

Detection of Altered Risk Factors in Hospitalized Patients with Coronary Artery Disease

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Objective - To assess biochemical, anthropometric, and dietary variables considered risk factors for coronary artery disease.

Methods - Using anthropometrics, dietary allowance, and blood biochemistry, we assessed 84 patients [54 males (mean age of 55 ± 8 years) and 30 females (mean age of 57 ± 7 years)], who had severe ($\geq 70\%$ coronary artery obstruction) and nonsevere forms of coronary artery disease determined by cardiac catheterization. The severe form of the disease prevailed in 70% of the males and 64% of the females, and a high frequency of familial antecedents (92% ' 88%) and history of acute myocardial infarction (80% ' 70%) were observed. Smoking predominated among males (65%) and diabetes mellitus among females (43%).

Results - Males and females had body mass index and body fat above the normal values. Females with nonsevere lesions had HDL > 35 mg/dL, and this constituted a discriminating intergroup indicator. Regardless of the severity of the disease, hyperglycemia and hypertriglyceridemia were found among females, and cholesterolemia > 200 mg/dL in both sexes, but only males had LDL fraction > 160 mg/dL and homocysteine > 11.7 mmol/L. The male dietary allowance was inadequate in nutrients for homocysteine metabolism and in nutrients with an antioxidant action, such as the vitamins B₆, C, and folate. Individuals of both sexes had a higher lipid and cholesterol intake and an inadequate consumption of fiber. The diet was classified as high-protein, high-fat, and low-carbohydrate.

Conclusion - The alterations found had no association with the severity of lesions, indicating the need for more effective nutritional intervention.

Key words: risk factors, individuals with coronary artery disease, hospitalization

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In the past few years, a marked reduction in mortality due to cardiovascular diseases has occurred, even though those diseases remain the major cause of mortality worldwide according to the American Heart Association¹.

The multifactorial etiology of coronary artery disease reveals the existence of several risk indicators, many of which may be modified by effective interventions². On the other hand, some studies show that the risk factors, when kept active, contribute to the progression of coronary lesions, worsening the patient's prognosis³.

According to dietary recommendations for preventing coronary artery disease, the factors related to its development or worsening, or both, are the following: total fat intake above 30% and saturated fatty acid intake above 10% of the total caloric value of the diet; dietary cholesterol above 300 mg/day; inadequate intake of vitamins and antioxidant minerals and of vitamins involved in the metabolism of methionine; dietary fiber below 20 g/day; sodium consumption above 6 g/day; and high-caloric diets⁴⁻⁷.

The current study assessed the levels of factors associated with coronary artery disease in patients hospitalized due to coronary artery disease, aiming at checking whether the severity of the coronary artery lesion was related to the alterations in risk factors.

Methods

We carried out a cross-sectional observational study with 84 patients hospitalized for the treatment of coronary artery disease in a ward of a public general hospital affiliated with the School of Medicine of Botucatu in the Central-Western region of the State of São Paulo, from March to August 1998. The inclusion criterion was the diagnosis of coronary artery disease through clinical examination and cardiac catheterization. The exclusion criteria were as follows: hospitalization time insufficient for data collection, presence of severe cardiac disease making the patient's assessment impossible, recent acute myocardial infarction (time ≤ 3 months in regard to the period studied), and presence of other chronic diseases, such

as decompensated diabetes mellitus, renal, respiratory, or hepatic insufficiency, and cancer.

The individuals were divided into 4 groups according to sex and the severity of the coronary artery lesion using the criterion of the Sociedade de Cardiologia do Estado de São Paulo⁸, which considers coronary artery obstruction $\geq 70\%$ as a severe lesion. The groups were as follows: groups 1 and 2 (G1 and G2) comprised 57 (38 males and 19 females) patients with severe coronary lesions; groups 3 and 4 (G3 and G4) comprised 27 (16 males and 11 females) patients with nonsevere coronary artery lesions.

This study was approved by the Committee on Ethics and Research in Human Beings of the School of Medicine of Botucatu.

A personal questionnaire was used to characterize the patients studied with information on sex, age, marital status, smoking status, occurrence of acute myocardial infarction, systemic hypertension, diabetes mellitus, angina pectoris, and hospitalization duration. The severity of the coronary artery disease was established with the analysis of the cardiac catheterization and after clinical examination.

The anthropometric examination comprised the following measurements: weight; height; triceps, biceps, subscapular, and supra-iliac skinfolds (using the Lange[®] caliper, USA); arm, waist, and hip circumferences (using the millimetric nonextendable tape); and subsequent calculation of the muscle circumference of the arm, waist/hip ratio, and body mass index⁹⁻¹¹. The sum of the skinfold values was determined and the Durnin and Wormesley method was applied¹².

The following reference values were used: the World Health Organization (WHO) standard¹³ for body mass index, the Frisancho¹⁴ standard for the arm circumference and the muscle circumference of the arm, and the Bray standard¹⁵ for the waist/hip ratio. The normal ranges for body fat were 15-18% for males and 20-25% for females¹⁶.

The dietary inquiry was applied on the 1st day of hospitalization using a 24-hour recall. To increase the reliability of the measuring spoon measurements reported by the interviewees, the manual of photographic record for dietary inquiries was used as support material¹⁷. In addition to the structured 24-hour recall, we used a questionnaire about the preferred way of preparing food, appetite, allergies, food aversions and preferences, number of meals/day, and use of vitamin and mineral supplements.

To analyze the quantitative data of food intake, measuring spoon measurements of food and beverages reported by the interviewees were converted into grams according to Soares et al¹⁸ and Pinheiro et al¹⁹.

The intake of energy, proteins, lipids, carbohydrates, unsaturated lipids, dietary cholesterol, vitamins C and E, folic acid, vitamins B₆ and B₁₂, and dietary fiber was calculated with the aid of Virtual Nutry software²⁰.

The values obtained were then compared with the dietary aliquots recommended by the National Research Council/Recommended Dietary Allowances (NRC/RDA-1989)²¹. In regard to adequacy, the individuals were grouped into the 3 following consumption ranges: < 67% of adequacy

(inadequate), from 67% to 100% (borderline), and $\geq 100\%$ of adequacy (adequate). The World Health Organization standards were adopted for daily dietary fiber intake⁷. Lipid consumption was compared with the values recommended by the National Cholesterol Education Program⁵ for the percent dietary fat in relation to the total energy value, dietary cholesterol, and unsaturated lipids.

The biochemical analyses performed in venous blood samples were obtained after nocturnal fasting ranging from 8 to 12 hours, through venous puncture with a closed vacuum system (Vacutainer[®] - England). The samples were then centrifuged for 10 minutes (3000 rpm) and the decanted plasma was analyzed with an automatic analyzer (model RAXT OU Ra 1000 - Technicon[®] - USA). The following plasma measurements were performed: glucose, total cholesterol, HDL-cholesterol, triglycerides, and total homocysteine, the latter with a high-performance liquid chromatographic assay²².

LDL-cholesterol was calculated with the Friedewald formula²³ and the total cholesterol/HDL-cholesterol ratio, and the values were compared with the normal values by Castelli et al²⁴.

The lipid levels were compared with those recommended by the 2^o Consenso Brasileiro sobre Dislipidemias²⁵ (2nd Brazilian Consensus on Dyslipidemias). The normal glycemia range was established from 70 to 110 mg/dL according to the criteria of the American Diabetes Association²⁶.

The reference values used for homocysteine ranged from 4.90 to 11.70 $\mu\text{mol/L}$ according to Ubbink et al²⁴.

The statistical analysis was performed with the analysis of variance (ANOVA) for the values of score-z and median, applying the study of comparison between the groups through the nonparametric analog of analysis of variance (Kruskal-Wallis test) complemented by its respective test of multiple comparisons²⁷.

The results were discussed based on the significance level of 5% ($p < 0.005$).

Results

Analyzing the characteristics of the sample, we observed that most patients were males (64%), acute myocardial infarction predominated in approximately 80% of the males and in 70% of the females, the mean age was similar for males and females (55 ± 8 and 57 ± 7 years, respectively), a positive familial history of coronary artery disease predominated in both sexes, and tobacco use was more prevalent among males (42%).

Other diseases, such as arterial hypertension and angina pectoris, were also observed in males and females. Severe coronary artery lesions were extremely prevalent and detected in 70% of the males and in 64% of the females (tab. I).

Of the anthropometric values, the percent body fat of males was above 18% and of females above 25%. In regard to the distribution of body fat, the waist/hip ratio was greater in the 2 male groups (G1 and G3) as compared with the female group with nonsevere lesions (tab. II).

The median values of body mass index did not statistically differ among the groups studied, and individuals of

Characteristics	Males (n= 54)	Females (n=30)
Hospitalization (days) *	10 ± 2	12 ± 3
Age (years) *	55 ± 8	57 ± 7
Menopause **	-	80% (24)
Smoking **	65% (35)	54% (16)
Cigarettes/day *	20 ± 8	15 ± 5
Positive familial history **	92% (50)	88% (27)
Severe coronary artery lesion**	70% (38)	64% (20)
Angina pectoris**	50% (27)	60% (18)
Diabetes mellitus **	18% (10)	43% (13)
Arterial hypertension **	50% (27)	60% (18)
Acute myocardial infarction **	80% (43)	70% (20)

* Mean and standard deviation; ** percentage and number of individuals.

both sexes were classified as preobese according to the Reports of WHO²⁸ (tab. II).

In regard to biochemical values, homocysteinemia was greater in the male sex, regardless of the severity of the coronary artery disease (tab. II).

Of the remaining plasma parameters analyzed, only triglycerides showed a statistical difference in the groups; lower values were found in the male groups (G1 and G3) than those found in females with severe coronary artery lesion (G2) (tab. II).

The HDL-cholesterol and LDL-cholesterol values were similar in both groups. Total cholesterol levels were above the recommended values in all groups, and they showed no significant differences according to the severity of the disease (tab. II).

The total cholesterol/HDL-cholesterol ratios showed significant difference with sexes, and both groups had increased values, which was compatible with an increased risk for coronary artery disease (tab. II). This ratio was higher in males with severe coronary artery lesions, showing a significant

correlation with the type of lesion in the male sex (tab. II). Both G3 and G2 had glycemia results above those recommended with no relation to the severity of the lesions (tab. II).

In regard to diet, the percentage contribution of macronutrients characterized the diet as high-fat, high-protein, and low-carbohydrate for both sexes (fig. 1). Analyzing the amount of protein consumed according to body weight, the diet was considered high-protein with protein consumption above 1g/kg/day for all groups studied. The assessment of dietary quantitative consumption revealed an increased ingestion of total lipids in both sexes. The excessive ingestion of dietary cholesterol was also significantly higher in males as compared with that in females in all groups. On the other hand, an insufficient ingestion of unsaturated lipids was observed in both sexes, and it was more significant in males than in females (tab. III). The consumption of dietary fiber was lower than that recommended, with no statistical differentiation between the groups studied (tab. III). In addition, only 13% of the males and 6% of the females reached the adequate level of at least 30 g/day proposed by WHO⁷.

In regard to dietary vitamin intake, the median intake observed in isolation showed no dietary inadequacy. However, when the percentage of individuals with adequate consumption according to RDA²¹ was analyzed, the results showed that of the vitamins with antioxidant potential, vitamin C was consumed more by the female groups, regardless of the severity of the coronary lesions (tab. III). This resulted in a significantly greater adequacy in the female groups as compared with that in the male groups. Vitamin E showed a better percentage of adequacy, and all females and almost all males had an adequate consumption of that vitamin (tab. III). Vitamin B6 was adequately consumed in 50% and 48% of the male groups 1 and 3, and in 60% and 62% of the female groups 2 and 4; therefore, no difference was observed among the groups. Vitamin B12 showed good levels of ade-

Variables	Group 1 (n=38)	Group 2 (n=19)	Group 3 (n=16)	Group 4 (n=11)	Result of the test *
BMI (kg/m ²)	28 ± 5	27 ± 6	26 ± 4	28 ± 6	6.30 (p>0.05)
Percent body fat (%)	25 ± 6 ^a	32 ± 6 ^b	25 ± 4 ^a	32 ± 6 ^b	23.44 (p<0.01)†
Waist/hip ratio	0.99 ± 0.05 ^a	0.94 ± 0.09 ^b	0.98 ± 0.05 ^a	0.92 ± 0.06 ^b	10.76 (p<0.05) †
Total cholesterol (mg%)	224 ± 45	226 ± 47	222 ± 40	220 ± 39	1.11 (p>0.05)
HDL-cholesterol (mg%)	30 ± 14	34 ± 12	31 ± 11	38 ± 13	1.57 (p>0.05)
LDL-cholesterol (mg%)	155 ± 37	164 ± 43	158 ± 35	163 ± 41	1.17 (p>0.05)
TC/HDL	11 ± 3 ^a	9 ± 2 ^b	7 ± 4 ^b	8 ± 3 ^b	20.30 (p>0.01) †
Glycemia (mg)	106 ± 20 ^a	132 ± 41 ^b	118 ± 21 ^a	128 ± 40 ^{ab}	10.67 (p<0.05) †
Homocysteine (µmol/l)	8.10 ± 3.57 ^a	6.00 ± 1.24 ^b	8.93 ± 3.32 ^a	5.75 ± 1.08 ^b	17.13 (p<0.05) †

BMI – body mass index; TC – total cholesterol; different letters mean difference between the groups; † significant result; * nonparametric analog of analysis of variance (Kruskal-Wallis test)

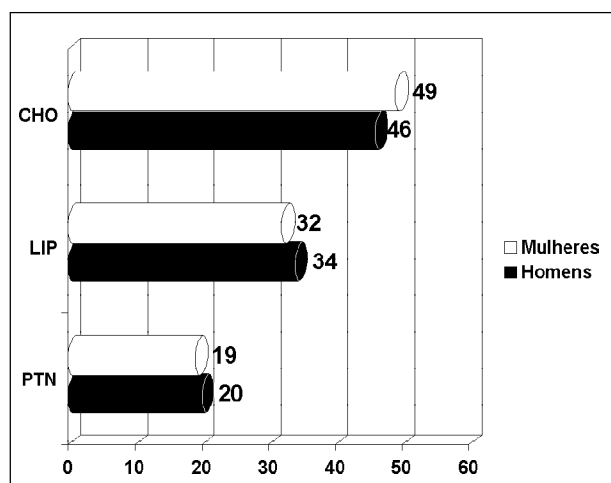


Fig. 1 - The percentage contribution of macronutrients in relation to daily total energy intake according to sex.

quacy for both sexes. Folic acid was inadequately consumed by males in both groups, significantly different from the female consumption, independent of the severity of the disease (tab. III).

Discussion

The results obtained in the present study show no significant difference between the groups studied in regard to the severity of coronary artery disease for the anthropometric, biochemical, and dietary parameters assessed, because of the stratification of the sample with a reduced number of individuals in each group. Relevant associations, however, occurred when males and females were compared.

In regard to the anthropometric study, some deviations

compatible with an increased risk for coronary artery disease were observed. These deviations were mainly represented by the following: body mass index > 25 kg/m²; percent body fat greater than 24 and 30 in males and females, respectively; and the waist/hip ratio greater than 0.98 and 0.90 in males and females, respectively. Gaudet et al²⁹ reported mean values of body mass index and waist/hip ratio in males with severe coronary artery disease of 28 kg/m² and 0.96, respectively, compatible with the subsequent risk for acute ischemic events, such as acute myocardial infarction. Those authors concluded that body mass index, percent body fat, and waist/hip ratio were above the recommended values also in patients with cardiac disease confirmed on coronary arteriography.

Deprés and Lamarche³⁰ related the accumulation of abdominal fat with dyslipidemia, and these individuals were more susceptible to an increase in triglycerides and a reduction in HDL-cholesterol. Korhonen et al³¹ observed significant differences in the lipid profile of patients with coronary artery disease with the degree of stenosis greater than 50%, lower than 50%, and individuals with no coronary artery disease, the profile of the first group having the greatest atherogenic potential. However, studies assessing the behavior of 2 or more risk indicators among individuals with coronary artery disease and coronary obstruction according to the severity of the lesion are still rare in the literature.

The biochemical analysis revealed a reduction in HDL-cholesterol in males, an increase in LDL-cholesterol in males and females, and total serum cholesterol above the recommended levels in all groups, according to the 2^o Consenso Brasileiro de Dislipidemias³². Similar results were observed in individuals undergoing coronary angiography for assessing coronary lesions in vivo³³ in a clinical assay carried out in postmenopausal females with coronary artery disease and previous acute myocardial infarction³⁴, and in a study³⁵ with

Table III - Median values, semi-amplitude, and percentage of individuals with an adequate dietary allowance

Variables	Group 1 (n= 38)	Group 2 (n=19)	Group 3 (n=16)	Group 4 (n= 11)	Result of the test *
Protein g/kg/day	1.50 ± 0.70	1.42 ± 0.69	1.40 ± 0.54	1.38 ± 0.73	1.00 (p > 0.05)
Total lipid (g)	64 ± 125	65 ± 100	68 ± 99	67 ± 55	5.75 (p>0.05)
Unsaturated lipids (g)	56 ± 29	34 ± 17 ^b	52 ± 36 ^a	26 ± 13 ^b	10.31 (p<0.05) †
Dietary cholesterol (mg)	311 ± 237	240 ± 174	315 ± 207	281 ± 259	2.86 (p>0.05)
Vitamin E	85% (32)	100% (19)	83% (13)	100% (11)	3.27 (p>0.05)
Vitamin C	35% (13) ^a	80% (15) ^b	68% (11) ^a	90% (10) ^b	10.09 (p<0.05) †
Vitamin B ₁	50% (19)	60% (11)	48% (8)	62% (7)	2.75 (p>0.05)
Vitamin B ₁₂ (mg)	87% (33)	73% (14)	88% (14)	75% (8)	2.47 (p>0.05)
Folacin (mg)	20% (7) ^a	60% (11) ^b	30% (5) ^a	78% (9) ^b	11.59 † (p<0.05)
Dietary fibers (g)	19 ± 8	16 ± 5	18 ± 10	14 ± 6	0.72 (p>0.05)

Different letters mean difference between the groups; † significant result; * nonparametric analog of analysis of variance (Kruskal-Wallis test).

dyslipidemic males and females with coronary artery disease. Individuals with these patterns of serum lipids have a greater predisposition to recurring events, such as angina pectoris, acutemyocardial infarction or sudden death, or both^{36,37}.

In the present study, the total cholesterol/HDL-c ratio was compatible with the risk for coronary artery disease³⁸, mainly in males with severe lesions, and this was the only discriminating indicator of the severity of the lesion.

Hypertriglyceridemia and hyperglycemia were observed mainly in the females of both groups, independent of the extension of the coronary lesion. Hyperglycemia and diabetes mellitus are frequently observed in females. Pyorala et al³⁹ related positively fasting glycemia and atherosclerotic complications in nondiabetic individuals. Glycemic control of individuals with coronary artery disease improves the prognosis of coronary artery disease and reduces mortality^{40,41}. Hokanson and Austin⁴² observed that high triglyceride levels correspond to a 75% higher risk in females with cardiac disease. Elisaf et al⁴³ found significant differences in the serum triglyceride levels of individuals with coronary artery lesions $\geq 70\%$ and those of individuals with coronary artery lesions $< 70\%$, strengthening the concept that triglyceride levels increase according to the severity of the coronary artery disease both in males and females, unlike our results⁴⁴.

Another biochemical parameter assessed that has been positively associated with the genesis of coronary artery disease is plasma homocysteine, considered by several authors an independent marker of early atherogenesis through still unclear mechanisms^{45,46}. Even though plasma homocysteine has been exhaustively studied, mainly in the past few years, its normal reference values are still a matter of controversy. The variations may be attributed to methodological differences in homocysteine measurement, in the processing of the sample, and in the selection of the individuals, because factors, such as age, sex, and menopause may influence homocysteinemia⁴⁷. In the present study, we used the values proposed by Ubbink et al⁶, who adopted a mathematical predictor model to establish the normal range of fasting homocysteine, and we found that a significant percentage of males (30%) had homocysteine levels above the recommended values.

Ueland et al⁴⁷ adopted the cut point $\geq 8.56 \mu\text{mol/L}$ for moderate homocysteinemia. When this cut point was adopted in our study, the percentage of hyperhomocysteinemic males increased to 45%. Bots et al⁴⁸ and Nygard et al⁴⁹ also reported increased plasma fasting homocysteine levels in males as compared with those of females, independent of the severity of the disease. The female homocysteine levels in our study were not comparable to those in the literature, because, according to Ridker et al⁵⁰, menopausal females are normally hyperhomocysteinemic.

Another important point to be considered is the low sensitivity of the measurements of fasting homocysteinemia. Dogamala et al⁵¹ identified, after the overload test with methionine, hyperhomocysteinemia in 39% of the patients who had normal or borderline basal levels.

Cunha⁵² reported that individuals with coronary artery disease and severe lesions had homocysteine levels

above those found in the group with no coronary artery disease. Mayer et al⁵³ reported a directly proportional association between the degree of coronary artery obstruction and homocysteine levels.

Even though extremely high median values have not been found, the importance of this alteration should not be disregarded, mainly because it refers to patients with established coronary artery disease, who have other risk factors, such as dyslipidemia, increased body fat, and inadequate dietary allowance.

According to Malinow et al⁵⁴, the percentage of abnormally high homocysteine levels among individuals with coronary artery disease is approximately 20 to 30%, which is identical to the percentage observed in the males of the present study.

Dietary composition has other implications in coronary artery disease, it being important to monitor some risk factors, such as dyslipidemia, obesity, and hyperhomocysteinemia. In our study, an excessive intake of total lipids and cholesterol and an inadequate intake of unsaturated lipids were observed in both sexes. In regard to caloric dietary distribution and macronutrients, we observed the ingestion of diets with a high percentage of proteins and lipids and a low percentage of carbohydrates. Watts et al⁵⁵, analyzing the progression of coronary artery disease in the male sex, observed a significant association with the amount of total and unsaturated fat in the diet. The intake of a similar diet was observed by Knoop et al⁵⁶ in individuals with coronary artery disease with a lipid intake of 36% in the diet and a mean dietary cholesterol consumption of 320 mg/day. Singh et al⁶⁴ observed the ingestion of high-fat and high-protein diets in their group of patients with coronary artery disease; however, the amount of dietary fiber intake of their patients was greater than that observed in the present study, in which that amount was extremely inadequate for both sexes.

The antioxidant components are significant dietary factors that prevailed in the diets of the females, of which a greater percentage showed adequate amounts of vitamin C and α -tocopherol according to the NRC/RDA²¹. These results were similar to those reported by Singh et al⁵⁸ in hospitalized patients with previous acute myocardial infarction.

Rosegren et al⁵⁹, studying patients who survived acute myocardial infarction, reported that the increased subsequent mortality risk was due to the maintenance of risk factors, such as smoking, dyslipidemia, and systemic arterial hypertension.

Our results showed that the individuals with coronary artery disease assessed in this study had alterations in risk factors, such as overweight, dyslipidemia, positive familial history for coronary artery disease, smoking, and inadequacy of dietary habits. These alterations were present in varied degrees according to sex and did not differ depending on the severity of the coronary artery lesion. Therefore, we observed the persistence of alterations in risk factors, even after the diagnosis of coronary artery disease, confirming the recurrence of ischemic events. This may have resulted from the lack of guidance and follow-up for correcting the risk factors that could be controlled.

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