Influence of Overall and Abdominal Adiposity on C-Reactive Protein Levels in Elderly Women

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Summary

Objective: To investigate how overall and abdominal adiposity, measured by waist circumference (WC), body mass index (BMI), and sum of skinfolds (∑SK), affect plasma C-reactive protein levels (CRP) in elderly women.

Methods: Study sample consisted of 387 women older than 60 years (mean age 68.9; standard deviation 5.9 years). BMI, WC, ∑SK, and CRP levels were all measured. One-way ANOVA was performed to detect differences in study variables among the CRP levels investigated. Logistic regression analysis was used to determine the influence of body fat measurements on CRP levels. The significance level was set at $p < 0.05$.

Results: The analysis of variance showed that mean WC was lower in women with normal CRP levels, as compared to those with high CRP levels. Logistic regression analysis examined the influence of BMI, WC, and ∑SK quartiles on CRP levels, yielding the following results: only WC was predictive of elevated CRP levels, its highest quartile (cut-off point of 94.0 cm) showing levels nearly two times higher than its lowest quartile (odds ratio = 2.23; 95% confidence interval = 1.92-4.18; $p = 0.012$).

Conclusion: The results of this study indicate that abdominal adiposity is a strong predictor of elevated CRP levels. (Arq Bras Cardiol 2007;88(6):624-628)

Key words: Adiposity; risk factors; atherosclerosis; women.

Introduction

Cardiovascular diseases have been a constant cause for concern of modern civilization, and they are the leading cause of death in the Western world and in the Brazilian population[1,2]. Most cardiovascular disorders result from atherosclerosis, a condition that may be influenced by risk factors such as obesity, smoking, diabetes, hypertension, and sedentariness[3,4].

The pathogenesis of atherosclerosis involves a chronic, persistent inflammatory process of the arterial wall, thereby activating cell proliferation, forming an atheroma and, ultimately, the fibroatheroma[3,5,6].

The development of atherosclerosis is asymptomatic and increases with age. Chronic atherosclerosis is a slow, progressive condition, but there are also acute cases. Clinical diagnosis depends on the progression of the atherosclerotic plaque, which, in turn, may be affected by both aging and factors that predispose to thrombosis, as well as genetic background and environmental factors[6].

Persistent inflammation of the arterial wall in the atherosclerotic process tends to elevate plasma C-reactive protein (CRP) levels, an acute-phase protein that increases in response to inflammation and infection[7]. For this reason, CRP measurement may be used as a diagnostic tool for predicting cardiovascular risks[8], provided it is performed in the absence of other inflammations and infections.

High plasma CRP levels are an independent risk factor for cardiovascular and coronary artery diseases[9,10]. Hypertension and diabetes may also be related to increased CRP levels[9]. Nevertheless, body adiposity seems to be the risk factor most related to these changes[11-16].

Excess (body) fat, particularly visceral fat, is an indicator of metabolic disorders, such as hypertriglyceridemia, high level of low-density lipoprotein cholesterol (LDL-cholesterol), low level of high-density lipoprotein cholesterol (HDL-cholesterol), and greater insulin resistance and glucose intolerance, all of which may potentiate atherosclerosis.

The relationship between abdominal adiposity and CRP levels increases when body fat distribution is measured by waist circumference (WC)[17,18]. Waist and hip circumferences have shown correlations of 0.62 and 0.65, respectively, with CRP levels adjusted for age, while body mass index (BMI) has shown lesser association (r = 0,14)[19]. Therefore, CRP appears to be a method that is easy to use and reproduce, both in clinical practice and epidemiological studies. The aim of this study is to determine how overall adiposity and abdominal

adiposity, measured by BMI, total sum of skinfolds ($\sum$SK), and waist circumference (WC), affect CRP levels in elderly women.

Methods

This was a cross-sectional, observational, descriptive study. Data were collected between April and July, 2006.

Sample population - In order to select a stratified sample, the following steps were taken: 1) Registering of community groups in Curitiba, state of Paraná, a joint effort with institutions focused on recreational activities for the population of the respective geographic area. 2) Mapping of all groups registered with the eight districts of the municipality. 3) Simple random selection of the groups that would be invited to participate in the study, per district. 4) Visit to the groups to explain study procedures and invite voluntary participation not only of the subjects but also of their family members and close friends.

After sample selection, as described, a timeframe for data collection was developed. Study sample included 387 women (mean age 68.9; standard deviation 5.9) who were 60 years or older at the time data were collected.

After being fully informed of the purpose of the study, as well as its procedures, benefits and potential risks, each subject signed an informed consent for voluntary participation in the study. The study protocol was approved by the Ethics Committee of the Setor de Ciências Biológicas of the Universidade Federal do Paraná, in accordance with the guidelines set forth in the Helsinki Declaration and also with Resolution No 196/96 of the Conselho Nacional de Saúde (National Health Board) for research involving human subjects.

Instruments and procedures - To avoid any influence of circadian variations, all measurements were performed at the same time of the day (8:00 to 10:00).In addition, subjects were instructed to refrain from vigorous physical activity on the preceding day and not to eat for two hours prior to the tests. Measurements were performed at the Physical Education Department - Physiology Laboratory of the Research Center Research Unit for Exercise and Sports of the Universidade Federal do Paraná.

Study variables - Anthropometric variables were taken as described by Lohman et al.[20]. Body height (in centimeters) was measured with subjects standing barefoot, feet together, and wearing as little clothing as possible. Also, patients were instructed to hold their breath and keep their head at 90 degrees, according to the Frankfurt plane, with heels, pelvic girdle, shoulder girdle, and occipital region against a wall-mounted stadiometer (SANNY, STANDARD model, accurate to 0.1 cm). Body mass (in kilograms) was measured with subjects standing barefoot and wearing as little clothing as possible. Body weight should be evenly distributed between both legs while standing on the weighing scale (2096 PP TOLEDO, accurate to 0.1 kg). Body mass index was calculated from the formula weight in kilograms divided by height in meters squared. Waist circumference (in centimeters) was measured midway between the iliac crest and the lowest rib, using a nonstretch measuring tape accurate to 0.1 cm.

Skinfolds were measured to the nearest 0.05 mm using a Lange skinfold caliper at the following anatomical sites: triceps, abdomen, supra-iliac, mid-thigh, and mid-calf, all on the right side of the body. Body fat was estimated according to the Jackson and Pollock's equation[21].

To prevent inter-rater variability, all anthropometric variables (BMI, height, WC, and skinfolds), in all subjects, were taken by the same previously trained rater.

C-reactive protein levels were determined by a particle-enhanced turbidimetric method using the COBAS MIRA PLUS spectrophotometer (Roche Diagnostics), with calibrator and control serum supplied by Biosystem (Bayer®).

Confounding variables – The presence of diseases was based on self-report through the following question: "Have you been diagnosed by your doctor as having… (disease)? Thus, this variable was coded as dichotomous (yes/no).

Statistical analysis - The Kolmogorov-Smirnov normality test was applied, indicating that variables had a parametric distribution. Measures of central tendency and variability were used to determine descriptive values (mean and standard deviation), as well as absolute and relative frequencies. One-way ANOVA was used to detect differences between independent variables in the CRP concentration ranges of $\leq$ 1.0 mg/dL and > 1.0 mg/dL.

Logistic regression analysis, adjusted for confounding variables, was used to check the relationship between the independent variables and CRP levels, which were treated as dichotomous variables (0 = CRP $\leq$ 1.0 mg/dL and 1 = CRP > 1.0 mg/dL). Our results indicate odds ratio and 95% confidence interval; the significance level was set at less than 0.05.

Confounding variables – Self-reported heart disease, hypertension, rheumatoid arthritis, diabetes, cancer, and tendinitis were included in the model as dichotomous variables, except for age, which was included as continuous variable. The other independent variables were treated as categorical and divided in quartiles, and the first quartile served as reference.

Data analysis was performed using Statistical Package for the Social Sciences (SPSS 13.0 for Windows).

Results

Table 1 presents means and frequencies according to CRP levels. The results demonstrate that the majority of population is within normal ranges (54.1%).

Table 2 shows the frequencies of self-reported diseases according to CRP levels. Hypertension was the most common disease, striking nearly half of the sample. However, less than 20% of the subjects reported heart disease.

Table 3 shows descriptive values for age and body fat, according to CRP levels. Subjects with values $\leq$ 1.0 mg/L are within normal ranges, while subject with values > 1.0 mg/L are at higher cardiovascular risk.

Mean WC values were lower in subjects with normal CRP levels. However, no significant differences were found in other measures of body fat between the CRP levels investigated.

The results of the logistic regression analysis are shown in Table 4. Only the highest quartile of waist circumference was found to be associated with increased CRP levels (> 1.0 mg/l), as compared to the lowest quartile; therefore, the risk of having CRP levels above the normal range (odds ratio 2.23) is twice as high in subjects with WC greater than 94.0 cm. Age, self-reported diseases, BMI, and ∑SF were not predictive of CRP levels.

Discussion

Obesity, which has been described as a secondary cardiovascular risk factor, is usually related to metabolic changes, hypertension, type-2 diabetes, and dyslipidemias[22]. These abnormalities contribute to the development of atherosclerosis[6,23,24]. In addition to its relationship with these factors, obesity is directly related to CRP levels[25].

Our results corroborate these findings, although only abdominal fat has been associated with increased CRP levels, regardless of the confounding variables, whereas BMI and ∑SK have shown no significant association. Nevertheless, the relationship between BMI and CRP levels has been demonstrated in epidemiological studies [11,13].

Body fat distribution based on WC shows a more accurate relationship with elevated CRP levels in overweight subjects than other measurements of overall adiposity, such as BMI or ∑SF[17,19,26]. However, waist-to-hip ratio (WHR), another method for assessing abdominal adiposity, seems to predict mortality causes, in addition to being associated with metabolic changes related to excess body fat in Brazilian elderly women[22,27]. These findings demonstrate that excess abdominal fat may affect general health in elderly women.

In a study correlating WC with atherosclerosis progression, subjects with waist circumference greater than 93 cm had increased carotid artery intima-media thickness (*p* = 0.035), as well as higher plaque size (*p* = 0.013)[17].   In another study on the risks associated with abdominal fat, a significant correlation was found between WC and CRP levels (0.37; *p* < 0.0001)[26]. In the present study, subjects with WC equal to or greater than 94.0 cm were twice as likely to have elevated CRP levels (odds ratio 2.23; 95% CI: 1.92-4.18) than subjects with WC less than 80.0 cm.

According to Ridker[28], CRP levels < 1, between 1 and 3, and > 3 mg/L are associated with low, moderate, and high cardiac risks, respectively. The highest quartile of waist circumference (≥ 94.0 cm), as demonstrated by regression analysis, has moderate cardiac risk. In this sample, however, 17.8% of these subjects were classified as having high cardiac risk (CRP > 3 mg/L; n = 69) (Table 1).

These reference values indicate that most elderly women in this study seem to be healthy, despite reporting several diseases; the diseases reported, however, failed to influence the analysis. Still, women with the largest WC were found to have the highest cardiovascular risk.

The metabolic disorders that usually come with this type of adiposity may explain the correlation between abdominal fat and CRP levels[17,29]. The primary concern regarding overweight subjects with high CRP levels is related with the development of atherosclerosis, since the low-level, persistent, chronic inflammatory process of the arterial wall is described as the main cause of endothelial dysfunction and insulin resistance[6,25].

C-reactive protein levels have shown to be independent predictors for mortality from coronary artery disease in patients with type-2 diabetes, and are positively associated with overall and cardiovascular mortality[30,31].

Today, obesity is highly prevalent in most countries, regardless of age, and this condition may cause a number of health problems, as stated previously. This may increase public health costs, in addition to making the elderly less functional and more vulnerable to other diseases, thereby triggering

Table 1 – Descriptive values for C-reactive protein

CRP	< 1.0 mg/L	> 1.0 mg/L and ≤ 3.0mg/L	> 3.0 mg/L
Absolute (relative) frequency	209 (54.1%)	109 (28.1%)	69 (17.8%)
Minimum-maximum	*	1.2-3.0	3.1-14.2
Mean (standard deviation)	*	2.2 (0.5)	4.6 (1.9)

* This mean could not be calculated because of the method used to measure CRP levels. CRP- C-reactive protein.

Table 2 – Absolute and relative frequencies (between parentheses) of self-reported diseases according to C-reactive protein concentration ranges.

	≤ 1.0 mg/L	> 1.0 and < 3.0 mg/L	3.0 mg/L
Heart disease	34 (17.2%)	23 (21.3%)	11 (16.2%)
Hypertension	116 (58.6%)	62 (57.4%)	35 (51.5%)
Rheumatoid arthritis	63 (31.8%)	31 (28.7%)	23 (33.8%)
Diabetes	32 (16.2%)	13 (12.50)	9 (13.2%)
Cancer	7 (3.5%)	4 (3.7%)	1 (1.5%)
Tendinitis	15 (7.6%)	4 (3.7%)	5 (7.4%)

Table 3 – Descriptive values (mean and standard deviation, between parentheses) according to C-reactive protein level (CRP mg/L).

CRP	< 1.0 mg/L	> 1.0 mg/L
Age (years)	60.3-84.1 68.4 (5.5)	60.0-87.5 69.5 (6.3)
Waist circumference (cm)	63.0-114.0 85.2 (9.7)	64.0-110.0 87.7 (9.1)*
BMI (kg/m2)	17.4-44.6 27.9 (4.5)	19.0-39.4 28.6 (4.0)
∑SF (mm)	52.0-239.0 151.9 (34.8)	76.0-254.0 157.9 (33.3)
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* ANOVA- differences between levels; p < 0.05. CRP- C-reactive protein; BMI- body mass index; ∑SF- sum of skinfolds.

Table 4 – Binary logistic regression analysis.

		Binary regression*		
	Cut-off points	Odds ratio	95% CI	p
WC	> 80.0 and < 87.0 ≥ 87.0 and < 94.0 ≥ 94.0	1.26 1.10 2.23	0.67-2.37 0.60-2.01 1.92-4.18	0.468 0.739 0.012
BMI	≥ 17.0 and < 23.0 ≥ 23.0 and < 27.0 ≥ 27.0	0.79 1.22 1.69	0.44-1.43 0.67-2.22 0.91-3.16	0.445 0.511 0.095
∑SF	≥ 122 and < 151 ≥ 151 and ≥ 176 ≥ 176	0.88 1.65 1.51	0.51-1.52 0.90-3.04 0.81-2.81	0.660 0.104 0.189

* Binary regression was performed after adjustment for confounding variables, but no variable was found to influence the analysis: age (p = 0.050); heart disease (p = 0.461); hypertension (p = 0.301); rheumatoid arthritis (p = 0.608); diabetes (p = 0.138); cancer (p = 0.718); and tendinitis (p = 0.381). 95% CI- confidence interval of 95%; WC- waist circumference; BMI- body mass index; ∑SF- sum of skinfolds.

other organic disorders. Therefore, controlling CRP levels in subjects with high abdominal fat may be effective to lower atherogenic and cardiovascular risks.

Limitations

The study sample consisted of elderly women living near the city of Curitiba, state of Paraná, who attended community groups. Thus, it did not reach subjects with a higher level of dependence, who usually remain in their homes. Abdominal fat was based solely on WC. Confounding variables, except for age, were determined by the self-report method, which, despite being widely used, may under- or overestimate the results. Moreover, CRP levels could have been measured using a high-sensitivity assay (hs-CRP); however, the method used in this study has been described in several studies assessing

cardiovascular risk.

To perform a binary logistic regression analysis, the dependent variable must be defined as dichotomous. Therefore, the CRP value of 1.0 mg/dL was used as the cut-off point, lower values being defined as normal and greater values, as increased risk. We suggest, therefore, that further studies be conducted using other indicators of abdominal obesity, methods more sensitive to determine CRP levels, and other cut-off points for different risk levels, to improve our understanding of the influence of body fat on CRP values.

Conclusions

It was concluded that, in this population of elderly women, abdominal fat was predictive of abnormal CRP

levels, regardless of the self-reported diseases. However, other indicators of overall adiposity, such as BMI and ∑SF, had no influence on CRP levels. This finding shows that women with greater abdominal fat are at higher cardiovascular risk.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any graduation program.

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