

# Risk Factors for Atherosclerosis in an Elderly out Patient Population in the City of São Paulo

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**Objective** - To analyze in out clinic elderly patients of both sexes for the prevalence of risk factors for atherosclerosis and study their association with the complications of atherosclerosis.

**Methods** - Five hundred and sixteen outpatients, 152 men and 364 women, 60 years or older, were studied. The prevalences of hypertension, dyslipidemia, diabetes mellitus, cigarette smoking and obesity were determined in both sexes and compared using the chi-square test. The association between these factors and the presence of atherosclerotic complications was analyzed by logistic regression.

**Results** - The comparative analysis of the factors in both sexes showed that hypertension, total cholesterol  $\geq 240$ mg/dL, LDL-cholesterol  $\geq 160$ mg/dL, and body mass index  $> 27.5$  were more frequent among women, but HDL-cholesterol  $< 35$ mg/dL and cigarette smoking were more frequent among men, and no difference occurred between sexes in relation to the frequency of triglycerides  $\geq 250$ mg/dL and diabetes mellitus. After adjustment of the variables in the regression model, we observed that in the total of elderly patients, risk factors for complications of atherosclerosis were: triglycerides  $\geq 250$ mg/dL, hypertension, and male sex. Among men, the risk factors were: LDL-cholesterol  $\geq 160$ mg/dL, diabetes mellitus, HDL-cholesterol  $< 35$ mg/dL and hypertension. Among women, the risk factors were: triglycerides  $\geq 250$ mg/dL and hypertension.

**Conclusion** - The results showed that, in the elderly, the risk factors for atherosclerosis persist, but with different behaviors between men and women. The study suggests that the relative importance of the risk factors can change with the aging process.

**Key words:** risk factors, atherosclerosis, elderly

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Cardiovascular disease as a complication of atherosclerosis is today the most important cause of morbidity and mortality among elderly people especially in the developed countries<sup>1-3</sup>. Although in the earlier decades of life women have a lower prevalence of cardiovascular disease, the latter increases with age, reaching a similar level to that of men around the age of 75<sup>4-6</sup>.

The same tendency has been observed in Brazil. According to the Sistema Estadual de Análise de Dados (SEADE) and the Instituto Brasileiro de Geografia e Estatística (IBGE), in 1995, in the city of São Paulo coronary artery disease was more prevalent in men up to the age of 75 years, but the prevalence became similar in both sexes after that age<sup>7</sup>.

Atherosclerosis is a disease in which multiple factors contribute to the degeneration of the arterial wall. It is evident that intensity and duration of injury define the severity of the alterations. Many risk factors were identified as having influence on the progression of atherosclerosis, mainly age, sex, heredity, diet composition, tobacco smoking, physical activity, obesity, systemic arterial hypertension, dyslipidemia, diabetes mellitus, plasma fibrinogen levels, hyperhomocysteinemia, left ventricular hypertrophy and psycho-social factors.

Researchers in the area agree that an order of risk factors exists and, in addition to age, sex, and heredity, hypertension, dyslipidemia, diabetes mellitus, tobacco smoking, and obesity must also be considered as major risk factors and deserve more attention. Most of the research, however, involves individuals of middle age and, more specifically, white males<sup>8</sup>. More recently, population studies have been aiming at the behavior of risk factors in the elderly, and some of these studies have cast doubt on their importance at this age<sup>1,2,9-12</sup>.

The goal of the present study was analyze in elderly individuals of both sexes the prevalence of the major risk factors and their correlation with atherosclerotic complications.

## Methods

A group of 859 outpatients from the Geriatric Service of Hospital das Clínicas of the University of São Paulo Medical

School, aged 60 or older, were randomly selected, being 245 males (28.5%) and 614 females (71.5%), during the years 1992 through 1994. All the patients enrolled in the outpatient department could potentially enter the study, and the patients were chosen alternately without any special selection criteria. The proportion of men and women was similar to that observed in the outpatient clinic.

Through the medical records and by direct interview of the patients, the following risk factors were analyzed: sex, systemic arterial hypertension, dyslipidemia, diabetes mellitus, tobacco smoking, and obesity. For the present study, we included only the elderly patients who had all the risk factors properly studied, or 516 patients, 152 (29.5%) males and 364 (70.5%) females. The patients were analyzed according to the presence or not of atherosclerotic complications. Three territories of atherosclerotic complications were considered: coronary, cerebral, and peripheral. Patients with angina pectoris, previous myocardial infarction, coronary angioplasty, or bypass surgery were included in the coronary artery disease group. Patients with previous cerebral infarction or clinical signs of transient ischemic attacks were included in the cerebrovascular disease group. Claudication with peripheral pulse reduction and surgical treatment for the re-establishment of arterial circulation were the criteria of inclusion in the peripheral artery disease group.

The diagnosis of systemic arterial hypertension was made in individuals with systolic pressure of 160 mmHg or higher, with diastolic pressure of 95 mmHg or higher, or with both of these<sup>13</sup>, with a minimum of two measurements on two different visits, or in patients already under drug treatment. The blood pressure was determined with the patient in the supine position, after resting for at least three minutes.

The diagnosis of dyslipidemia was based on total cholesterol (TC) levels of 240mg/dL or higher, low-density lipoprotein cholesterol (LDL-C) levels of 160mg/dL or higher, high-density lipoprotein cholesterol (HDL-C) lower than 35mg/dL or triglycerides levels of 250mg/dL or higher. Total cholesterol and triglycerides levels were determined by enzymatic methods<sup>14</sup> and HDL-cholesterol levels were determined by the Warnick-Albers method<sup>15</sup>. The other fractions were calculated as follows<sup>16</sup>: very low-density lipoprotein cholesterol (VLDL-C) by the division of triglycerides/5, when triglycerides levels were lower than 400mg/dL and LDL-cholesterol by the following equation:  $LDL-C = TC - (HDL-C + VLDL-C)$ .

Diabetes mellitus was diagnosed when fasting plasma glucose levels were above 140mg/dL on at least two occasions, or when the patient was under drug treatment. Plasma glucose levels were determined by colorimetry after precipitation<sup>17</sup>. Blood samples for glucose and lipid determinations were obtained after 10 to 12 hours of fasting.

The patients were divided in two groups according to their smoking habits: smokers or nonsmokers. Patients who were smokers in the past, but not presently, were excluded.

Obesity was defined by body mass index or Quetelet index, obtained by the formula:  $[\text{body mass index} = \text{weight (kg)}/\text{height (m)}^2]$ <sup>18,19</sup>. The diagnosis of obesity was made

when body mass index was greater than 27.5. For weight and height determination, the patients wore light clothes and were barefoot. Height was measured with the patient in the upright position, with the patient's back against a wall.

The comparative analysis of the prevalences of the factors among men and women was done by the chi-square ( $X^2$ ) test, and the comparison between the mean of ages by Student's *t* test with the significance level established at 0.05.

The relationship of each risk factor with atherosclerotic complications was defined by logistic regression analysis<sup>20</sup>.

Initially, a univariate analysis was performed as a strategy for the selection of variables to be adjusted in a logistic regression model. In the final analysis, we included in the model the variables with the Pearson's *p* value of up to 0.494 for the men, up to 0.503 for the women, and up to 0.560 for the total of the elderly patients, indicating that the number of variables was small and that clinical interest existed for testing them in the model.

Each one of the logistic regression models, namely, that of the men, the women, and the total of the elderly patients was adjusted by means of a forward stepwise model technique. For example, in the analysis of the total of the elderly patients, we first included the variables sex and systemic arterial hypertension that had small *p* values in univariate analysis. In the analysis of the men, the first variables included were diabetes mellitus and systemic arterial hypertension; in the analysis of the women, the first variables were systemic arterial hypertension and triglycerides. Subsequently, the other variables were included, following a sequence of the *p* values obtained in univariate analysis. In this manner, we tried to estimate the independent effect of each variable adjusted to the model, controlling the respective confounding effects. The likelihood ratio test of each final model was performed, defining its significance, which permitted the evaluation of the adequacy of the model.

## Results

Among the 516 elderly patients studied, the average age was 75.6 years, with no statistically significant difference between men and women ( $p=0.276$ ).

The prevalences of the various risk factors are shown in figure 1 and in the first two left columns of the tables I, II, and III.

The comparative analysis of the prevalences of the variables among the elderly patients of both sexes showed that systemic arterial hypertension ( $p=0.05$ ), total cholesterol  $\geq 240\text{mg/dL}$  ( $p=0.001$ ), LDL-cholesterol  $\geq 160\text{mg/dL}$  ( $p=0.012$ ), and body mass index  $>27.5$  ( $p=0.009$ ) were more frequent among women, HDL-cholesterol  $<35\text{mg/dL}$  ( $p=0.024$ ) and tobacco smoking ( $p=0.044$ ) were more frequent among men, and no significant difference was noted in relation to triglycerides ( $p=0.458$ ) and diabetes mellitus ( $p=0.706$ ).

Atherosclerotic complications were observed in 110 (21.3%) elderly patients, being 45 (29.6%) among men and 65 (17.9%) among women (table I), showing that the risk was significantly greater among men [odds ratio (OR) = 1.93;  $p=0.003$ ; confidence interval of 95% ( $CI_{95\%}$ ) = 1.22-3.07].

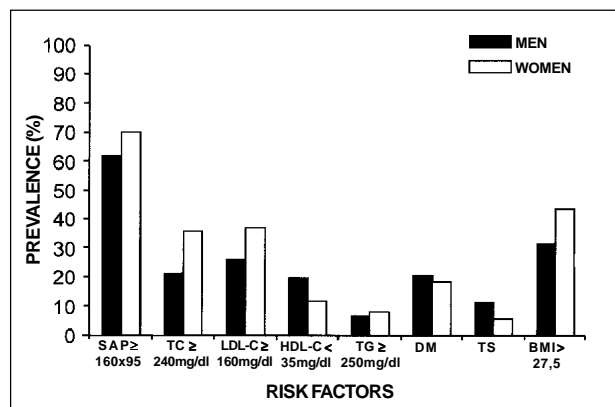


Fig. 1 - Prevalence of the risk factors for atherosclerosis in the elderly (152 men and 364 women). SAP- systemic arterial pressure; TC- total cholesterol; LDL-C- LDL-cholesterol; HDL-C- HDL-cholesterol; TG- triglycerides; DM- Diabetes mellitus; TS- tobacco smoking habit; BMI- body mass index.

In all the elderly patients, an association existed between complications of atherosclerosis and systemic arterial hypertension (odds ratio = 1.97), triglycerides levels  $\geq 250\text{mg/dL}$  (odds ratio = 2.05), diabetes mellitus (odds ratio = 1.69), HDL-cholesterol level  $< 35\text{mg/dL}$  (odds ratio = 1.70), the last one with a p value of 0.056 (table I).

Among men, an association existed between complications of atherosclerosis and systemic arterial hypertension (odds ratio = 2.51), LDL- cholesterol level  $\geq 160\text{mg/dL}$

(odds ratio = 2.22), diabetes mellitus (odds ratio = 3.38), total cholesterol level  $\geq 240\text{mg/dL}$  (odds ratio = 2.23), the last one with a p value of 0.052 (table II).

Among women, no significant association between complications of atherosclerosis and the risk factors was observed (table III). However, one may point out the odds ratio values of the following variables: systemic arterial hypertension (OR=1.89;  $p=0.056$ ;  $CI_{95\%} = 0.98-3.64$ ) and triglycerides level  $\geq 250\text{mg/dL}$  (OR=2.02;  $p=0.095$ ;  $CI_{95\%} = 0.89-4.63$ ).

After adjustment of the variables to the regression model (table IV), we observed that in the total of the elderly patients, by the decreasing order of the odds ratio values, the risk factors for atherosclerotic complications were: triglycerides level  $\geq 250\text{mg/dL}$  (odds ratio = 2.27), systemic arterial hypertension (odds ratio = 2.17), and male sex (odds ratio = 2.14).

For the men, the risk factors were LDL-cholesterol level  $\geq 160\text{mg/dL}$  (odds ratio = 2.82), diabetes mellitus (odds ratio = 2.57), HDL-cholesterol level  $< 35\text{mg/dL}$  (odds ratio = 2.17), and systemic arterial hypertension (odds ratio = 2.09); for the women, the risk factors were: triglycerides level  $\geq 250\text{mg/dL}$  (odds ratio = 2.17) and systemic arterial hypertension (odds ratio = 1.97).

As for the adequacy of each one of the three models of logistic regression, we found that the likelihood ratio test for the final model of the total of the elderly patients was 22.73 ( $p=0.0000$ ), 19.02 ( $p=0.0008$ ) for the men, and 6.99

Table I – Prevalence and crude odds ratio (OR) for the presence of complications of atherosclerosis in 516 elderly patients according to biological-behavioral variables

Variables	N°	Total		Complications of atherosclerosis				
		N°	%	N°	%	OR	p	$CI_{95\%}$
Sex								
Female	364		70.5	65	17.9	1		
Male	152		29.5	45	29.6	1.93	0.003	1.22 - 3.07
SAH								
<160 e/ou 95	168		32.6	24	14.3	1		
$\geq 160$ e/ou 95	348		67.4	86	24.7	1.97	0.007	1.20 - 3.23
TC								
<240mg/dl	352		68.2	74	21.0	1		
$\geq 240\text{mg/dl}$	164		31.8	36	22.0	1.06	0.811	0.67 - 1.66
LDL-C								
<160mg/dl	338		65.5	67	19.8	1		
$\geq 160\text{mg/dl}$	178		34.5	43	24.2	1.29	0.254	0.83 - 2.00
HDL-C								
$\geq 35\text{mg/dl}$	442		85.7	88	19.9	1		
<35mg/dl	74		14.3	22	29.7	1.70	0.056	0.95 - 3.05
Triglycerides								
<250mg/dl	475		92.0	96	20.2	1		
$\geq 250\text{mg/dl}$	41		8.0	14	34.2	2.05	0.040	1.03 - 4.05
Diabetes mellitus								
Absent	416		80.6	81	19.5	1		
Present	100		19.4	29	29.0	1.69	0.038	1.03 - 2.77
Tabacco smoking								
No	477		92.4	102	21.4	1		
Yes	39		7.6	8	20.5	0.95	0.898	0.42 - 2.13
BMI								
$\leq 27.5$	308		59.7	63	20.5	1		
$> 27.5$	208		40.3	47	22.6	1.14	0.560	0.74 - 1.74

CI- confidence interval; SAH - systemic arterial hypertension; TC - total cholesterol; LDL-C - LDL-cholesterol; HDL-C - HDL-cholesterol; DM- diabetes mellitus; BMI - body mass index.

**Table II – Prevalence and crude odds ratio (OR) for the presence of complications of atherosclerosis in 152 elderly men according to biological behavioral variable**

Variables	Total		Complications of atherosclerosis				
	N°	%	N°	%	OR	p	IC <sub>95%</sub>
SAH							
<160 x 95	59	38.8	11	18.6	1		
≥160 x 95	93	61.2	34	36.6	2.51	0.020	1.53 - 5.48
TC							
<240mg/dl	120	79.0	31	25.8	1		
≥240mg/dl	32	21.1	14	43.8	2.23	0,052	0.99 - 5.02
LDL-C							
<160mg/dl	112	73.7	28	25.0	1		
≥160mg/dl	40	26.3	17	42.5	2.22	0.040	1.04 - 4.74
HDL-C							
≥35mg/dl	122	80.3	32	26.2	1		
<35mg/dl	30	19,7	13	43.3	1.30	0.070	0.94 - 1.81
Triglycerides							
<250mg/dl	142	93.4	40	28.2	1		
≥250mg/dl	10	6.6	5	50.0	2.55	0.156	0.70 - 9.28
DM							
Absent	121	79.6	29	23.9	1		
Present	31	20.4	16	51.6	3.38	0.004	1.49 - 7.67
Tobacco smoking							
No	135	88.8	41	30.4	1		
Yes	17	11.2	4	23.5	0.71	0.562	0.22 - 2.29
BMI							
≤27.5	104	68.4	29	27.9	1		
>27.5	48	31.6	16	33.3	1.29	0.494	0.62 - 2.70

CI- confidence interval; SAH - systemic arterial hypertension; TC - total cholesterol; LDL-C – LDL-cholesterol; HDL-C - HDL-cholesterol; DM- *diabetes mellitus*; BMI - body mass index.

**Table III – Prevalence and crude odds ratio (OR) for the presence of complications of atherosclerosis in 364 elderly women according to biological-behavioral variables**

Variables	Total		Complications of atherosclerosis				
	N°	%	N°	%	OR	p	IC <sub>95%</sub>
SAH							
<160 x 95	109	30.0	13	11.9	1		
≥160 x 95	255	70.1	52	20.4	1.89	0.056	0.98 - 3.64
TC							
<240mg/dl	232	63.7	43	18.5	1		
≥240mg/dl	132	36.3	22	16.7	0.88	0.655	0.50 - 1.55
LDL-C							
<160mg/dl	226	62.1	39	17.3	1		
≥160mg/dl	138	37.9	26	18.8	2.11	0.702	0.64 - 1.93
HDL-C							
≥35mg/dl	320	87.9	56	17.5	1		
<35mg/dl	44	12.1	9	20.5	1.21	0.632	0.51 - 2.81
Triglycerides							
<250mg/dl	333	91.5	56	16.8	1		
≥250mg/dl	31	8.5	9	29.0	2.02	0.095	0.89 - 4.63
DM							
Absent	295	81.0	52	17.6	1		
Present	69	19.0	13	18.8	1.08	0.813	0.55 - 2.13
Tobacco smoking							
No	342	94.0	61	17.8	1		
Yes	22	6.0	4	18.2	1.02	0.967	0.33 - 3.13
BMI							
≤27.5	204	56.0	34	16.7	1		
>27.5	160	44.0	31	19.4	1.20	0.503	0.70 - 2.06

CI- confidence interval; SAH - systemic arterial hypertension; TC - total cholesterol; LDL-C – LDL-cholesterol; HDL-C - HDL-cholesterol; DM- *diabetes mellitus*; BMI - body mass index.

( $p=0.0304$ ) for the women. Therefore, all the likelihood ratio test values were significant, permitting the affirmative that the models were adequate.

This significance of the likelihood ratio test in the three models of logistic regression was an important criterion for identifying the variables considered risk factors for of-atherosclerosis. Another classic criterion was the significance of the variable individually, in our case by the  $p$  value of Wald (table IV).

The identification of the risk factors was accomplished, therefore, by the interaction of the above two criteria, plus the capacity of the variable to influence the odds ratio of the others, with its removal or inclusion in the model.

## Discussion

Identification of risk factors for atherosclerosis is essential for the adoption of preventive measures. This study evaluated 516 elderly outpatients of both sexes, in order to determine the impact of systemic arterial hypertension, dyslipidemia, diabetes mellitus, tobacco smoking, and obesity, considered risk factors of cardinal importance that can be controlled or even removed.

Among the individuals analyzed, 21.3% presented with at least one complication of atherosclerosis. Although in this age group, the prevalence of atherosclerotic disease has shown an important increase in women<sup>4-7</sup>, this study showed that after age 60 a significantly greater prevalence of complications of atherosclerosis persists among men (29.6% x 17.9%; OR=1.93; CI<sub>95%</sub>=1.22-3.07).

Systemic arterial hypertension was the most prevalent of the risk factors analyzed, affecting 61.2% of the men and 70.1% of the women, and the difference in prevalence

between the two sexes was statistically significant. These values were similar to those observed by the National Health and Nutrition Examination Survey (NHANES-II)<sup>21,22</sup> in the United States where the authors, using the same diagnostic criteria, observed in elderly patients systemic arterial hypertension in 59.2% and 66.2% of white men and women, and in 67.1% and 82.9% of black men and women, respectively.

Systemic arterial hypertension is considered one of the most important causes of morbidity and mortality in the adult population of the civilized world, both by its high prevalence and by its complications.

In the Framingham Study, higher morbidity and mortality by cardiovascular and cerebrovascular disease were found in hypertensive patients, but the risk was lower in the elderly<sup>22,23</sup>. Comparing the elderly patients of both sexes, Hall<sup>24</sup> observed that with the same level of blood pressure, the risk of atherosclerotic complications was greater in men.

In our study, the importance of systemic arterial hypertension as a risk factor for atherosclerosis and its complications was demonstrated by univariate analysis and confirmed by multivariate analysis both for the total of the elderly patients and for the men and the women separately. Thus, systemic arterial hypertension was the only factors that proved to be of risk in the three groups of subjects studied. This fact, along with the high prevalence of systemic arterial hypertension, shows the great importance of this illness as a cause of atherosclerotic complications in the elderly.

The plasma lipids as risk factors for atherosclerotic disease have been extensively studied in young and middle-aged adults. However, few investigations have been conducted in the elderly<sup>3,8,9,25</sup>.

The prevalences of total cholesterol and LDL-cholesterol were significantly greater among women. These results are

Table IV – Multivariate analysis\* for factors associated with complications of atherosclerosis in univariate analysis

Fatores	Complications of atherosclerosis OR	$\rho$	IC <sub>95%</sub>
<b>All the elderly patients</b>			
Sex	2.14	0.001	1.36 - 3.36
Systemic arterial hypertension	2.17	0.003	1.31 - 3.61
Diabetes mellitus	1.43	0.175	0.85 - 2.39
Triglycerides $\geq 250$ mg/dl	2.27	0.023	1.12 - 4.59
HDL-cholesterol $< 35$ mg/dl	1.82	0.350	0.63 - 4.02
LDL-cholesterol $\geq 160$ mg/dl	1.42	0.125	0.91 - 2.24
Body mass index $> 27.5$	1.14	0.574	0.73 - 1.78
<b>Elderly men</b>			
Diabetes mellitus	2.57	0.034	1.08 - 6.16
Systemic arterial hypertension	2.09	0.085	0.90 - 4.84
LDL-cholesterol $\geq 160$ mg/dl	2.82	0.015	1.23 - 6.46
Total cholesterol $\geq 240$ mg/dl	1.30	0.646	0.43 - 3.93
HDL-cholesterol $< 35$ mg/dl	2.17	0.094	0.86 - 5.39
Triglycerides $\geq 250$ mg/dl	1.50	0.583	0.36 - 6.30
Body mass index $> 27.5$	0.82	0.641	0.36 - 1.87
<b>Elderly women</b>			
Systemic arterial hypertension	1.97	0.044	1.02 - 3.81
Triglycerides $\geq 250$ mg/dl	2.17	0.069	0.94 - 5.03
Body mass index $> 27.5$	1.15	0.615	0.66 - 1.99

\* Adjusted for all the variables included in the final model. Likelihood ratio statistics. All the elderly patients (6 df) = 22.73,  $\rho=0.0000$ ; elderly men (6 df) = 19.02,  $\rho=0.0008$ ; elderly women (2 df) = 6.99,  $\rho=0.0304$ . OR- odds ratio; CI- confidence interval.

in agreement with a previous study carried out in the Geriatric Service that showed that total cholesterol and LDL-cholesterol increase in both sexes with advancing age, but mainly in women<sup>25</sup>.

In our study we observed by univariate analysis that total cholesterol  $\geq 240$ mg/dL and LDL-cholesterol  $\geq 160$ mg/dL were risk factors for complications of atherosclerosis among men, but not among women, nor in the whole group of elderly patients. Multivariate analysis partially confirmed these results, because only LDL-cholesterol was shown to be a risk-factor in men.

The role of total cholesterol and LDL-cholesterol as risk factors for atherosclerosis in the elderly is a subject open for discussion<sup>26</sup>. Several studies have reached the conclusion that they are important risk factors for coronary artery disease; however, these studies also agree on their lesser impact in the elderly as compared with middle-aged subjects<sup>12,27-31</sup>.

Papaléo Netto et al<sup>9</sup> compared total cholesterol and LDL-cholesterol levels of 31 aged patients of both sexes with atherosclerotic complications with total cholesterol and LDL-cholesterol levels of a group of healthy elderly individuals and found no significant difference between the two groups.

Krumholz et al<sup>11</sup> followed 997 individuals of both sexes 70 years or older for four years and did not find any correlation between total cholesterol  $\geq 240$ mg/dL and higher mortality due to coronary artery disease or more frequent hospital admissions for acute myocardial infarction and unstable angina.

According to La Rosa<sup>28</sup> and Crouse<sup>29</sup>, LDL-cholesterol may be more harmful to men. Studies performed in primates suggest that the presence of circulating estrogen in women could may interfere with the uptake of LDL-cholesterol by the artery wall, which may be related to its antioxidant effect<sup>32</sup>.

Capurso<sup>33</sup> believes that the conflicting results obtained by several investigators may be caused by the fact that in the elderly, dyslipidemia is frequently related to nongenetic causes, such as hypothyroidism and the use of drugs like diuretics. These secondary forms of dyslipidemia could be less related to cardiovascular risk, because they are of later onset and thus exert atherogenic effect for a shorter period of time.

In 19.7% of men and 12.1% of women, plasma HDL-cholesterol was below 35mg/dL, and this difference was statistically significant.

In a previous study of the Geriatric Service, Figueira et al<sup>25</sup> observed that HDL-cholesterol levels diminished with age in both sexes, but more markedly in males.

The analysis of the importance of HDL-cholesterol as a risk factor for atherosclerotic vascular disease in the elderly has been done in several studies<sup>34-37</sup>. In the Framingham study, HDL-cholesterol  $< 35$ mg/dL correlated with a greater prevalence of cardiovascular disease in elderly patients of both sexes<sup>34</sup>. According to La Rosa<sup>28,35</sup> the HDL-cholesterol levels, usually higher in women, could be one of the reasons why they have a lesser risk of atherosclerotic

complications than men. On the other hand, the Bronx Aging Study showed HDL-cholesterol  $< 35$ mg/dL as an important risk factor for coronary artery disease only in men<sup>36</sup>.

In our study, we observed that HDL-cholesterol  $< 35$ mg/dL corresponded to a greater prevalence of atherosclerotic complications in men (43.3%) as compared with women (20.5%). The comparison, by univariate analysis, between the subjects with HDL-cholesterol  $< \text{and} \geq 35$ dL, as to the presence of atherosclerotic complications did not show any difference in the women, but in the men the prevalences of complications were 43.3% and 26.2%, respectively. The comparative study by multivariate analysis also showed that HDL-cholesterol  $< 35$ mg/dL was a risk factor for atherosclerotic complications only in men.

It has been demonstrated by comparing normal individuals, both young and aged, that triglycerides rise significantly during the aging process in both sexes<sup>25</sup>. In our study, only 8.0% of the patients showed triglycerides levels of  $\geq 250$ mg/dL, with no significant difference between men and women.

The importance of triglycerides as a risk factor for atherosclerosis, both in elderly and middle-aged individuals, and its complications has been debated in the literature<sup>36,38</sup>, with a good deal of controversy. Recently, several studies have called attention to triglycerides as an important risk factor of cardiovascular disease, independently of the association with other factors such as diabetes mellitus and low HDL-cholesterol<sup>39-41</sup>.

In our study, analyzing the total of patients by univariate analysis, we observed a significant association between triglycerides  $\geq 250$ mg/dL and atherosclerotic complications. When the male and female subjects were analyzed separately, in spite of the greater prevalence of atherosclerotic complications in those with triglycerides  $\geq 250$ mg/dL in relation to those with triglycerides  $< 250$ mg/dL (respectively 50.0% x 28.2% and 29.0% x 16.8%), no significant difference was noted. However, we have to emphasize the odds ratio value observed in women (OR=2.02;  $p=0.095$ ;  $CI_{95\%}=0.89-4.63$ ). Multivariate analysis confirmed these results, maintaining triglycerides  $\geq 250$ mg/dL as a risk factor for the total of elderly patients and for the women.

Diabetes mellitus was diagnosed in 20.4% of the men and 19.0% of the women, with no significant difference between the two sexes.

In the Framingham Study, the risk of death by cardiovascular disease was 1.7 times greater in men and 3.3 times greater in women with diabetes, when compared with that in nondiabetic patients<sup>42</sup>. The Tecumseh Study showed even more striking results, with the risk of atherosclerotic complications 1.9 times greater in diabetic men and 5.3 times greater in diabetic women, when compared with nondiabetic patients<sup>43</sup>.

In the present study, we showed by univariate analysis a significant association between diabetes mellitus and the presence of atherosclerotic complications among the patients as a whole and among the men separately; this was confirmed by multivariate analysis only in the men. In the women, univariate analysis showed that the prevalence of

atherosclerotic complications among diabetic and nondiabetic patients was practically equal (18.8% x 17.6%; OR = 1.08;  $p=0.813$ ;  $CI_{95\%}=0.55-2.13$ ).

The fact that diabetes mellitus, in spite of its high prevalence (19.0%), did not prove to be a risk factor among the women is in disagreement with the data in the literature, but this could mean that, among the elderly women of our group, other risk factors such as age causing senile atherosclerosis, and estrogen deficiency, may have been of primordial importance.

As for tobacco smoking, the behavior of the 516 elderly patients varied a great deal. Many were past smokers but had abandoned the smoking habit for variable periods of time. The number of cigarettes consumed per day also had great variation. For these reasons, two groups were considered: a) smokers, made up of patients who were smoking at the time of the interview, and b) nonsmokers, made up of patients who had never smoked.

It was shown that the prevalence of smokers in this outpatient population was low (7.6%), with a significant predominance of the men (11.2%) in relation to the women (6.0%).

The smoking habit is frequently associated with other factors related to atherosclerosis and its complications, such as lower HDL-cholesterol levels, elevation of blood viscosity, hyper-fibrinogenemia, greater platelet aggregation, and anti-estrogen effect<sup>44,45</sup>.

The role of tobacco smoking as a risk factor was demonstrated in experimental, clinical, and anatomopathological studies. The deleterious changes caused by tobacco smoking are proportional to the number of cigarettes consumed, the duration of the smoking habit and the age of onset of smoking<sup>12,46,47</sup>.

Among elderly smoker the risk of atherosclerotic complications seems lower than that observed in middle-aged smokers, but still higher than that in elderly nonsmokers<sup>12,45</sup>.

The low prevalence of smokers among the elderly patients in our study, much lower than that observed in younger age groups, could mean that the patients more susceptible to the harmful effects of smoking had complications and died prematurely. This supposition plus the fact that during the aging process other factors such as age itself may predominate could explain why smokers and nonsmokers of both sexes showed no difference in the prevalence of atherosclerotic complications.

The relationship between obesity and atherosclerotic complications has been a subject of controversy. Several studies have suggested this association; however, only a few demonstrated a specific effect of obesity as a risk factor, because it is usually associated with other factors, such as

systemic arterial hypertension, dyslipidemia and diabetes mellitus.

Our study observed that obesity, defined by a body mass index  $>27.5$ , was present in 31.6% of the men and 44.0% of the women; this difference was statistically significant.

By univariate analysis, no significant difference was found between complications of atherosclerosis in obese and nonobese patients in both sexes. It is possible that an analysis directed to the distribution of body fat could yield a different result, because individuals with abdominal obesity present with a greater prevalence of complications than those with gluteo-femoral obesity<sup>48,49</sup>.

In summary, among the elderly patients analyzed in the present study, the prevalence of atherosclerotic complications was significantly greater in the men compared with that in the women.

The data obtained showed that in the elderly; the risk factors for atherosclerosis and its complications have a different prevalence between males and females.

Comparative analysis revealed that systemic arterial hypertension, total cholesterol  $\geq 240$ mg/dL, LDL-cholesterol  $\geq 160$ mg/dL, and body mass index  $>27.5$  were more frequent in the women, HDL-cholesterol  $<35$ mg/dL and tobacco smoking were more frequent in the men, and no difference was noted in relation to triglycerides  $\geq 250$ mg/dL and diabetes mellitus.

The risk of complications of atherosclerosis in relation to each one of the factors analyzed also showed an important difference between elderly men and women. Thus, LDL-cholesterol  $\geq 160$ mg/dL, HDL-cholesterol  $<35$ mg/dL, diabetes mellitus, and systemic arterial hypertension were risk factors for the men, but triglycerides  $\geq 250$ mg/dL and systemic arterial hypertension were risk factors for the women.

Based on these findings, we can affirm that the factors considered of risk for atherosclerosis and its complications in the elderly have different consequences in men and women. Therefore, the evaluation of these factors should be done by different weights in each sex, so that adequate preventive and therapeutic measures can be taken in the respective situation.

The results of this investigation also suggest, confirming the opinion of other authors<sup>2,50</sup>, that the order of importance of the risk factors can change with the aging process, as in the case of tobacco smoking for example.

Undoubtedly, further investigations are necessary to evaluate adequately the importance of the risk factors for atherosclerosis in elderly patients, comparing people of different age groups, including the very elderly, studying patients of different socio-economic conditions, and analyzing the impact of preventive and therapeutic measures on the prevalence of the risk factors and their complications.

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