the chi-square test was used to evaluate categorical variables. All statistical analyzes were performed using commercially available statistical software (InStat, version 3.0, GraphPad Software Inc, USA). A  $p$  value  $< 0.05$  was considered statistically significant.

## Results

### Sudden cardiac death cases

Between 2006 and 2010, 4,501 autopsies were performed in Ribeirão Preto. Initially, 2,053 cases were selected as possible SCD; however, after careful analysis, 718 cases were excluded for not meeting all the criteria for SCD, as well as 256 cases due to incomplete information. In 180 cases, a noncardiac cause of sudden death was identified: 99 cases of acute aortic syndrome, 58 cases of pulmonary embolism, 21 cases of hemorrhagic CVA and two cases of asthma. Therefore, 899 cases (20% of all autopsies) were defined as SCD (Figure 1). SCD rates ranged from 28/100,000 inhabitants in 2009 to 32/100,000 inhabitants in 2007 and 2008 (Figure 2). There was no difference in SCD rates between the years ( $p = 0.88$ ).

### Demographic characteristics of the population

The demographic characteristics of the study population are summarized in Table 1. Men were more affected than women (67% x 33%). Most of the victims were Caucasians (75% x 25%), between the sixth and seventh decade of life (mean age  $62.7 \pm 13.2$  years).

### Cause of death

The most prevalent cause of death was acute coronary syndrome, accounting for approximately two-thirds (64%) of all cases of SCD. The second cause was cardiomyopathy (32%), including both etiologies, ischemic and nonischemic. A diagnosis of myocardial bridge in eight cases, a case of myocarditis confirmed by histopathological analysis and, in another case, severe hypoplasia of the left anterior descending coronary artery in a 35-year-old woman were also observed. In 24 victims (3%) the cause of death could not be diagnosed, with these cases being considered sudden death of unknown cause (Table 2).

### Risk factors for sudden cardiac death

More than one-fifth of the patients (21.1%) victims of SCD had some type of previously known cardiac disease. Several risk factors for SCD were found in these patients, with the most prevalent being systemic arterial hypertension (57.3%). Furthermore, we observed 56 patients (6.2%) with a history of alcohol abuse (Table 3).

### Chagas Disease

Forty-nine patients (5.5%) had a diagnosis of Chagas disease, including those with previously known chagasic cardiomyopathy and those with positive serology at the time of the autopsy. It is noteworthy the fact that the proportion of patients with Chagas disease decreased from 2006 to 2010 (12 patients: 7.1% in 2006, 13 patients: 7.0% in 2007, 11 patients: 5.8% in 2008; five patients: 3.0% in 2009, eight patients: 4.3% in 2010), but the difference over the years did not reach statistical significance ( $p = 0.14$ ).

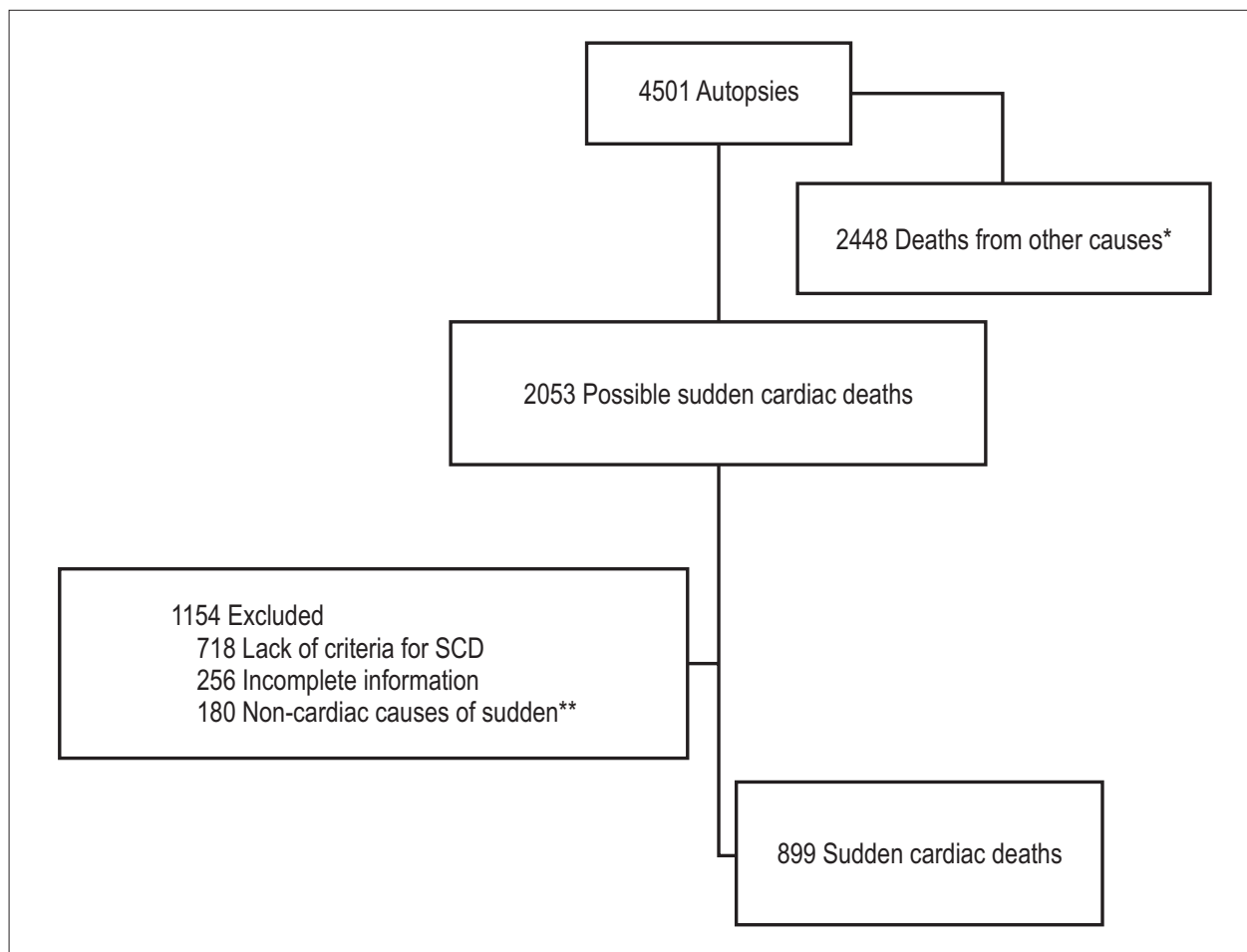


Figure 1 – Study flowchart.

\*Deaths from other causes: infectious diseases, advanced malignancies, abdominal diseases, cachexia, prolonged bed rest. \*\* Non-cardiac causes of sudden death: acute aortic syndromes, pulmonary embolism, hemorrhagic stroke, asthma.

### Temporal variation of sudden cardiac death

The analysis of cases of SCD showed a circadian variation, with fewer cases during the night ( $p < 0.05$  in comparison to other periods of the day) followed by a significant increase in the early hours of the morning, which was the period with the highest number of SCD events ( $p < 0.05$  in comparison to other periods of the day). It was not possible to determine the hour of the event in 10% of cases, (Figure 3A).

Further analyses showed no predominance of any day of the week ( $p = 0.79$ , Figure 3B) or any month of the year ( $p = 0.06$ ); however, the events tended to occur more frequently in the months of May and June (Figure 3C).

### Place of death

More than half of the deaths occurred at home (53.3%). Of the remaining, the deaths occurred in emergency rooms (37.8%), where most patients arrived in cardiorespiratory arrest, called "death on arrival"<sup>16</sup>. It is worth noting that 8.2% of all events occurred in public places and six men died (0.7%) during physical activity practice (mean age 35 years).

### Cardiopulmonary resuscitation

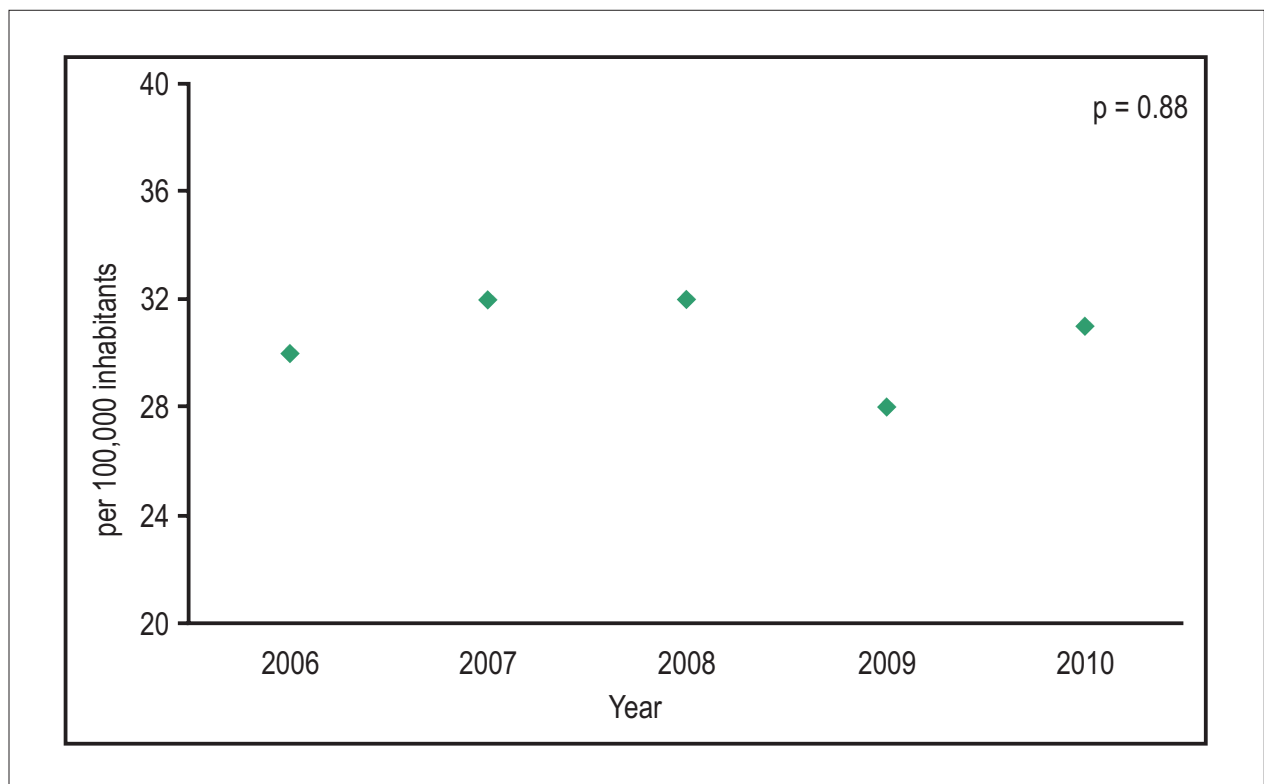
In total, 447 patients of 899 received CPR maneuvers (49.7%). In 2006, CPR was performed in 43.4% of patients, and this proportion increased over the years, reaching 54.4% of the victims submitted to CPR in 2010. An increasing tendency in CPR maneuvers is observed (Figure 4), but with marginal statistical significance ( $p = 0.05$ ).

### Additional considerations

Although SCD is included in the International Classification of Diseases 10 (ICD-10), code I46-1<sup>17</sup>, only 3.6% of the forms completed by physicians who treated the victims and 2.2% of the autopsy reports issued by the pathologists specified this diagnosis as "cause of death". Finally, in 26 cases (2.9%) microscopic examination of the heart was performed based on the diagnostic hypothesis of myocarditis; however, the diagnosis was confirmed in only one case.

### Discussion

To the best of our knowledge, this is the first study that characterizes different aspects related to SCD in Brazil.



**Figure 2** – SCD rates (per 100,000 inhabitants) in Ribeirão Preto from 2006 to 2010. The mean rate of SCD was 30/100,000 inhabitants per year, ranging from 28/100,000 inhabitants in 2009 to 32/100,000 inhabitants in 2007 and 2008.

Because there are scarce data on this topic, both in Brazil and in other Latin American countries, it is very important to know the rates of SCD in our community, the event circumstances and the characteristics of the victims, so that prevention strategies are developed and tested, of which some are specific to our population.

The rate of SCD in Ribeirão Preto was approximately 30/100,000 inhabitants. In other communities around the world, the incidence of SCD ranged from 37/100,000 inhabitants in Okinawa, Japan<sup>18</sup> and 90-100 / 100,000 in Maastricht, in the Netherlands<sup>19</sup>, with most of the studies reporting similar SCD incidence, little over 50/100,000 residents: in Oregon, United States (53/100,000 residents)<sup>20</sup> and a community located in western Ireland (51.2 / 100,000)<sup>21</sup>.

In comparison to data from other communities, the mean rate of SCD in our population was lower. There are several possible reasons for this difference. First, we analyzed only data from the SVOi, and thus, our data may be underestimated because not all deaths that occurred in Ribeirão Preto during the analyzed period were referred for autopsy. Moreover, SCD survivors were not considered. Another reason for this difference was the exclusion of cases with inconclusive data. However, it is known that the epidemiology of SCD is strongly associated to the incidence of CAD and, in Brazil, CAD mortality is estimated at 48 / 100,000 inhabitants<sup>22</sup>, whereas in the United States, it is approximately three times higher (135/100,000)<sup>23</sup>. These factors may be related to the lower economic development

of our country; however, as there is no reliable data available, both related to our population and to other developing countries, one cannot establish adequate comparisons.

In our study, most of the victims were males, Caucasians, aged 60 to 80 years. According to recent data, SCD occurs most often between the sixth and seventh decade of life<sup>7</sup>, in accordance with our findings. Regarding the distribution of SCD by gender, there was a change in the pattern over the years, with an increase in the proportion of events in women<sup>3</sup>. Previous studies showed a women / men ratio of 25:75<sup>4</sup>; however, in more recent studies, the women/men ratio increased to 40:60<sup>7</sup>, probably due to the increase in CAD prevalence and mortality among women over the years<sup>24</sup>. We found 67% of events in men, similar to what is described in the literature. Finally, most SCD victims were Caucasians (75%). However, it is important to note that we have a heterogeneous racial distribution in different regions of Brazil and thus, this finding should not be extrapolated or considered representative of the entire country.

Acute coronary syndrome was responsible for most cases of SCD (64%), and cardiomyopathy was the second most common cause in our series (32%), including myocardial diseases of ischemic and nonischemic etiology. Studies have shown that up to 80% of cases of SCD are associated with CAD. Approximately 10-15% of cases occur in patients with myocardial diseases such as hypertrophic cardiomyopathy, idiopathic dilated cardiomyopathy, right ventricular arrhythmogenic dysplasia or infiltrative myocardial diseases<sup>3,4</sup>.

**Table 1 – Demographic characteristics of victims of SCD in Ribeirão Preto between 2006-2010**

| Characteristics   | N.º | %    |
|-------------------|-----|------|
| Gender            |     |      |
| Male              | 599 | 67   |
| Female            | 300 | 33   |
| <b>Age, years</b> |     |      |
| 10-19             | 3   | 0.3  |
| 20-29             | 7   | 0.7  |
| 30-39             | 33  | 3.5  |
| 40-49             | 114 | 12.5 |
| 50-59             | 190 | 21   |
| 60-69             | 241 | 27   |
| 70-79             | 231 | 26   |
| 80                | 80  | 9    |
| <b>Ethnicity</b>  |     |      |
| Caucasian         | 675 | 75   |
| Black             | 100 | 11   |
| Mixed-race        | 119 | 13   |
| Asians            | 5   | 1    |

SCD: sudden cardiac death.

In our study it was not possible to separate SCD victims due to ischemic or nonischemic myocardial diseases, due to the difficulty in differentiating some cases according to the information provided in the analyzed reports. As an example of this limitation, some SCD victims had CAD and Chagas disease, and both diseases can induce lethal arrhythmias, making it impossible to define what the pathology responsible for the event was. This may explain the lower rates of CAD as cause of SCD and the higher number of events per myocardial diseases.

Regarding Chagas disease, 49 SCD victims (5.5%) had this diagnosis in their autopsy reports. Although the WHO certified in 2006 that the vector-borne transmission of Chagas disease was eliminated in our country, Brazil is considered as having high prevalence of human infection (1% of our population, 1.9 million infected individuals in 2005)<sup>25</sup>, with chagasic cardiomyopathy still having a very important role in cardiovascular mortality in our country, especially in cases of sudden death<sup>10</sup>.

The cause of death could not be identified in 24 cases (2.2%). The victims had a structurally normal heart and some of these cases could be related to genetic diseases such as channelopathies, undiagnosed accessory pathways or coronary vasospasm<sup>26</sup>.

The presence of structural heart disease, such as previous myocardial infarction or left ventricular dysfunction is an important risk factor for SCD<sup>3</sup>. In our study, more than 20% of the victims had some type of heart disease reported by

**Table 2 – Distribution of SCD causes among SCD victims in Ribeirão Preto: 2006-2010**

| Cause of death          | N.º | %    |
|-------------------------|-----|------|
| Acute coronary syndrome | 576 | 64.1 |
| Cardiomyopathies*       | 289 | 32.1 |
| Myocardial bridge       | 8   | 0.9  |
| Myocarditis             | 1   | 0.1  |
| Coronary artery anomaly | 1   | 0.1  |
| Undetermined            | 24  | 2.7  |

\* Ischemic and nonischemic cardiomyopathies; SCD: sudden cardiac death

**Table 3 – Risk factors for SCD among victims of SCD in Ribeirão Preto: 2006-2010**

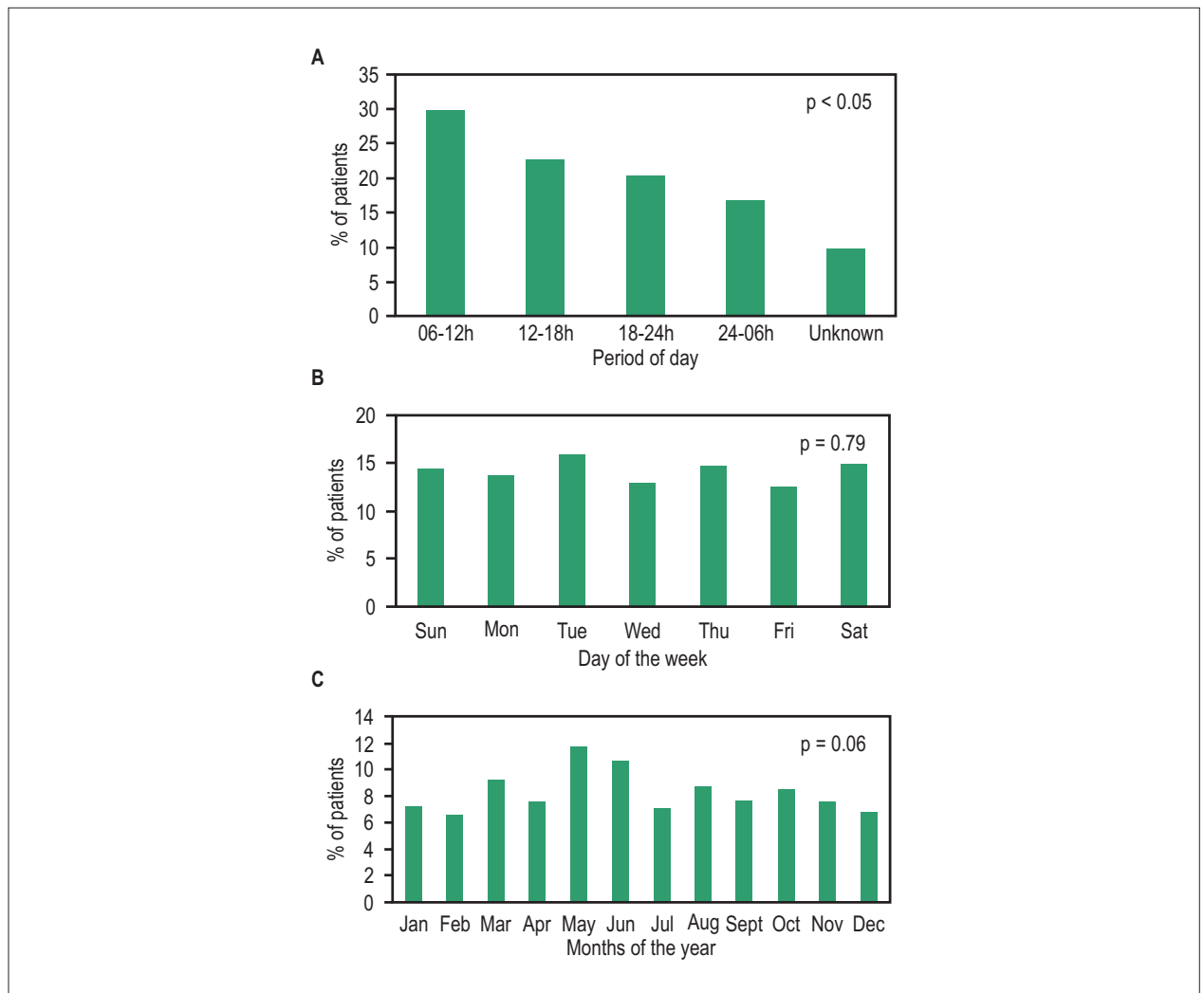
| Risk factors for SCD     | %    | N.º |
|--------------------------|------|-----|
| SAH                      | 57.3 | 515 |
| Structural heart disease | 21.1 | 190 |
| Diabetes                 | 15.3 | 138 |
| Smoking                  | 8.8  | 79  |
| Obesity                  | 8.6  | 77  |
| Dyslipidemia             | 1.2  | 11  |
| Alcohol abuse            | 6.2  | 56  |
| Chagas disease           | 5.5  | 49  |

SAH: systemic arterial hypertension; SCD: sudden cardiac death

relatives. Furthermore, we observed that systemic arterial hypertension was the most prevalent risk factor among SCD victims (57.3%) and hypertensive patients, especially those with left ventricular hypertrophy, had a higher risk of SCD than the overall population<sup>27</sup>.

Other risk factors such as diabetes, smoking, obesity and dyslipidemia, were also found, but in smaller proportions, suggesting that these data are underestimated, for some reasons described as follows: first, retrospective data were collected and there were no specific questionnaires in the analyzed forms. The victims' medical records were not evaluated. Finally, some diseases, such as diabetes or dyslipidemia, may be underdiagnosed in our population, as diagnosis depends on laboratory tests that are often not routinely performed. Alcohol abuse was detected in 6.2% of the cases, similar to the study carried out in a community located in western Ireland<sup>21</sup>.

It is known that the temporal distribution of SCD has an established pattern, with most events occurring in the morning, on Mondays during winter months<sup>11</sup>. In our series, there were a higher number of events in the morning, with no difference regarding the days of the week or months of the year, with the latter being explained by the absence of well-defined seasons in our region. The higher number of events in the morning was previously attributed to increased



**Figure 3** – Histogram of the temporal variation of SCD. A) Histogram of the circadian variation of SCD. The morning period is the period with the most SCD events ( $p < 0.05$  in comparison to other periods). B) Histogram of the weekly variation of SCD. There was no difference between days of the week ( $p = 0.79$ ). C) Histogram of monthly variation of SCD. SCD events tended to occur more frequently in the months of May and June, but without statistical significance ( $p = 0.06$ ).

sympathetic discharge that occurs at waking up, causing the higher number of CVAs, acute coronary syndromes and sudden deaths<sup>28</sup>.

Regarding the place of death, more than half of the events occurred at home (53.3%), which is known to be associated with lower success rates after attempted CPR<sup>29</sup>. It can be observed that 49.7% of victims received CPR maneuvers, a result similar to that found in Maastricht, Netherlands, where 51% of SCD victims received CPR maneuvers<sup>19</sup>. Despite not reaching statistical significance, the number of SCD victims that received CPR increased over the years, which may reflect improvements in the health system, with a larger number of ambulances and emergency rooms in public and private hospitals.

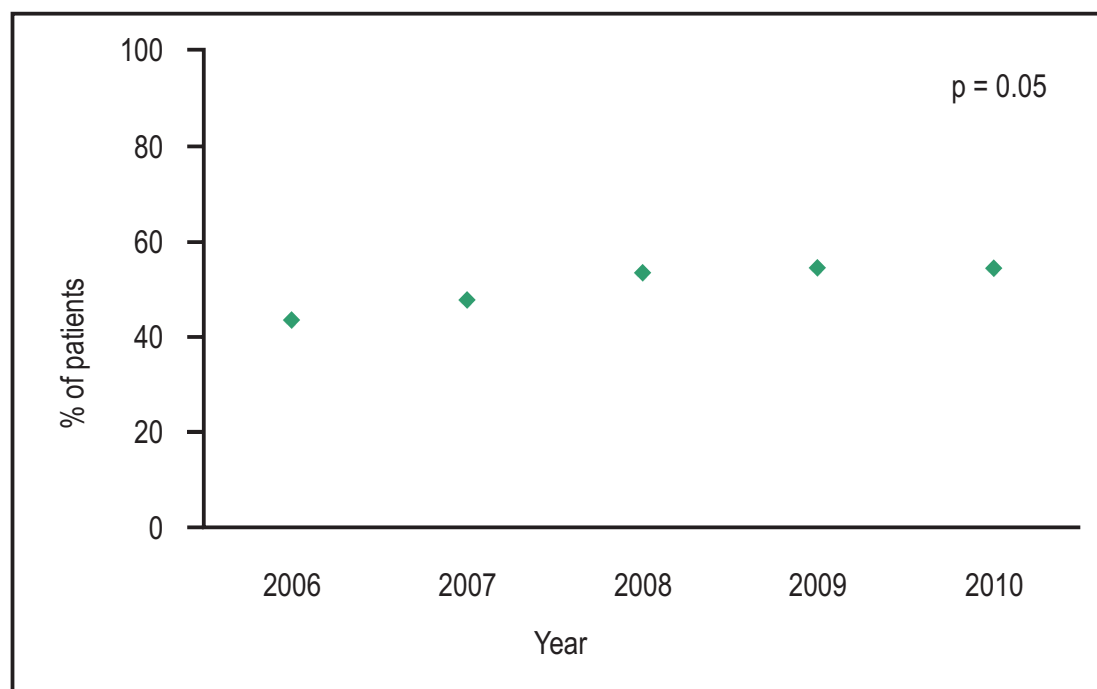
#### Study limitations

As mentioned before, SCD rates may be underestimated. Because this is a retrospective study, some specific data are

lacking regarding events such as complete profile of risk factors for SCD victims, better description of the clinical manifestations presented by victims before death in witnessed cases and CPR procedures performed or autopsy protocols.

Although the institution of reference for performing autopsies of our region is the SVOi, not all cases of SCD are referred to this service, as, according to Brazilian laws, if the death resulted from non-traumatic causes and if there is a physician aware of the case that is willing to sign the death certificate, referral of the victim to the autopsy examination is not mandatory. Finally, there are not specific forms for the investigation of SCD in SVOi.

Although the study has several limitations, we believe our findings provide very important information about the characteristics of SCD in Brazil, also showing flaws in our medical documentation, which should be readily improved, e.g., by establishing specific autopsy protocols<sup>30</sup>.



**Figure 4** – Proportion of SCD victims submitted to CPR maneuvers in Ribeirão Preto (2006-2010). Altogether, 447 of the 899 victims received CPR (49.7%). There was a clear tendency to an increase in the number of patients that received CPR between 2006 and 2010 ( $p = 0.05$ ).

## Conclusion

Sudden cardiac death accounted for about 20% of all non-traumatic deaths in this large Brazilian community, based on autopsy reports. Most SCD cases occurred due to ACS in men between the sixth and seventh decade of life. Most events occurred in the morning, at home and CPR maneuvers were performed on half of the victims. This study is particularly significant because it is the first to comprehensively evaluate the scenario of SCD in Brazil and to contribute to the development of preventive strategies in our social context.

## Author contributions

Conception and design of the research: Braggion-Santos MF, Volpe GJ, Pazin-Filho A, Maciel BC, Marin-Neto JA, Schmidt A; Acquisition of data: Braggion-Santos MF; Analysis and interpretation of the data: Braggion-Santos MF, Volpe GJ,

Schmidt A; Statistical analysis: Braggion-Santos MF, Schmidt A; Writing of the manuscript: Braggion-Santos MF, Volpe GJ; Critical revision of the manuscript for intellectual content: Pazin-Filho A, Maciel BC, Marin-Neto JA, Schmidt A.

## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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## Study Association

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