

Distribution of Risk Factors in Parents and Siblings of Patients with Early Coronary Artery Disease

Antonio de Padua Mansur, André P. L. Mattar, Anderson L. Rolim, Fábio R. Yoshi, José F.G. Marin, Luíz Antonio M. César, José Antonio F. Ramires

São Paulo, SP - Brazil

Objective – Early coronary artery disease (CAD) is associated with risk factors (RF). Offspring of parents with a RF have a greater prevalence of them. However, the distribution of RF in parents and siblings of patients with early CAD is unknown.

Methods – The study comprised the parents and siblings of 42 patients with early CAD (≤ 45 years), 29 males. Their mean age was 39.5 ± 3.7 years. The following major RF were analyzed: smoking (≥ 5 cigarettes/day), hypercholesterolemia (total cholesterol ≥ 200 mg/dL), hypertension (diastolic blood pressure ≥ 90 mmHg), and diabetes (glycemia ≥ 126 mg/dL).

Results – Of a total of 102 RF, 4, 3, 2, and 1 were observed in, respectively, 5, 15, 15, and 7 patients with early CAD, the most prevalent being smoking (86%) and hypercholesterolemia (83%). Diabetes was observed in 15 (36%) and hypertension in 16 (38%) patients. Smoking was more prevalent in the fathers (76%) and hypercholesterolemia in the mothers (30%). In 183 siblings, 131 RF were observed (1 patient with the disease had a mean of 4.7 siblings). The prevalences of smoking, hypertension, hypercholesterolemia, and diabetes in the siblings were, respectively, 32%, 18%, 14%, and 9%. The incidence of RF was as follows: 72 (39%) siblings had 1 RF, 25 (14%) siblings had 2 RF, and 3 (2%) siblings had 3 RF. In parents and their offspring, smoking was moderately correlated ($r=0.43$; $P=0.02$) with CAD.

Conclusion – Smoking habit of parents is passed on to offspring, and, in association with hypercholesterolemia, it was the major cause of early CAD in offspring. High prevalence of smoking in offspring shows the potential responsibility of parents in the incidence of the disease in offspring.

Key words: coronary artery disease, risk factors, familial history, smoking

Coronary artery disease is the major cause of death in the Brazilian population¹ and is directly related to the number and intensity of risk factors², which may be generically divided into unchangeable (age and sex) and changeable. The major changeable risk factors are obesity, sedentary lifestyle, systemic arterial hypertension, smoking, dyslipidemia, and diabetes. Smoking and sedentary lifestyle are basically behavioral, and the remaining risk factors are associated with genetic and environmental components. Studies in different populations have shown the greater importance of environmental and behavioral components in the genesis of the atherosclerotic process³. A classical example is the greater prevalence of the disease in individuals migrating from a more favorable environment to one with a more atherogenic profile⁴. Likewise, some studies^{5,6} have shown the importance of the microenvironment, in particular the family, where genetic influences and lifestyle are equally important. Offspring of parents with systemic arterial hypertension or with dyslipidemia have a greater incidence of diseases whose phenotypes are influenced by the familiar lifestyle. The result of this interaction is responsible for atherosclerotic disease, which normally affects males after the 6th decade and females almost 1 decade later⁷. In younger patients with coronary artery disease, a greater participation of the genetic component has been discussed. Despite the existing controversies, a familiar analysis may directly or indirectly facilitate the detection and quantification of which component, genetic or environmental, has the greatest impact on early atherosclerotic disease, and, consequently, on its future control. Therefore, the major objective of this study was to analyze the prevalence of risk factors in families of patients with early systemic arterial disease, and to detect the importance of parents in the vertical transmission of these risk factors.

Methods

This study prospectively analyzed the distribution of the major risk factors of parents and siblings of 42 conse-

Instituto do Coração do Hospital das Clínicas - FMUSP
Mailing address: Antonio de Padua Mansur – InCor - Av. Dr. Enéas C. Aguiar, 44
05403-090 - São Paulo, SP, Brazil - E-mail: corantonio@incor.usp.br
English version by Stela Maris C. e Gandour

cutive patients of the outpatient care clinics of the Group of Chronic Coronary Heart Diseases of the Instituto do Coração (InCor) of the Hospital das Clínicas of the Medical School of the University of São Paulo diagnosed with early coronary artery disease (≤ 45 years) from August to November 1999. Their ages ranged from 30 to 45 years (mean \pm SD = 39.5 ± 3.7 years). Twenty-nine (69%) patients were males and 13 (31%) were females. The diagnosis of coronary artery disease was angiographic and defined as obstructive atherosclerotic lesions $\geq 50\%$ in at least 1 subepicardial coronary artery. The major risk factors studied were as follows: smoking (≥ 5 cigarettes/day), systemic arterial hypertension (diastolic pressure ≥ 90 mmHg)⁸, and diabetes (glycemia ≥ 126 mg/dL)⁹. Hypercholesterolemia was diagnosed as total cholesterol levels ≥ 200 mg/dL or LDL-cholesterol levels ≥ 130 mg/dL¹⁰.

The calculation of the sample size (N = 15 families) for the study was based on proportion-type variables with a significance level of $\alpha = 0.05$, a statistical power of $1 - \beta = 80\%$, and transmission of at least 50% of the risk factors. The statistical analysis used the chi-square test for categorical variables, the Student *t* test for analysis of the fractions comprising the lipid profile, and the Pearson test for the correlations between the risk factors of parents and offspring. The statistical significance level of $P < 0.05$ was adopted.

Results

A total of 102 risk factors were observed in the patients with early coronary artery disease, and their distribution of 4, 3, 2, and 1 was respectively detected in 5, 15, 15, and 7 patients. The most prevalent risk factors were smoking (86%) and hypercholesterolemia (83%) followed by diabetes (38%) and systemic arterial hypertension (36%). Smoking was more prevalent in the father (48%) and hypertension in the mother (24%). Table I shows the distribution of the general characteristics and lipid profile.

At least 1 risk factor was observed in 50% of the mothers and in 55% of the fathers (NS). In 183 siblings, 131 risk factors were observed as follows: 54 (41%) siblings had 1 risk factor, 25 (19%) had 2 risk factors, and 9 (7%) siblings had 3 risk factors. The relation of 1 patient with coronary artery disease had a mean of 4.7 siblings and 1.3 risk factors.

Only 2 siblings also had coronary artery disease. The prevalence of smoking, hypertension, hypercholesterolemia, and diabetes in the siblings was, respectively, 31%, 17%, 13%, and 8%. A moderate correlation ($r=0.43$; $P=0.02$) between the smoking habit of parents and offspring and the disease was observed. No correlation was detected between the risk factors of mothers and offspring or their siblings and the disease, or fathers and offspring also with the disease. Among ill offspring, 35 (83%), 6 (14%), and 1 (2%) patients had, respectively, single-, double-, or triple vessel disease, depending on the number of impaired coronary arteries. The lipid profile of the population was similar in the groups, except for HDL-cholesterol in mothers and offspring with coronary artery disease ($P=0.008$). All

Table I – Clinical characteristics and distribution of risk factors in parents and offspring with coronary artery disease (CAD) and their siblings

	Fathers (N=40)	Mother (N=40)	Offspring with CAD (N=42)	Siblings (N=183)
Mean age (years)	68.4 \pm 9.5	65.2 \pm 7.3	39.5 \pm 3.7	38.4 \pm 4.6
Sex (male/female)	40 / 0	0 / 40	29 / 13	87 / 96
Smoking	19 (76%)	8 (20%)	36 (86%)	58 (32%)
Hypercholesterolemia	5 (12%)	12 (30%)	35 (83%)	32 (18%)
Systemic arterial hypertension	4 (10%)	7 (17%)	16 (38%)	25 (14%)
Diabetes	4 (10%)	7 (17%)	15 (36%)	16 (9%)
Risk factors (total)	32	34	102	131
0	18 (45%)	20 (50%)	0	83 (45%)
1	17 (42%)	11 (27%)	7 (16%)	72 (39%)
2	4 (10%)	7 (17%)	15 (36%)	25 (14%)
3	1 (2%)	3 (7%)	15 (36%)	3 (2%)
4	1 (2%)	0	5 (12%)	0
Triglycerides (mg/dL)	229 \pm 86	230 \pm 75	220 \pm 46	232 \pm 86
Total cholesterol (mg/dL)	245 \pm 59	236 \pm 62	232 \pm 49	229 \pm 29
HDL-cholesterol (mg/dL)	43 \pm 9	46 \pm 8	38 \pm 17**	41 \pm 6
LDL-cholesterol (mg/dL)	152 \pm 38	149 \pm 32	140 \pm 35	138 \pm 26

* $P < 0.0001$ for the prevalence of familial antecedents among offspring with CAD and their siblings; ** $P = 0.008$ for HDL levels between mothers and offspring with CAD

patients with the disease were taking lipid-lowering drugs (statins). Two patients used fibrates concomitantly.

Discussion

This study stresses 2 important points: 1) the great majority of patients with early coronary artery disease has an important changeable risk factor; and 2) the vertical transmission of risk factors from parents to offspring was more environmental or related to lifestyle than to the genetic component. Some studies have shown that offspring or siblings of patients with coronary artery disease may have conditions ranging from phenotypic correspondence of a certain risk factor to a greater mortality due to cardiovascular diseases¹¹, suggesting the important participation of the genetic component passed on by parents^{12,13}. However, genetic studies in animals and human beings have shown difficulties in identifying the genes directly related to coronary artery disease^{14,15}. Some of these genes have been more constantly associated with coronary artery disease, either in its acute (acute coronary syndromes) or in its chronic form in case-control or meta-analysis studies¹⁶⁻¹⁸. However, these associations disappear in longitudinal studies¹⁹⁻²¹, suggesting the greater importance of the environmental component. Inadequate diet and lifestyle potentiate a risk factor with some degree of genetic influence (systemic arterial hypertension, dyslipidemia and diabetes) and favor other mainly behavioral risk factors, such as smoking and a sedentary lifestyle. Lifestyle and diet are, therefore, the major determinants of the phenotypic expression of major changeable risk factors (systemic arterial hypertension, dyslipidemia and diabetes). A recent study²² has emphasized that smoking and diet were the major

risk factors responsible for postprandial hyperlipemia, which is known to be a condition associated with the atherosclerotic process. An improvement in these determinants is associated with better control of these risk factors and a reduction in the incidence of the coronary artery disease²³. Recommendations, although not systematic, to change lifestyle and life habits result in improvement in the control of risk factors²⁴. Therefore, families with individuals at high risk for developing coronary artery disease may benefit from this educational process, which will cause an improvement in all risk factors. This process applied to our population could reduce the incidence of the disease in young individuals, because our data showed that 86% of our study population were smokers and 83% had some degree of dyslipidemia, smoking being considered the most important factor for coronary artery disease. A recent study²⁵ showed an al-

most 6-time greater risk for coronary artery disease in female smokers. As smoking is a behavioral risk factor, quitting smoking offers the best cost-benefit ratio for reducing the disease. Medications, in addition to being expensive, are usually associated with side effects; however, most of the time, they are not required. In developing countries, where the social cost is usually high due to other diseases, a reduction in smoking through an educational process is the major approach for reducing cardiovascular diseases. This educational process will influence parents to quit smoking, and, consequently, reduce smoking in offspring.

This study reveals the important participation of the parental habit of smoking in offspring. Therefore, it is the responsibility of parents to control the smoking habit as early as possible, because the incidence of smoking among young people has been increasing.

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