Original Article

Risk Factors Associated With Acute Myocardial Infarction in the São Paulo Metropolitan Region. A Developed Region in a Developing Country

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Objective

To identify the risk factors associated with acute myocardial infarction (AMI) and their respective powers of association in the São Paulo metropolitan region.

Methods

The cases comprised patients diagnosed with first AMI with an ST segment elevation. The controls were individuals with no known cardiovascular disease. The study comprised 271 cases and 282 controls from 12 hospitals. Risk factors were as follows: ethnic group; educational level; marital status; family income; family history of coronary artery disease; antecedents of arterial hypertension and of diabetes mellitus; hormonal replacement in women; smoking; physical activity; alcohol consumption; total cholesterol, LDL-cholesterol, HDL-cholesterol, triglyceride, and glucose levels; body mass index; and waist-hip ratio (WHR).

Results

The following risk factors showed and independent association with AMI: smoking [odds ratio (OR)=5.86; 95% confidence interval (CI) 3.25-10.57; P < 0.00001); waist-hip ratio (first vs. third tertile) (OR=4.27; 95% CI 2.28-8.00; P<0.00001); antecedents of arterial hypertension (OR=3.26; 95% CI 1.95-5.46; P< 0.00001); waist-hip ratio (first vs second tertile) (OR=3.07; 95% CI 1.66-5.66; P=0.0003); LDL-cholesterol level (OR=2.75; 95% CI 1.45-5.19; P=0.0018); antecedents of diabetes mellitus (OR= 2.51; 95% CI 1.45-5.19; P=0.023); family history of coronary artery disease (OR=2.33; 95% CI 1.44-3.75; P=0.0005); and HDL-cholesterol level (OR=0.53; 95% CI 0.32-0.87; P=0.011).

Conclusion

Smoking, waist-hip ratio, antecedents of arterial hypertension and of diabetes mellitus, family history of coronary artery disease, and LDL-cholesterol and HDL-cholesterol levels showed to be independently associated with AMI within the São Paulo metropolitan region.

Key words

acute myocardial infarction, risk factors, case-control study

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According to projections for the year 2020, cardiovascular disease (CVD) will remain as the major cause of mortality and disability. Currently, developing regions more greatly contribute to the CVD burden than developed ones [1]. Such rise in CVD within developing regions may result from the following 3 factors: a decrease in mortality due to parasite infections, with an increase in life expectancy; lifestyle and socioeconomic changes associated with urbanization, resulting in higher levels of CVD risk factors; and special susceptibility of certain populations (due to specific genes), leading to a greater impact on clinical events when compared with populations from developed western regions [1].

The age-specific coefficients for mortality due to acute myocardial infarction (AMI) and cerebrovascular disease (CbVD) within the metropolitan regions in Brazil have risk profiles that differ from those of other countries. About 50% of male deaths due to coronary artery disease (CAD) occur in the age group below 65 years, whilst in other countries (United States, Cuba and England) this proportion is found to be around 25% [1]. In the São Paulo municipality, despite the decline in mortality due to CAD and CbVD from the mid-70s onwards, CVDs related to atherosclerosis still represent the major group of causes of death within the state, as in developed countries [2,3].

The knowledge about risk factors for CVD or CAD originates from studies carried out in developed countries in North America and Western Europe. Thus, it is neither entirely safe, nor perfectly acceptable, to extrapolate the results obtained primarily in those countries to the Brazilian population. Not only can the prevalence of risk factors differ significantly, but also the impact of each factor on a certain population can be drastically different. In addition, the protective factors for CAD may be different, thereby generating impacts that are not clinically similar.

Thus, one may conclude that any health policy considering the individual, institutional or governmental point of view must be based, preferably, on data obtained from the local population. Consequently, a case-control study assessing the risk factors associated with AMI in our region is a fundamental stage for analyzing the real impact of the risk factors on our population. The aim of this present study is the identification of the power of association between cardiovascular risk factors and AMI in the São Paulo metropolitan region.

Methods

A multicenter (12 hospitals in the São Paulo metropolitan region), hospital-based, case-control study was carried out with

prospective data collection using an anthropometric measure form and with blood collection for lipid profile and glucose level assessment. The study's population comprised individuals diagnosed with AMI (first manifestation) and an ST segment elevation (cases) and individuals with no diagnosis of cardiovascular disease (controls).

The inclusion criteria for the cases were as follows: patients admitted into Emergency or Coronary Units diagnosed with first AMI and an ST segment elevation, presenting with chest pain initiated ≤ 24 hours, electrocardiographic (ECG) alterations compatible with AMI, an ST segment elevation, an increase in the levels of the MB fraction of creatine kinase (CKMB) and/or total creatine kinase (CK) of at least twice the normal reference value of the local laboratory. Patients with the following conditions were excluded: valvular heart disease; chronic consumptive disease; and clinical conditions that, according to the investigator, could prevent the patient's inclusion or jeopardize the study's analysis.

The inclusion criteria for controls were as follows: absence of known diagnosis of CVD; ECG within the normal limits (except for isolated atrial ectopy); patients with SAH with no ECG alteration; and diabetic patients with no suspected association with CVD. In general hospitals, the selection of controls included patients admitted into the hospital, originating from the ophthalmology, otorhinolaryngology, orthopedics, or plastic surgery clinics. In cardiology-specialized hospitals, the selection of controls included the following: individuals who sought the hospital for blood donation or for performance of routine check-up exams; the institution's employees; and family members of hospitalized patients. The exclusion criteria were as follows: previous diagnosis of CAD or any other CVD, including cerebral and peripheral vascular disease; liver and renal diseases; history of chest pain suggestive of coronary ischemia; neoplasias, or any other significant comorbidity; pregnancy; recent (< 30 days) change in eating habits; and clinical conditions that, according to the investigator, could prevent the patient's inclusion or jeopardize the study's analysis.

The following data were obtained: a 10-mL blood sample was collected and analyzed at the hospitals participating in the study. For the cases, the blood sample for lipid profile was collected within the first 24 hours of AMI symptom onset, and that for glucose measurement was collected between 5 and 8 days of hospital admission. For the controls, the blood sample for lipid and glucose measurement was collected within the first 30 days of inclusion in the study. The measurements of total cholesterol, HDL-cholesterol, triglyceride, and glucose levels were performed through the direct method, while the LDL-cholesterol level was calculated through the indirect method by using the Friedewald equation (LDL-cholesterol = total cholesterol – HDL-cholesterol – triglycerides/5).

The dependent variable was AMI, and the independent variables were the following cardiovascular risk factors of interest for this case-control study: ethnic group; educational level; marital status; family income; family history of coronary artery disease; antecedents of arterial hypertension and of diabetes mellitus; smoking; physical activity; alcohol consumption; total cholesterol, LDL-cholesterol, HDL-cholesterol, triglyceride, and glucose levels; body mass index; and waist-hip ratio.

The variables were compared after adjustment for age and sex. Univariate analysis was used as a strategy for evaluating the relations between disease and exposure to the variables studied. For the continuous variables, the means, standard deviations, medians, and the maximum and minimum intervals were calculated, and the cases and controls were compared by using parametric and nonparametric tests, as required. For the logistic model, all variables that had statistical significance ($p < 0.05$) in the univariate analysis were considered. The interactions of the variables selected as described were examined in a correlation matrix, and all interactions with a correlation coefficient > 0.5 were incorporated to the model. The odds ratio and 95% confidence interval were calculated for each variable. All variables were categorized for the construction of a multivariate model, and the category of reference for the risk estimate was previously established. The forward stepwise was the method used for logistic regression; the significance level of 0.05 was established for inclusion of the variables in the study, and 0.10 was the significance level established for their exclusion. The variables were analyzed by using unconditional logistic regression [4,5]. Aiming at detecting any differences in the results of multivariate analysis, due to the potential heterogeneity of the cases and controls included in the 12 hospitals participating in the study, an additional analysis was performed. The sample size was calculated based on the prevalence of cardiovascular risk factors in the Brazilian population by using the odds ratio of 2.0, the proportion of one case to one control, 2-tailed test, statistical power of 90%, and an alpha value of 0.05.

This study was approved by the committees on ethics and research at the 12 hospitals participating in the project.

Results

This study comprised 553 individuals (271 cases and 282 controls). The total number of individuals represented in the multivariate analysis was 494 due to lack of data regarding some independent variables necessary to this analysis. The continuous variables and their respective means and standard deviations are shown in table I.

According to the univariate analysis, the following variables were associated with an increased or reduced risk of developing AMI: marital status; retirement; family history of coronary artery disease; antecedents of SAH and DM; smoking; physical activity; LDL-cholesterol, HDL-cholesterol, and glucose levels; BMI; and

Table I - Continuous independent variables with their means and standard deviations

Independent variable	Case		Control	
	Mean	Standard deviation	Mean	Standard deviation
Age	58.00	13.00	47.00	12.00
Total cholesterol	195.74	47.66	195.46	51.97
HDL-cholesterol	36.20	10.38	42.36	14.05
LDL-cholesterol	130.79	43.24	123.52	44.34
Triglycerides	146.73	93.18	150.84	93.99
Glucose	130.58	66.98	104.31	32.89
BMI	26.78	4.12	25.64	4.61
WHR	0.98	0.10	0.91	0.11

BMI - body mass index; WHR - waist-hip ratio.

WHR. Through multivariate analysis, the following variables showed a positive independent association with AMI: smoking; antecedent of SAH; antecedent of DM; family history of coronary artery disease; WHR; and LDL-cholesterol level. Smoking had the greatest independent power of association for the development of AMI (OR = 5.86; 95% CI = 3.25-10.57), whilst family history of coronary artery disease had the lowest (OR = 2.33; 95% CI = 1.44-3.75). The HDL-cholesterol level showed a negative independent association with AMI. Table II shows those variables with their respective odds ratios, 95% confidence intervals, and P values.

Figure 1 depicts the graphic representation of those variables with their respective powers of association.

After controlling the variable "participant hospital" in the multivariate model, the results previously obtained were maintained. Therefore, the numeric difference between the cases and controls, causing qualitative differences between them, was ruled out due to the homogeneity of the results.

Discussion

These data allowed us to determine the risk factors independently associated with AMI in a sample of the São Paulo metropolitan population. The unconditional logistic regression analysis showed that the risk factors smoking, WHR, antecedent of SAH, antecedent of DM, family history of CAD, and LDL-cholesterol level were independently associated with an elevated risk of AMI. Smoking was the strongest independent risk factor identified.

This study depicts smoking as the most important independent risk factor for AMI. The importance of smoking has been demonstrated over the years through a series of intra- and interpopulational proofs. An ecological study, assessing smoking and mortality due to CAD and comparing the capitals of some Brazilian metropolitan regions in 1988, suggested the existence of a clear association between smoking and mortality due to CAD [6]. Recently, a hospital-based, case-control study, assessing the risk factors for AMI in Indians, has reported that the most important predictive factor of AMI is smoking (OR = 3.6) [7]. Comparatively, the study conducted in the São Paulo metropolitan region has reported a greater potency for smoking (≥ 5 cigarettes/day) than that in the Indian study (OR = 5.86 vs. 6.7). Another hospital-based, case-control study conducted in Argentina has also reported similar results [8]. In the study by Moraes and Souza [9], a significant independent association of smoking with the increased risk for CAD was observed in men [ex-smokers (OR = 2.24), and smokers (OR = 1.84)]; in women, a significant independent association with the increased risk of CAD was observed only in ex-smokers (OR = 2.68), confirming our results. However, the power of association was smaller than that in our study, and the association was more intense in ex-smokers than that in current smokers. One possible explanation could be the fact that, in the present study, AMI was assessed, an event in which coronary thrombosis has a predominant effect on the genesis of the acute occurrence, while in the study by Moraes and Souza [9], CAD was analyzed, not only AMI. One may suggest that smoking has a more potent power of association with the atherothrombotic event of AMI than coronary atherosclerosis in isolation. In this study, the increased risk resulting from smoking was 5.86 as compared with 1.80 in the FHS. As AMI is the major cause of death in the State of São Paulo, data on smoking and mortality complement the understanding of the link between smoking, AMI, and death due to CAD. The results of the Multiple Risk Factor Intervention Trial (MRFIT) [10] have also confirmed the gradual relation between the number of cigarettes and death due to CAD.

In this study, the antecedent of DM showed to be a risk factor independently associated with AMI. This finding is consistent with that obtained in population-based cohort studies, showing that type 2 DM represents an approximately 2-fold greater risk for CAD in men and 3-fold greater risk for CAD in women. In the FHS [11], the presence of DM doubled the risk of CVD adjusted for age in men and tripled the risk in women. Myocardial infarction, angina, and sudden death were twice more frequent in diabetic individuals as compared with those in nondiabetic individuals. After adjusting for all the other risk factors, DM continues to be the major independent cardiovascular risk factor. In the MRFIT study [10], the risk of cardiovascular death in 12 years of follow-up was approximately 3-fold greater in men as compared with that in nondiabetic controls. In the study by Moraes and Souza [9], one of the interpretations for

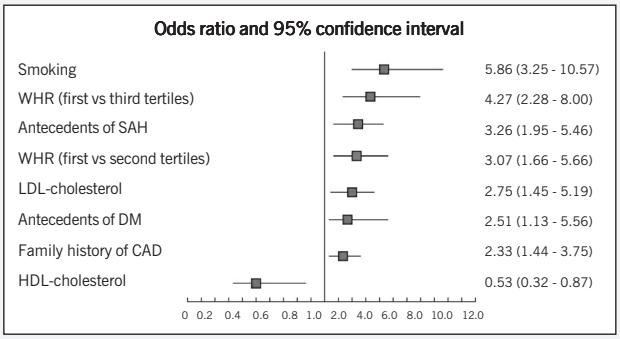

Fig. 1 - Variables independently associated with acute myocardial infarction. WHR – waist-hip ratio; SAH - systemic arterial hypertension; LDL – low-density lipoprotein; DM - diabetes mellitus; CAD – coronary artery disease; HDL – high-density lipoprotein; CI – confidence interval.

Table II - Variables independently associated with AMI*

Independent variable	OR	95% CI	p
Smoking (≥ 5 cigarettes/day vs. never)	5.86	3.20-10.57	< 0.00001
Waist-hip ratio (first vs third tertile)	4.27	2.28-8.00	< 0.00001
Antecedents of arterial hypertension (present vs. absent)	3.26	1.95-5.46	< 0.00001
Waist-hip ratio (first vs second tertile)	3.07	1.66-5.66	0.0003
LDL-cholesterol (< 100 mg/dL vs ≥ 100 mg/dL)	2.75	1.45-5.19	0.0018
Antecedents of diabetes (present vs absent)	2.51	1.13-5.56	0.0230
Family history of coronary artery disease (present vs absent)	2.33	1.44-3.75	0.0005
HDL-cholesterol (≥ 40 mg/dL vs < 40 mg/dL)	0.53	0.32-0.87	0.011

OR - Odds ratio; CI - 95% confidence interval; * Multivariate analysis through unconditional logistic regression.

the disappearance of DM as an independent predictive factor for CAD may be the presence of more potent risk factors than DM in the occurrence of the coronary events evaluated, such as CAD, in the multivariate model; in addition, the diabetic individuals may have been adequately treated, reducing the risk for CVD.

Data of the current study strongly suggest that the presence of an antecedent of SAH is a potent risk factor independently associated with AMI. This correlation has been demonstrated in several epidemiological studies, and the reduction in the risk for CVD with SAH control has been reported in several clinical studies on primary prevention [12-14]. In their study, Moraes and Souza [9] showed that SAH is an independent predictive factor for the occurrence of CAD (OR = 3.67 in women, and OR = 4.38 in men). According to the Seven Countries Study [12], each 10 mmHg increase in the median systolic blood pressure of the population corresponded to a duplication in the risk of coronary death. The MRFIT study [13] has also shown a direct correlation between the elevation in the systolic and diastolic blood pressure levels and the subsequent incidence of mortality due to CAD during an 11.6-year follow-up in men initially without CAD. Finally, the results of a meta-analysis of 9 prospective observational studies, including 418,343 individuals initially free from CAD, showed that the increase in the risk of mortality due to CAD initiated at diastolic blood pressure levels between 73 mmHg and 78 mmHg, and that increase was greater than 5 times for levels between 73 mmHg and 105 mmHg [14].

The data of the study of the São Paulo metropolitan region have been confirmed by those of other case-control studies showing the importance of the family history of coronary artery disease for the risk of AMI. A case-control study carried out in Argentina has assessed the relation between family history of AMI and the risk for AMI [8]. That study assessed 1,070 individuals and showed that the fact of having a first-degree relative with a history of AMI increases the risk for AMI (OR = 2.18). When the history involved only one family member with AMI, the risk was smaller (OR = 2.04) as compared with that when 2 or more relatives had AMI (OR = 3.18). It is worth noting that the association was stronger for younger individuals (OR = 4.42 for individuals aged < 55 years) as compared with older ones (OR = 3.0 for individuals ≥ 55 years) with 2 or more relatives with AMI. Moraes and Souza [9] have demonstrated the independent association of family antecedents of heart disease with an increased risk for CAD (OR = 2.71 in women, and OR = 3.29 in men). In Brazil, the FRICAS (Fatores de Risco para Infarto Agudo do Miocárdio no Brasil – risk factors for acute myocardial infarction in Brazil) study, comprising 591 individuals in 20 cities, 13 of which in the State of São Paulo, has associated the family history of coronary artery disease with the risk for AMI through univariate analysis [15]. A large proportion of CVD may be attributed to inherited or familial predisposition.

This case-control study analyzed BMI and WHR for assessing obesity. The BMI was not independently associated with the occurrence of AMI. The Nurses' Health Study has shown that a BMI between 27 and 29 was associated with a 1.6 relative risk of death, a BMI between 29 and 32 was associated with a 2.1 relative risk, and a BMI ≥ 32 was associated with a 2.2 relative risk as compared with the group with a BMI below 19 [16]. The NHANES study has reported a 1.5 relative risk for CVD late in life for women with a BMI above 29, when compared with the reference population (BMI < 21) [17]. In addition, obesity has been associated with myocardial hypertrophy, independently of SAH, and with higher rates of heart failure in the FHS [18]. Furthermore, observational studies have suggested an association between BMI and CVD or CAD, but not with AMI in isolation.

The WHR was an extremely strong factor independently associated with the development of AMI. This measure has been considered to bear great sensitivity, because it has allowed a statistically significant association to be reported, even when comparing the second and third tertiles. According to data obtained in this study, the WHR is a more sensitive measure than BMI for identifying the risk independently associated with AMI. Among the larger studies assessing the relation between abdominal obesity and CAD, the Nurses' Health Study stands out. That study has assessed the WHR and has reported that a WHR ≥ 0.88 was associated with a 3.25 relative risk for CAD, as compared with that of a WHR < 0.72 [19]. Abdominal obesity has also been identified as a predictive risk factor for stroke in the Physician's Health Study [20]. A WHR above 0.9 in men or 0.8 in women indicates abdominal obesity [21,22].

In this study, total cholesterol level has not been identified as an independent predictor of the occurrence of AMI. The mean total cholesterol levels in the cases were similar to those in the controls (195.74 vs. 195.46 mg/dL). The descriptive analysis involving the median of the total cholesterol levels has shown more elevated values in the cases as compared with those in the controls (193.0 vs. 199.0 mg/dL). As already previously specified, the methodologically plausible explanation may be the possibility of insufficient statistical power. The direction of the difference (greater cholesterol levels in the cases than those in the controls) and the biological plausibility allow us to interpret these findings as promising. We could also suggest that the total cholesterol levels in the controls were reasonably elevated, nearing those of the cases, and, therefore, hindering the detection of the difference. Although this possibility cannot be ruled out, 2 scenarios can be considered to better explain the current data. On the one hand, if selection bias occurred in the recruitment of controls, allowing the unconscious inclusion of controls with total cholesterol levels above the mean of the general population, attenuation of that difference would have been observed. On the other hand, when comparing the total cholesterol levels of controls with those obtained in a cross-sectional study involving 8,045 individuals in 9 capitals, the results showed that the levels in that study were greater than those obtained in this case-control study, indicating that a selection bias may not have been sufficient to invalidate the results obtained (198.40 mg/dL vs. 195.46 mg/dL) [23]. Corroborating the results of this study, the FHS [24] has shown that, although the significantly elevated cholesterol levels represent a risk factor for CAD, approximately 80% of the individuals experiencing myocardial infarction had total cholesterol levels in the same range of those who did not develop myocardial infarction.

In this study, the greater HDL-cholesterol levels (> 40 mg/dL according to the recommendations of the NCEP) were shown to be significantly associated with protection against AMI. The study conducted in the metropolitan region has confirmed, in our population, the results of the studies previously described, establishing LDL-cholesterol and HDL-cholesterol levels as risk factors independently associated with AMI.

This study has found no independent association of AMI with the marital status evaluated (single vs. nonsingle). We prefer to interpret the findings as having insufficient biological plausibility. However, further studies with a greater number of individuals could guarantee sufficient statistical power to evaluate that hypothesis. Regarding that hypothesis, it has been postulated that, the level of mental stress could vary depending on the marital status, and, therefore, it could be a potential risk factor associated with AMI. A prospective study carried out with Swedish men has reported an association between mental stress and an increased risk for subsequent coronary events [25]. In addition, in 12 Russian regions, from 1989 to 1994, the greater the mental stress caused by important events in life, such as death in the family and job loss, the greater the decline in life expectancy for men [26].

No independent association has been detected between physical activity and the occurrence of AMI. However, biological plausibility suggests that physical activity may provide a protective effect against AMI. In addition, a great potential exists for reducing the risk for CVD among those who initially had a sedentary lifestyle and became moderately active [27]; however, those who maintained their sedentary lifestyle had a greater risk for CVD and all-cause mortality [28]. Multiple prospective studies published during the past 35 years have shown a strong, consistent and gradual correlation between recreational and occupational physical activity reported by individuals and cardiovascular events, all-cause mortality, and cardiovascular mortality [29-33].

Several studies have suggested a progressive correlation between glucose levels and the increased risk for CVD in nondiabetic and diabetic individuals. In addition, in a meta-regression analysis of all cohort studies with nondiabetic individuals, the baseline glucose levels were related to cardiovascular events and subsequent mortality [34]. In the present study, although the cases had mean serum levels greater than those of controls (130.58 mg/dL vs. 104.31 mg/dL), that difference showed no independent association with the occurrence of AMI through multivariate analysis. Again, the fact that serum levels equal to or greater than 126 mg/dL (32.8% in the cases vs. 13.2% in controls) were not considered independent predictive factors associated with AMI should be attributed lack of sufficient statistical power.

Our results showed that triglyceride levels were not independently associated with the occurrence of AMI. Unlike the behavior of other lipids, the mean triglyceride levels in the cases were lower than those in controls (146.73 mg/dL vs. 150.84 mg/dL). Selection bias may have occurred, allowing the inclusion of controls with levels similar to or higher than those of the cases. Considering that triglyceride levels are an independent risk factor for AMI according to other studies, selection bias may be a plausible alternative. Data on the association between AMI and elevated triglyceride levels are, however, controversial according to current evidence, allowing us to suggest that triglycerides may not constitute an independent risk factor for AMI in the population studied.

Caucasians were compared with other ethnic groups, denominated non-Caucasians (blacks, mulattos, Asians, and others), and no ethnic association was observed with the occurrence of AMI. Once again, insufficient statistical power to detect those differences may be postulated as a potential explanation.

Ethnic group has been described as a factor with different risk rates for cardiovascular events. The MONICA project [35] has reported the rates of events related to CAD and has shown that, according to the country (including the female and male sexes), those rates have ranged from under 50/100,000 to over 900/100,000. In the United States, the greatest negative impact of CVD has been found among African Americans, with greater mortality rates due to CAD in men than in women [36]. In the SHARE study [37] (Study of Health Assessment and Risk in Ethnic Groups), carotid atherosclerosis determined by using ultrasound was more prevalent among South Asians as compared with that in Europeans and Chinese (11%, 5%, and 2%, respectively; $P = 0.0004$).

According to our data, no significant independent association was found between educational level and family income and the occurrence of AMI. Despite the biological plausibility of those factors, the statistical power may not have been sufficient to detect that difference in this study. On the other hand, in the Indian case-control study, whose statistical power was similar to ours, those differences could be detected. Similar to other epidemic diseases, CAD has a close relation with the social level, and its prevalence seems to be strongly related to social and cultural conditions of the population. This assumption is evidenced by the rapid decline in the CAD rates in parallel with the economic changes in the United States and Japan, as well as by the increase in those rates observed in Eastern European and Latin American countries [7].

Our study has shown that alcohol consumption (3 to 6 times per week) as compared with lack thereof (abstention) does not protect against the occurrence of AMI. The possibility of insufficient statistical power cannot be ruled out. In addition, multicolinearity may have occurred. This means that, as several factors were analyzed, those that were somehow related (alcohol and smoking, for example) could have influenced each other to the extent that the factor in question (alcohol) could not be detected.

Some observational studies have reported a J curve correlating alcohol consumption and total mortality [38]. The point of lower mortality occurred among those ingesting one or two drinks per day [39], and total mortality increased in those ingesting more than 2 drinks per day. Although the mortality rates for CAD gradually decline with the increase in alcohol consumption, mortality due to other diseases increases according to the number of drinks. Excessive alcohol consumption may have several adverse effects on health, including SAH and stroke [40,41]. Recent data have shown that protection against CAD seems not to differ according to the type of alcoholic beverage ingested [42]. Adding plausibility to this hypothesis, a population-based, case-control study carried out in the Czech Republic has reported a lower risk for CAD among individuals on a daily or almost daily alcohol consumption (OR = 0.38) and those ingesting from 4 to 8 liters of beer per week (OR = 0.34).

The following limitations may be considered in this study: selection bias regarding the inclusion of controls, statistical power insufficient to detect significant associations with certain factors, and the presence of confounding factors.

The definition of cases involved well-established criteria for the diagnosis of AMI. Therefore, the likelihood of selection bias for the cases is remote. Although the definition of the controls was adequate, the inclusion of individuals with undiagnosed cardiovascular disease may have occurred, evidencing selection bias for the controls. If that bias, in addition to being present, had a moderate or important magnitude, the detection of the associations

between the risk factors and AMI may have been attenuated. Some centers included more cases, others more controls, and others included even more cases and controls than the mean of the hospitals. To determine whether the controls included at specialized hospitals were similar or had no substantial differences as compared with the controls included at the 10 general hospitals, the demographic characteristics of the controls were compared. When comparing the variables of the controls at 2 specialized hospitals with those at 10 general hospitals, no statistically significant difference was observed, except for family income and physical activity (more frequent at specialized hospitals), and total cholesterol level < 200 mg/dL and LDL-cholesterol level < 100 mg/dL (more frequent at general hospitals).

As already emphasized, small differences may have passed undetected because of the sample size and the statistical power of this study. That is why the sample size and the statistical power of this study were previously calculated, and the minimum odds ratio with interest to be detected was established as 2.0. Odds ratios below 2.0, due to their questionable relevance for the clinical practice, were ruled out.

The preventive objectives in patients with CAD, as well as in high-risk individuals, involve the same principles as follows: a reduction in the risk of clinically relevant ischemic events, with a consequent decrease in mortality and early disability, and an extension in survival. As CAD is multifactorial in its origin, the absolute risk of the individual (risk of developing fatal or nonfatal CAD during the next 10 years) should be estimated through the presence of risk factors. Individuals with greater multifactorial risk should be identified and selected for interventions in their lifestyle, and, when appropriate, for pharmacological interventions. Actions in preventive cardiology should be based on the prevalence and mortality rate of the disease in question. Within that context, AMI is an extremely prevalent condition, the major cause of death in the São Paulo population. Consequently, the decrease in the CAD burden, particularly of AMI, should be initiated with a reduction in the risk factors that are assuredly and independently associated with its occurrence. This study was able to detect these factors and their respective powers of association, fundamental to the establishment of preventive health policies in the São Paulo metropolitan region, regarding both population strategies and the daily clinical practice. Based on the data obtained, preventive cardiovascular health-promoting actions can be hierarchized.

The results of this case-control study allow us to guide policies in preventive cardiology, aiming at reducing the incidence of AMI and its consequences regarding morbidity and mortality, through the effective control of the risk factors identified.

Acknowledgement

We thank the individuals who took part in this study and the major and associated investigators of the hospitals (Annex A) for their inestimable contribution.

In addition to the major authors, the following investigators also took part in this study:

Annex A – List of the hospitals, major and associated investigators participating in the study, and respective number of cases and controls included

Hospital	City	Major investigator	Associated investigator	Cases	Controls
Hospital do Coração da Associação do Sanatório Sírio	São Paulo	J. Farran	I. Fernandes	87	51
Instituto Dante Pazzanese de Cardiologia	São Paulo	R. Ramos	A. Timerman	26	65
Hospital São Luiz	São Paulo	R. Dreicon	L. Ferreira	18	34
Hospital São Paulo	São Paulo	A. Carvalho	F. Fonseca	20	24
Hospital do Servidor Público Municipal	São Paulo	E. Sales Filho	J. Almeida	16	25
Santa Casa de São Paulo (emergency unit)	São Paulo	V. Golin	A. Pereira	11	11
Santa Casa de São Paulo (coronary unit)	São Paulo	R. Franken	Y. Francisco	14	2
Hospital Santa Marcelina	São Paulo	C. Del Carlo	C. Blecher	20	19
Hospital Santa Paula	São Paulo	O. Gebara	G. Cividanes	14	5
Hospital Universitário Wladimir Arruda	Santo Amaro	C. Gun	E. Araújo Jr.	11	17
Hospital Municipal de Santo André	Santo André	E. Dancini	E. Daminello	29	9
Hospital e Maternidade Brasil	Santo André	F. Borelli	G. Amarante	5	20
Total				271	282

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