

Cardiovascular Risk Factors in Critical Coronary Lesions: Myth or Reality?

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Abstract

Background: Cardiovascular disease (CVD) is responsible for the greatest morbidity and mortality rates in the world, and acute myocardial infarction (AMI) and cerebral ischemic attack are its main manifestations. Risk factors that contribute to the development of the disease are widely known, but there remains the question of whether a higher number of risk factors explains more serious illnesses, or if the isolated impact of a risk factor could also be determinant in patients.

Objective: The study correlates the risk factors for coronary artery disease (CAD) and patients undergoing angioplasty and / or coronary artery bypass graft (CABG) due to critical injuries, clarifying the role of classic risk factors for cardiovascular disease (CVD) and analyzing if factors such as gender, marital status and education level are related to a greater presence of these risk factors.

Methods: We used questionnaires of risk factors for CVD with patients at the Hemodynamics Department and Cardiac Surgery Charity Hospital Portuguese São Paulo, in São Paulo, Brazil, followed by statistical analysis.

Results: In our sample most patients showed two risk factors for CVD, and hypertension, dyslipidemia and diabetes mellitus were the most prevalent ones in this population.

Conclusion: The study confirmed that the role of classic risk factors in cardiovascular disease is not a myth but a reality, especially when patients with fewer risk factors presented obstructive situations similarly to patients with more risk factors. (Int J Cardiovasc Sci. 2016;29(5):378-384)

Keywords: Cardiovascular Diseases; Myocardial Infarction / surgery; Risk Factors; Myocardial Revascularization.

Introduction

CAD is the imbalance between the supply and demand of oxygen in the myocardial tissue when the dilating capacity of the arteriolar bed to increase myocardial perfusion in stress situations is insufficient, which happens mainly through the process of atherosclerosis.¹

Vascular deposits mostly affect medium-sized and large caliber arteries, and coronary arteries are a common site for the phenomenon. As the process advances, there is obstruction of the lumen and a decrease in oxygen supply to the myocardium, generating chest pains in

75-85% of cases. Compromising of the lumen may be partial or total, and obstructions $\geq 70\%$ are considered serious lesions.¹

Studies show that AMI is the main evolution of CAD and has a high rate of prevalence, morbidity and mortality. Mortality, which can reach up to 30% of cases, is related to the first place where assistance is provided, and half of all deaths occur in the first two hours. Early treatment prioritizes pain relief and coronary recanalization through the use of fibrinolytics and/or mechanicals. Among the mechanical techniques, there is angioplasty – which is considered the best option

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for reperfusion – if performed in up to 90 minutes after diagnosis, following the Brazilian and International Guidelines concerning the handling of these patients. Another form of reperfusion is through CABG, which is generally elective and performed 3 to 7 days after the AMI episode. CABG cases are rare, recommended only when there is no licensed operator to perform an angioplasty, or if there are complications in the procedure.²

It is known that risk cardiovascular risk factors are difficult to handle and very prevalent in the population because they are present in a cultural and economic conditions context, but it is believed that there is a possibility to decrease mortality in at least 50% by controlling those risks. Arterial hypertension, diabetes mellitus (DM), dyslipidemia, and smoking are the biggest villains.³

Thus, the objective of this work is to show the relation of these factors, and evaluate the presence of other factors, such as education level, marital status, number of children, and occupation, in an attempt to show the impact of CVD in the healthcare system and in the lives of those affected by serious coronary lesions.

Methodology

The retrospective research for descriptive and observational purposes was done in the department of Hemodynamics and Cardiac Surgery of the Brazilian Hospital *Beneficência Portuguesa de São Paulo*, in the city of São Paulo, between October 2015 and February 2016, after approval by the Research Ethics Committee of the University *Universidade Anhembi Morumbi*.

The active search gathered 200 patients of both genders, ≥ 18 years of age, undergoing percutaneous transluminal coronary angioplasty (PTCA) and/or CABG. We excluded those who presented difficulty to understand the assessment questions and those without critical lesions (lumen stenosis $< 70\%$).

All participants signed a free consent form.

The data were collected through a questionnaire filled out by the researchers, patient charts, and contemplated several clinical variables such as weight, age, height, personal background, life-style, demographic information, marital status, level of education, clinical history and lab exams.

Statistical analysis

To evaluate the normal distribution of quantitative variables, we used the Kolmogorov-Smirnov test. Quantitative data were described as mean and standard deviation, and categorical variables were described as absolute frequencies and percentages. For continuous variables, we used unpaired Student's t test, and for categorical variables, the chi-square test.

To estimate the conditional or expected value, we used a linear regression between the number of risk factors and age, and the results were considered significant when $p < 0.05$. All the tests were two-tailed. Statistical calculations were done through the software SPSS 22.

Results

We analysed 200 patients – 53 women (26.5%) and 147 men (73.5%) – who underwent PTCA or CABG. A total of 72 patients (36%) underwent PTCA and the other 128 (64%) underwent CABG. The type of treatment was decided by the heart team, according to the patients' wishes and angiographic conditions.

After statistical treatment, we concluded that most patients were male, over 60 years of age (64%) (Table 1), had a low level of education (elementary school – 55.5%) (Table 2), were married (57%) (Table 3), had a body mass index (BMI) between 18 and 24.99 (54.5%), had a clinical history of chest pains complaints (74%) and presented, in most cases, "classic and modifiable risk factors" for CVD, such as smoking, systemic arterial hypertension (SAH), DM, obesity, and dyslipidemia. Among these factors, SAH was the most prevalent at 80% (Table 4).

Most patients ($n=89$; 44.5%) presented two cardiovascular risk factors, excluding the male gender, and including smoking, obesity, SAH, DM, and dyslipidemia. There was no difference in the correlation of gender and quantity of risk factors ($p=0.89$).

Table 1
Distribution per age group

	Frequency	%	
Valid	< 45 years	3	1.5
	45-60 years	69	34.5
	> 60 years	128	64.0
	Total	200	100.0

Table 2
Population distribution according to level of education

	Frequency	%
Illiterate	27	13.5
Elementary school	111	55.5
High school	50	25
University	8	4
Post graduate	4	2
Total	200	100

Table 3
Distribution per marital status

	Frequency	%
Single	23	11.5
Married	114	57
Divorced	43	21.5
Widowed	20	10
Total	200	100

Table 4
Modifiable risk factors

Factor	N	%
SAH	160	80
Obesity	33	16.5
Smoking	48	24
Dyslipidemia	135	67.5
DM	76	38

HAS: systemic arterial hypertension, DM: diabetes mellitus.

The presence of risk factors can also be analysed by grouping the patients according to the number of factors in which 0 (zero) represents their absence, and

5 (five) represents the presence of five or more risk factors (Table 5).

Table 5
Distribution of risk factor frequency

	Frequency	%
0	6	3
1	31	15.5
2	89	44.5
3	55	27.5
4	17	8.5
5	2	1
Total	200	100

By analysing marital status and the distribution of the factors in questions, we concluded that married individuals are generally less obese ($p=0.013$) (Table 6); however, DM, SAH, smoking and dyslipidemia were not altered according to marital status.

Regarding the level of education, no correlation was found between level of education and the presence of risk factors; there was also no correlation between the number of children and the frequency of risk factors.

There was significant difference between gender and age – women presented a higher mean age (66.1 years) than men (62.1 years) in the researched situation ($p=0.008$).

Discussion

CVD is responsible for a high frequency of hospital admissions and generates significant costs for patients and for the public healthcare system. These costs may be direct, as in the case of hospital admissions, medical fees, surgical material, and medications, or indirect, such as loss of productivity, absence from work, and increase of social security costs, among others.

According to the Brazilian Ministry of Health – Mortality Information System (SIM) – in 2013, AMI was the second greatest cause of death in Brazil,

Table 6
Marital status and obesity according to BMI

		Marital status				Total
		Single	Married	Divorced	Widowed	
Obesity	N	18	103	33	13	167
	%	78.3	90.4	76.7	65.0	83.5
Total	N	5	11	10	7	33
	%	21.7	9.6	23.3	35.0	16.5
Total	N	23	114	43	20	200
	%	100.0	100.0	100.0	100.0	100.0

with approximately 85,900 deaths (almost 236 per day), which represents an increase of 2% over the previous year.⁴

It is estimated that, in 2007, there were 1,157,509 hospital admissions for CVD; a very impactful number that shows the high incidence of this infirmity requiring urgent medical intervention, bed occupancy at coronary units, ICUs and infirmary. Costs are expressive; for example, in November of 2009, there were 91,970 admissions for CVD, which amounted to R\$ 165,461,644.33 in expenses.⁵

A study done at the State Hospital of the Brazilian city of Bauru, between January and June of 2007, showed that around 12% of the service costs go to CVD assistance, amounting to over R\$ 600,000.00 in monthly expenses with the infirmity group. Still in this research, it was concluded that 80% of the money is destined to admitted patients – one day in the cardiology ICU costs around R\$ 684.00, a coronary arteriography is R\$ 996.00, and cardiac surgery for CABG is approximately R\$ 9,000.00.⁶

Having the USA as a base, where treatment resources are more comprehensive, in 2002 annual expenses with atherosclerosis surpassed US\$ 329 billion, while expenses with neoplasia and HIV combined were \$178 billion.⁷

There are studies, like the multicenter INTERHEART and the Brazilian AFIRMAR, that show that there are modifiable risk factors (sedentary life style, smoking, arterial hypertension, DM, etc.) and non-modifiable risk factors (age, gender, ethnicity) related to CVD, and that interventions significantly alter the risk for diseases of the circulatory system.⁸

Moreover, the pioneer study Framingham, done approximately 60 years ago (1948) in the State of Massachusetts, showed, throughout generations and years, the importance of risk factors for the development of cardiac and cerebrovascular disease in a Caucasian population, proving that the atherosclerotic event is not a natural and inevitable process, exclusive of the aging process.

When we associate the data of the high prevalence and mortality and the high financial costs CVDs generate to the Brazilian healthcare system, it becomes relevant to confirm that certain risk factors, such as DM, SAH, dyslipidemia, sedentary life styles, smoking, age, heredity – in isolation or associated – in fact contribute to the pathophysiological development of CAD.

The relevance of CVD studies is fully known, having as a background its extremely elevated incidence, prevalence, mortality and morbidity. The identification of risk factors is of pivotal importance for the clinical management and elaboration of public healthcare policies for primary and secondary prevention of its group of pathologies, among which is AMI.

After statistical analysis of the collected data, it is possible to ponder that, even though most interviewed patients presented at least two classic risk factors, there were those who reported a lack of contributing factors, or mentioned the presence of only one factor in their clinical histories, in addition to those who never even had chest pains (18.5%) – which is the main sign of coronary compromise and myocardial ischemia – but still had an ischemic episode.

Another important observation is that risk factors such as SAH may be controlled and still take part in the coronary event – since 80% of the interviewees reported arterial hypertension – however, there was no discrimination of whether there was current decompensation of the disease. This same rationale can be considered when patients reported dyslipidemia, because not all of them had the real values of the cholesterol dosage in their charts, and non-normal values of LDL and HDL-cholesterol did not necessarily place them in high risk groups for CVD.⁹

Considering such information, it is possible to raise the question that the role of classic risk factors in coronary events presents gaps and other possible elements, which are still unclear and that also influence the pathophysiology of CVD. Thus, it is pivotal to study new risk factors implicated in the pathogenesis of CVD. A good example of these factors that are being studied is homocysteine, an intermediate amino acid formed by the enzymatic action from methionine, whose metabolism depends on the appropriate intake of vitamins B6, B12, and folic acid.¹⁰ The mechanisms suggested, through which hyperhomocysteinemia causes CAD, are endothelial dysfunction with reduced vascular relaxation, mitogenic effect in vascular smooth muscle cells, activation of factor V, activation of the tissue plasminogen activator (tPA), and endovascular inflammation.¹¹

The hypothesis of hyperhomocysteinemia as a risk factor for CVD came from studies with children with homozygous homocystinuria – a genetic disease affecting one in every 50,000 – 200,000 new born babies who develop early atherosclerosis (coronary, cerebral, and peripheral) and whose life expectancy is < 30 years of age.^{12,13}

The Physician's Health Study, done in the USA, monitored, for 5 years, 15,000 American doctors with no history of CVD, concluding that around 7% of infarctions attributed to CVDs were related to hyperhomocysteinemia with a relative risk of 3.4 (confidence interval of 95%: 1.3 – 8.8; $p=0.01$). Similarly Nygard et al., in a study with 802 individuals with coronary disease confirmed by angiography, reported that homocysteine levels are linearly correlated to the risk of cardiovascular events and global mortality.^{14,15}

Homocysteine metabolism depends on vitamins B6, B12, and folic acid, and may be one of the numerous explanations for a higher incidence of CVDs in

the population with low socio-economical power, considering they are more exposed to malnutrition. These facts can be correlated by some of the data collected, in which 55.5% of interviewees finished only elementary school and 13.5% were illiterate, while only 2% had post graduate degrees. It is worth mentioning that the financial situation of the participants was not researched, and that a low level of education is suggestive of lower income. However, it is possible to think of another strand for the role of homocysteine in CVD, in which the increase of this amino acid would be a consequence, and not a cause of the pathology.¹⁶

Considering the modifiable risk factors of social-economical nature, such as marital status, level of education, and number of children, the literature is still divided.

The study 'Association of Marital Status with Vascular Disease in Different Arterial Territories: A population based study of over 3.5 million subjects', presented at the 63^o Annual Meeting of the American College of Cardiology, similarly to a Brazilian study by Santos e Ramos in 2012, showed that married individuals have lower rates of CVD in comparison to other marital statuses. This same study reported that those with a larger number of children and university level education present more cardiovascular events, and demonstrated that the "singles" group was the one most affected by CVDs, differently from this research where we did not find a relation between these data. An important observation in the data collected in this study is that the patients were part of an urban context with a rich flow of information, which may have influenced the appearance of CVD. Also, with regards to level of education, we highlight the fact that our sample had a very small number of participants.^{17,18}

Considering that the main mechanism for cardiovascular events is atherosclerosis, it is inevitable to not associate inflammatory factors and components of coagulation to the pathophysiology of CVD. Thus, C-reactive protein was suggested as a direct contributor to vascular damage, independently increasing the risk for AMI, stroke, and peripheral vascular disease, and it is part of the indication for some FDA-approved statins.¹¹⁻¹⁶

The collected data demonstrated that the age group related to the episode responsible for surgical intervention, in this case CABG or angioplasty, was higher in women (66.1 years), which is in line with the

tendency of menopause being seen as a risk factor for the development of the atherosclerotic process, considering that after 55 years of age, most women have completed the menopausal process.¹⁹

There is still the need for further studies regarding new risk factors, and it is noteworthy that, other than factors mentioned here, other factors related to homeostasis, inflammation, and thrombogenesis can also be related to CVD. Among them, are fibrinogen, platelet hyperreactivity, resistance to aspirin, lipoprotein "a", and other serum markers of inflammation, such as tumor necrosis factor alpha and interleukin 6. There have been over 100 new risk factors identified, some with a direct relation with CVD; however it is currently not recommended to use them until substantial data and protocols be evaluated.¹¹

Conclusion

In this study, we concluded that classic risk factors for CVD are real and, despite being supposedly known, there has been an increase in the incidence of this group of diseases, suggesting that the efficacy in their approach is below the necessity.

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Author contributions

Conception and design of the research: Costa FAA, Clemente CET, Ueno FH, Motta AR. Acquisition of data: Costa FAA, Clemente CET, Ueno FH, Motta AR. Analysis and interpretation of the data: Costa FAA. Statistical analysis: Costa FAA. Writing of the manuscript: Clemente CET, Ueno FH, Motta AR. Critical revision of the manuscript for intellectual content: Costa FAA.

Potential Conflict of Interest

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