

Gender-Related Associations of Increased Body Mass Index with Clinical and Laboratory Variables in Individuals with no Evidence of Heart Disease

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Summary

Background: In clinical practice, the patients we care for display a wide range of body mass indices, from lean to obese. This finding may be the sole apparent clinical abnormality.

Objective: To evaluate clinical and laboratory variables that might be associated with increased body mass index in asymptomatic men and women with no evidence of heart disease, to provide data to substantiate medical recommendations in a study sample from our everyday practice.

Methods: The subjects aged 14 to 74 years (mean 40.6 years), 295 men (43.1%) and 389 women (56.9%) The associations between body mass index stratified by gender and clinical and laboratory variables were analyzed using the Spearman correlation coefficient and multiple linear regression.

Results: The mean body mass index (BMI) did not differ significantly between women (26.15 Kg/m²) and men (26.33 Kg/m²). In the multiple linear regression model, the ratios of total cholesterol/high-density lipoprotein cholesterol (TC/HDL-C) ($\beta = 1.1320$; $p < 0.001$) and serum glucose ($\beta = 0.0233$; $p = 0.023$) were independently correlated with body mass index in women. In men, the variables independently correlated with BMI were the TC/HDL-C ($\beta = 0.793$; $p < 0.001$) and age ($\beta = 0.0464$; $p = 0.030$).

Conclusion: In men and women with no evidence of heart disease, TC/HDL-C increased with body mass index in both genders. Other indices associated with BMI included serum glucose in women and age in men. Clinical and laboratory variables associated with body mass index may differ in relation to gender. (Arq Bras Cardiol 2007;88(6):549-554)

Key words: Body mass index; dyslipidemias/epidemiology; risk factors; public health.

Introduction

Body mass index (BMI) has been defined as weight in kilograms divided by the square of the height in meters (kg/m²) and is a surrogate measure of overweight and obesity in clinical practice and in epidemiological studies¹. Overweight and obesity, evaluated by body mass index, is currently recognized as an important public health problem in several countries^{2,3}, including Brazil⁴, and is associated with increased risk of cardiovascular diseases⁵ among men⁶⁻⁸ and women⁹⁻¹¹. In previous studies, the relationship of body mass index to cardiovascular diseases demonstrated a strong and consistent association with risk factors for cardiovascular diseases, such as high blood pressure, glucose intolerance, diabetes and dyslipidemia¹²⁻¹⁴.

In clinical practice, in addition to patients with increased risk of cardiovascular diseases, we also care for patients of low cardiovascular risk that seek cardiac health evaluation (check

up) and who present a wide range of body mass indices, from lean to obese. In many of these patients, the main abnormality identified in clinical evaluation may be an increase in the body mass index. In addition to medical advice for changes in life style aimed at weight loss, it would be interesting to assess the clinical and laboratory variables associated with increased body mass index to obtain data from patients we care, in order to provide medical advice regarding cardiovascular disease prevention.

We hypothesized that certain clinical and laboratory variables regularly obtained in everyday practice might be associated with increases in body mass index, and that such an association might differ depending on gender.

The objectives of this study were to evaluate clinical and laboratory variables relative to body mass index increases and to evaluate these variables in relation to gender in a cohort of asymptomatic outpatients with no evidence of heart disease after careful clinical and laboratory examinations.

Methods

Type of study and setting - A cohort of asymptomatic individuals, with no evidence of heart disease after careful

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clinical and laboratory examinations, was established in a General Outpatient Clinics Unit of a tertiary care university hospital that provides also primary and secondary levels of care (cardiovascular health examination, second opinion and preoperative cardiac evaluation).

Sample and procedures - The evaluation included careful clinical examination, electrocardiogram and chest X-ray. Ethnic groups were categorized as white, black and mulatto (a person of mixed white and black ancestry). Smoking habits were assessed by questioning during clinical examination and subjects were categorized as either nonsmokers or current smokers. Asymptomatic individuals with normal clinical examination, as well as normal electrocardiogram and chest X-rays, were invited to participate in this study. Individuals who agreed to participate were submitted to further laboratory work-up, including treadmill electrocardiographic exercise stress test and two-dimensional transthoracic Doppler echocardiography.

Laboratory work-up included serum glucose, total cholesterol, high-density lipoprotein cholesterol (HDL-cholesterol), low-density lipoprotein cholesterol (LDL-cholesterol), total cholesterol/HDL-cholesterol ratio, LDL-cholesterol/HDL-cholesterol ratio, triglycerides, uric acid, thyroid-stimulating hormone (TSH), creatinine and urine analysis.

Inclusion criteria - We included in the study asymptomatic Brazilian men and women older than 14 years of age and with normal clinical examination, as well as normal electrocardiogram and chest X-rays.

Exclusion criteria - We excluded individuals with past medical history of cardiovascular disease, systemic hypertension, *Trypanosoma cruzi* infection (Chagas' disease microorganism), diabetes mellitus, TSH < 0.05 or > 8 mg/dl, chronic obstructive pulmonary disease, asthma, renal failure, chronic inflammatory diseases, osteoarticular diseases, chronic anemia or neoplasia, and abnormal echocardiogram or electrocardiographic exercise stress test.

Study population - Six hundred and eighty-four individuals were eligible for the study. Ages ranged from 14 to 74 (mean 40.6) years, 295 (43.1%) were men and 389 (56.9%) women. Five hundred and sixteen individuals (75%) were white, 117 (17.1%) were mulatto, 32 (4.7%) were Asian and 22 (3.2%) were black.

Studied variables - We studied body mass index (kg/m²) in relation to gender, smoking status (by questioning about being nonsmokers or current smokers at the time of the clinical examination), serum glucose (mg/dl), total cholesterol (mg/dl), HDL-cholesterol (mg/dl), LDL-cholesterol (mg/dl), VLDL-cholesterol (mg/dl), total cholesterol/HDL-cholesterol ratio (TC/HDL-C), LDL-cholesterol/HDL-cholesterol ratio (LDL-C/HDL-C), triglycerides (mg/dl).

Statistical analysis - Goodness of fit for normal distribution was evaluated using the Kolmogorov-Smirnov test. Means of age, body mass index, heart rate, systolic and diastolic blood pressure, serum glucose, triglycerides and total and partial cholesterol were compared by gender using the Mann-Whitney test (as distribution of variables was not Normal). Subsequently, the analysis was further detailed to evaluate

body mass index comparing men and women also in relation to smoking status. The relationship between body mass index stratified by gender and other quantitative variables was analyzed using the Spearman correlation coefficient and multiple linear regression analysis.

Variables with $p < 0.20$ in univariate analysis were selected to be included in multiple linear regression model. The multiple linear regression model was developed with the stepwise forward procedure. The independent variable was kept in the final model when p values were < 0.05 . The multiple linear regression model that was developed for the entire sample was also applied in the analysis of each stratum. Final models for each stratum by body mass index and gender were found to be similar (data not shown). In the multiple regression model, log-transformed β results were expressed as 10 ^{β} . Statistical calculations were performed with the Statistical Package for Social Science (SPSS) Statistics Set for Windows (version 10.0).

Ethical aspects - The study protocol was approved by the Human Research Ethics Committee of the Hospital and all patients signed an informed consent.

Results

Six hundred and eighty-four individuals were eligible for the study, 389 (56.9%) being women and 295 (43.1%) men. There were 285 (73%) white women and 228 white men (77%). Eighty-five (22%) women and 75 (25%) men were current smokers. In this study sample, 130 (33.6%) women and 128 (43.2%) men were overweight (BMI 25 – 29 Kg/m²) and 76 (19.4%) women and 167 (43.2%) men were obese (BMI > 30 Kg/m²).

Baseline characteristics of study participants in relation to gender revealed that there was a significant difference in mean values of serum glucose ($p < 0.001$), triglycerides ($p < 0.001$), and HDL-cholesterol ($p < 0.001$) between women and men. Other baseline characteristics of study participants are shown in Table 1.

Comparison of mean body mass index between women (26.15 Kg/m²) and men (26.33 Kg/m²) did not reveal a statistically significant difference. There was neither a statistically significant difference in the comparison of body mass index of women who were smokers in relation to nonsmokers, nor of men who were smokers in relation to nonsmokers (Table 2).

In women and men, univariate analysis revealed a significant correlation between body mass index and age, serum glucose, serum triglycerides and total and partial cholesterol (Table 3).

In multiple regression analysis adjusted by gender, independent variables associated with increased body mass index were identified in men: TC/HDL-C ($\beta = 0.793$; $p < 0.001$) and age ($\beta = 0.0464$; $p = 0.030$); and in women: TC/HDL-C ($\beta = 1.1320$; $p < 0.001$) and serum glucose ($\beta = 0.0233$; $p = 0.023$) (Table 4).

Discussion

In this study sample, no statistical significant difference was

Table 1 - Demographic, clinical and laboratory characteristics of the study participants relative to gender

Variables	Female (n = 389) mean (standard error); median	Male (n = 295) mean (standard error); median	p value ⁽¹⁾
Age (years)	40.9 (0.59); 41	40.3 (0.66); 41	0.534
Body mass index (kg/m ²)	26.15 (0.24); 25.5	26.33 (0.24); 26.0	0.258
Heart rate (beats/min)	70.3 (0.40); 70	67.8 (0.43); 68	< 0.001
Systolic blood pressure (mmHg)	123.5 (0.57); 120	124.4 (0.69); 120.5	0.145
Diastolic blood pressure (mmHg)	78.8 (0.37); 80	80.1 (0.41); 80	0.020
Serum glucose (mg/dl)	90.2 (1.17); 88	95.3 (1.67); 90	< 0.001
Triglycerides (mg/dl)	97.3 (2.81); 82	141.4 (6.24); 112	< 0.001
Total Cholesterol (mg/dl)	195.7 (1.93); 189	199.39 (2.38); 197	0.175
HDL-Cholesterol (mg/dl)	52.6 (0.71); 51	43.0 (0.63); 41	< 0.001
LDL-Cholesterol (mg/dl)	123.8 (1.72); 119	128.5 (2.05); 127	0.058
VLDL-Cholesterol (mg/dl)	19.7 (0.57); 17	26.6 (0.89); 22	< 0.001
TC/HDL-C ratio	3.9 (0.06); 3.8	4.9 (0.09); 4.7	< 0.001
LDL-C/HDL-C ratio	2.5 (0.05); 2.4	3.2 (0.08); 3	< 0.001

⁽¹⁾ Mann Whitney Test. HDL - high-density lipoprotein; LDL - low-density lipoprotein; VLDL - very low-density lipoprotein; TC/HDL-C - total cholesterol/high-density lipoprotein cholesterol; LDL-C/HDL-C - low-density lipoprotein cholesterol/high-density lipoprotein cholesterol.

Table 2 - Comparison of mean body mass index by gender and smoking

Gender	BMI of nonsmokers n (mean; standard deviation)	BMI of smokers n (mean; standard deviation)	p ⁽¹⁾
Women	304 (26.31; 4.94)	85 (25.55; 3.81)	0.362
Men	220 (26.53; 4.13)	75 (25.74; 3.74)	0.093

⁽¹⁾ Mann-Whitney Test. BMI - body mass index.

found in body mass index between women and men, which is in agreement with previous studies¹⁵⁻¹⁷. In other report, body mass index was demonstrated to be influenced by gender¹⁸. Thus, in our practice, increased the body mass index warrants medical advice to both men and women.

Body mass index values in this study sample were within the range of lower body mass index observed in Asian¹⁹ and higher body mass index observed in European²⁰ and American populations²¹. These findings may be related to differences in the characteristics of the studied populations and other demographic and clinical variables. In the outpatient sample we studied, individuals are reaching the body mass index of European and American populations.

There was no significant difference in body mass index when we compared smokers to nonsmokers either in men or in women. Smoking cessation and reduced physical activity were demonstrated to increase the risk of gaining weight in both men and women²². In other study, sedentary lifestyle

in either previous or current smokers and obesity in women were strong risk factors for poor health either as the main effect of each variable or a combined (interactions) effect²³. There was no relationship between body mass index and duration of smoking cessation²⁴. Former smokers had a larger increase in body mass index than those who had never smoked²⁵. This is an interesting finding in our study sample that helps us to counsel patients on the relationship between smoking and body weight.

In our study, age was independently correlated with body mass index in men. In other studies, aging was demonstrated to be associated with an increase in body mass index in men^{26,27}. Even when being overweight does not represent a serious problem in old age, obese elderly people are certainly at risk of disability, morbidity and mortality²⁸. The increase in body mass index related to aging was suggested to be related with cardiovascular disease²⁹. These findings suggest that gender-related factors may participate in weight

Table 3 - Correlation coefficients (r) among body mass index and variables of the study by gender

Variables	BMI of women r (p)	BMI of men R (p)
Age (years)	0.22 (<0.001)	0.18 (0.001)
Serum glucose (mg/dl)	0.35 (<0.001)	0,21 (<0.001)
Triglycerides (mg/dl)	0.28 (<0.001)	0.32 (<0.001)
Total cholesterol (mg/dl)	0.18 (<0.001)	0.25 (<0.001)
HDL-Cholesterol (mg/dl)	-0.25 (<0.001)	-0.20 (0.001)
LDL-Cholesterol (mg/dl)	0.23 (<0.001)	0.19 (0.001)
VLDL-Cholesterol (mg/dl)	0.27 (<0.001)	0.32 (<0.001)
TC/HDL-C ratio	0.34 (<0.001)	0.33 (<0.001)
LDL-C/HDL-C ratio	0.32 (<0.001)	0.27 (<0.001)

BMI - body mass index; HDL - high-density lipoprotein; LDL - low-density lipoprotein; VLDL - very low-density lipoprotein; TC/HDL-C - total cholesterol/high-density lipoprotein cholesterol; LDL-C/HDL-C - low-density lipoprotein cholesterol/high-density lipoprotein cholesterol.

The total cholesterol/HDL-cholesterol ratio in our study sample was independently correlated with body mass index in men and women. We did not detect an independent correlation between total cholesterol, LDL-cholesterol and HDL-cholesterol with body mass index. These findings are in agreement with previous studies among men³⁶ and women³⁷ and with both men and women^{38,39}. Some studies have shown that the total cholesterol/HDL cholesterol ratio is a powerful lipoprotein marker for the development of coronary heart disease^{40,41}, regardless of the absolute LDL-cholesterol, HDL-cholesterol⁴² and LDL-cholesterol/HDL-cholesterol ratio⁴³. Patients with a high total cholesterol/HDL-cholesterol ratio were also significantly more insulin resistant⁴⁴. Insulin resistance is also related to obesity⁴⁵. Thus, other metabolic characteristics may be involved in the pathophysiology of the association of total cholesterol/HDL cholesterol ratio and increase in body mass index.

Our study has limitations. We screened a sample of asymptomatic patients with normal clinical examination that may not be representative of the whole population. Correlation indices of clinical and laboratory variables associated with the increase in body mass index was modest, but significant. Clinical implications of these results, specifically when we analyzed the clinical

Table 4 - Models of multiple linear regression of body mass index by gender

Variables	Women		Men	
	Coefficient regression	p	Coefficient regression	p
Age (years)	0.0341	0.109	0.0464	0.030
Serum glucose (mg/dl)	0.0233	0.023	0.0024	0.789
LDL-Cholesterol (mg/dl)	-0.0057	0.532	-0.0088	0.328
TC/HDL-C ratio	1.1320	< 0.001	0.793	< 0.001
r ² aj	0.10		0.08	
p (model)	< 0.001		< 0.001	

LDL - low-density lipoprotein; TC/HDL-C - total cholesterol/high-density lipoprotein cholesterol.

gain and may warrant further studies.

Body mass index was independently correlated with serum glucose in women in this study sample. In previous studies, body mass index was positively correlated with glucose in men and women^{30,31}. Both men and women, during 10 years of follow-up, demonstrated an increase in the incidence of diabetes together with increases in the degree of overweight³². Weight loss was effective in reducing coronary heart disease risk in insulin-resistant, obese women^{33,34}. The results of a study that included men and women substantiate evidence to sharpen target levels for serum glucose and body mass index among patients with low HDL-C and high triglycerides³⁵. In our study sample some unknown factors other than obesity-related well-known risk factors may be responsible for this observation.

meaning of increased body mass index, must be taken into a wider context in the study of associated clinical and laboratory variables. Hormone replacement therapy may also influence body mass index⁴⁶ and was not evaluated at the time the study was launched. However, hormone replacement therapy is not commonplace in the population we care for.

In conclusion, our data demonstrated that in healthy men and women showing no evidence of heart disease, total cholesterol/HDL-cholesterol ratio increased with increased body mass index in both men and women. Other indices that are associated with body mass index included serum glucose in women and age in men. Clinical interpretation of clinical and laboratory variables associated with body mass index may benefit from being more gender-specific.

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