



Original/Síndrome metabólico

Hypertriglyceridemic waist phenotype and cardiometabolic alterations in Brazilian adults

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Abstract

Aims: the present study aims to evaluate the prevalence of cardiometabolic changes according to the hypertriglyceridemic waist (HW) phenotype in Brazilian adults.

Methods: it is a population based transversal study with 976 adults (n = 533 women) 20-59 years old. Phenotype was defined by triglycerides concentration (TGL) ≥ 150 mg/dl and waist circumference (WC) ≥ 80 cm in females and ≥ 90 cm in males. All the analyses were adjusted according to the study design and pondered by gender, age and schooling. A descriptive analysis was performed through averages and ratios; their respective confidence intervals were herein presented (CI 95%). The prevalence of cardiometabolic changes due to the presence of HW and to gender was calculated and compared by means of Pearson's chi-square test. Statistic significance level was 0.05. The probability of coronary event risk was estimated in 10 years and calculated from Framingham score, using Kernel density graph.

Results: no difference in phenotype prevalence between genders was observed. Higher averages in all the cardiometabolic risk factors analyzed and higher probability of evolving to a cardiovascular event in 10 years were observed in individuals with the HW phenotype. Lower HDL values were only verified in this group.

Conclusion: the HW phenotype is an important cardiovascular risk sign and allows the premature identification of individuals with higher risk, so that its use in clinical practice must be encouraged, mainly because it is a simple low cost asset.

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Key words: *Hypertriglyceridemic waist. Cardiovascular diseases. Obesity. Metabolic diseases. Risk factors.*

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FENOTIPO CINTURA HIPERTRIGLICERIDÉMICA Y ALTERACIONES CARDIOMETABÓLICAS EN ADULTOS BRASILEÑOS

Resumen

Objetivos: evaluar la prevalencia de alteraciones cardiometabólicas según el fenotipo cintura hipertriglicéridémica (CH) en adultos brasileños.

Métodos: estudio transversal, de base poblacional, con 976 (n = 533 mujeres) individuos de 20 a 59 años. El CH fue definido por un aumento en las concentraciones de triglicéridos y en la circunferencia de la cintura (CC). Todos los análisis fueron ajustados por el efecto del diseño del estudio y ponderados por género, edad y escolaridad. Fue realizado un análisis descriptivo de promedio y presentados sus respectivos intervalos de confianza (IC 95%). La prevalencia de las alteraciones cardiometabólicas según la presencia o no del fenotipo CH y según el sexo fue calculada y comparada a través del test chi-cuadrado de Pearson. El nivel de significancia estadística adoptado fue de 0,05. Se estimó la probabilidad de riesgo de evento coronario en 10 años, a partir del score de Framingham a través del gráfico de densidad de Kernel.

Resultados: la prevalencia del fenotipo CH en la muestra fue de 17,32% (IC 95% 13,54-21,89), no se observó diferencia entre sexos. Se observaron mayores promedios para todos los factores de riesgo cardiometabólico analizados en aquellos con CH. Sólo se verificaron menores valores medianos para el HDL en este grupo. Los individuos con CH presentaban mayor probabilidad de evolucionar hacia un evento cardiovascular en 10 años que aquellos sin el fenotipo.

Conclusión: el fenotipo CH constituye un importante marcador precoz del riesgo cardiovascular. Su utilización en la práctica clínica debe ser incentivada, ya que se trata de una herramienta sencilla y de bajo coste.

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Palabras clave: *Cintura hipertriglicéridémica. Enfermedades cardiovasculares. Obesidad. Enfermedades metabólicas. Factores de riesgo.*

Introduction

The non-transmissible chronic diseases are the main causes of morbimortality in the world, among them there are the cardiovascular diseases and type 2 diabetes mellitus¹. It is known that the presence of cardiometabolic disorders such as dyslipidemia, hyperuricemia, high blood pressure, insulin resistance and obesity are capable of raising the risk of cardiovascular diseases²⁻⁴ and it makes the early identification and appropriate treatment of cardiovascular risk of fundamental importance to change this condition⁵. The study by Framingham is highlighted within this context. It is considered that cardiovascular risk factors are multifactorial and they interact to each other over time, fact that can lead to cardiovascular diseases^{6,7}.

Similarly to the Framingham Risk Score, the hypertriglyceridemic waist (HW) phenotype has been recently assumed as a simple and low cost asset. It is defined by the simultaneous presence of triglycerides plasma concentrations (TGL) and change in waist circumference (WC) to predict cardiovascular risk. This phenotype can indicate the presence of the atherogenic metabolic triad (hyperinsulinemia, high apolipoprotein B serum concentration and small dense LDL particles) and it allows tracking the high cardiometabolic risk in individuals with no symptoms; thus it is of great use in clinic practices, prevention strategies and health promotion^{8,9}.

Only few studies¹⁰⁻¹² evaluate the cardiovascular risk factors related to the HW phenotype, therefore it makes further investigation necessary. Hence, the current study aims to evaluate the prevalence of cardiometabolic alterations according to the hypertriglyceridemic waist phenotype in Brazilian adults.

Methods

It is a population based cross-sectional study developed in the urban zone of Viçosa County, southeast of Brazil. The town is a university city located in Zona da Mata region, Minas Gerais State. Its total area is equivalent to 299.397 Km², the demographic density is of 241.2 inhabitants per square kilometer and the population is 72,220 inhabitants³, 95% out of this total live in the urban zone (68.609 individuals).

The population used as reference in the current study was formed by adults between 20-59 years old, from both genders. The mentioned age group consists of approximately 60% of the total population in the county (43,431 people)¹³.

The size of the sampling group was calculated based on the prevalence estimation formula considering the population of reference equal to 43,431, confidence interval equals 95%, expected prevalence of the phenotype as 22%¹², sampling error 3.5 percentage points and effect of the study design (cluster sampling) estimated as 1.5. Ten percent (10%) was added to the sampling size calculation in order to compensate refusals

and losses. Other 10% was added to the sampling size calculation for confusion factors control, The sampling group came, then, to a total of 958 individuals. The calculation was done in Epi-Info version 3.5.2® software¹⁴.

The sampling process was carried out by conglomerate in two stages. Firstly, 30 out of 99 sectors were randomly selected by simple random sampling without replacement; then one block and one corner were picked to be the starting point for the field work¹⁵. All adults in the household were considered eligible and the households unsuccessfully visited at least four times (including a visit on the weekend and another in the evening) were considered losses. Non-inclusion criteria were: pregnant women, amputees, the bedridden, individuals using plaster cast, individuals with psychiatric disorders and who, for some other reason, could not stay in the appropriate position for anthropometric measures.

Data collection was done by pairs of interviewers during household visits, through a face to face interview and the application of a structured questionnaire. Training and a pre-test of the questionnaire were performed in 30 adults between 20-59 years old randomly selected at the university, in order to achieve standardization. The pilot study was performed with 81 people (7% of the total sampling group) in one of the selected census sectors, which was excluded from the analysis. The research was widely disseminated in the regional mainstream media to provide greater adhesion. The quality control of data collection was done by telephone interview, by one of the supervisors, with 10% of the sampling group. After filling up the questionnaire, participants were invited to attend the population group laboratory of Federal University of Viçosa to have their blood samples, anthropometric measurements and body composition collected.

The dependent variable was the HW phenotype verified when the individual showed plasma TGL concentration higher than or equal to 150 mg/dl, WC greater than or equal to 80 cc for females and greater than or equal to 90 cm for males^{8,9,16}.

The independent variables were: gender, age, smoking habits, body mass index (BMI), WC, total body fat, glucose and fasting insulin, Homeostatic Model Assessment Index for Insulin Resistance (HOMA-IR), C-reactive protein (CRP), systolic blood pressure (SBP), diastolic blood pressure (DBP), uric acid and plasmatic lipids. Body weight, height, and WC were measured as standard international techniques¹⁶⁻¹⁸. Body weight was obtained through a portable anthropometric scale by Tanita (with capacity of 130 kg) and height was directly measured, using the 2.5 meters long stem fixed stadiometer by Welmy coupled to the wall. After the measurements, BMI was calculated from individuals who were classified as overweight (BMI >25 kg/m²) and normal weight (BMI <25 kg/m²)¹⁹. The WC measurement was made by inelastic millimeter tape with 1.5 meters capacity.

Blood pressure was measured in duplicate, the first measurement after 5 minutes of rest and the second 20 minutes after the first one. Equipment for blood pressure measurement was the Automatic Blood Pressure Monitor with clamp, model Omron HEM-742INT IntelliSense®. Blood samples were obtained after 12 hours of fasting in a tube containing gel clot activator by peripheral venipuncture using vacuum system, and material was centrifuged up to 40 minutes after collection, for 15 minutes at 3000 rpm (2000 G). After centrifugation, serum samples were obtained for the following determinations: Glucose, total cholesterol, HDL and LDL cholesterol, triglycerides and uric acid using enzymatic colorimetric methods, Bioclin® kits, quantitative RCP using turbidimetric method, Bioclin® kit and insulin by ELISA using Human Insulin ELISA- Linco Research® kit. We evaluated the presence of insulin resistance through HOMA-IR index, calculated using the formula proposed in previous studies²⁰. Body fat was assessed using the equipment of X-ray absorptiometry Dual Energy (DEXA) (Lunar Prodigy Advance DXA System-analysis version: 13.31, GE Health care, Madison, WCI, USA). All evaluations were performed by the same technician, using standard procedures described in the Core Users Manual.

Participants' Framingham score was calculated according to the presence or absence of the HW phenotype or to changes in any of the phenotype's components. It was done by following the proposed cardiovascular risk algorithm model based on the data of study²¹. Points were set to the following items: gender, age, systolic blood pressure level, total cholesterol and HDL cholesterol plasma concentrations, smoking and diabetes mellitus diagnosis. Subsequently, these items would convert to risk estimation of developing cardiovascular disease, in a time span of 10 years. Thereby, the participants were classified as low, medium or high risk according to their probability of developing cardiovascular disease in 10 years - less than 10%, between 10 and 20% and over 20%, respectively^{7,21,22}.

The field work was performed between September 2012 and May 2014. Data were tabulated in duplicate using the Epidata software and checked by the "compare date" module. Sample weights -considering the variables gender, age and education- were calculated to balance differences in the socio-demographic composition of the sampling group and the composition of the city's total adult population, according to the census distribution of 2010¹³. Data analysis was performed using the Stata version 13.1 statistic pack on

Table I
Anthropometrical, clinical and biochemical characteristics and body composition of the studied adults, according to the presence or absence of hypertriglyceridemic waist phenotype, Viçosa, 2014

Variables	Hypertriglyceridemic Waist Phenotype			
	No		Yes	
	Average	CI 95%	Average	CI 95%
BMI (kg/m ²) ¹	22.9	22.5-23.4	28.1	27.5-28.6
WC (cm) ²	75.8	74.9-76.7	91.9	90.4-93.3
Total body fat (%) ³	25.4	24.1-26.7	34.8	33.8-35.8
Fasting glucose (mg/dl)	82.7	81.2-84.2	88.6	86.2-90.9
Insulin (mg/dl)	6.8	6.3-7.3	10.7	9.9-11.6
HOMA-IR ⁴	1.4	1.3-1.5	2.4	2.1-2.6
ASBP (mmHg) ⁵	114.6	112.8-116.5	124.9	123.0-126.9
ADBP (mmHg) ⁶	73.2	71.4-74.9	80.7	79.5-81.9
RCP ⁷	1.36	1.17-1.55	2.13	1.94-2.32
Uric Acid (mg/dl)	3.8	3.7-4.0	4.4	4.2-4.5
Total cholesterol (mg/dl)	178.1	175.1-181.0	203.2	198.1-208.2
VLDL (mg/dl) ⁸	17.3	16.9-17.8	34.4	31.5-37.3
HDL (mg/dl) ⁹	52.4	50.9-53.9	46.1	43.7-48.4
LDL (mg/dl) ¹⁰	108.3	105.5-111.1	122.5	118.7-126.3
TGL (mg/dl) ¹¹	86.8	84.4-89.2	172.4	158.0-186.9

¹Body Mass Index; ²Waist circumference; ³Total body fat measured by DEXA;

⁴Homeostatic Model Assessment for Insulin Resistance; ⁵Average systolic blood pressure;

⁶Average diastolic blood pressure; ⁷Reactive C-Protein; ⁸Very low density lipoprotein or VLDL-cholesterol;

⁹High density lipoprotein or HDL-cholesterol; ¹⁰Low density lipoprotein or LDL-cholesterol; ¹¹Triglycerids.

the set of svy commands, which considers the complex sampling design.

Initially, the descriptive analysis was conducted through averages and ratios. Their respective confidence intervals (CI 95%) were presented. The prevalence of cardiometabolic changes, related to the presence or absence of the HW phenotype and in accordance to gender, was calculated and compared using Pearson chi-square test. The adopted level of Statistic significance was 0.05. Additionally, the risk probability of coronary event in 10 years was calculated from Framingham score by means of Kernel density graph.

The project was approved by the Research Ethics Committee of UFV under Protocol number - 008/2012. Signatures were requested to the participants in the terms of the free and informed consent.

Results

The final sample consisted of 959 individuals, after 2.7% losses. Among the examined individuals, 50.80% (CI-95% 47.6-54.3) were women, approximately 61% were men. Little more than 50% of women were between 20-40 years old. It was verified that

13.34% of the participants (CI 95% 11.33-15.65) were smokers and 16.05% (CI 95% 13.86-18.52) were former smokers.

The prevalence of the HW phenotype in the sampling group was 17.32% (CI 95% 13.54-21.89); no difference was observed in the phenotype prevalence between women and men. The mean age of those who have the HW phenotype was 39.52 years (CI 95% 38.40-40.64) and 29.98 years (CI 95% 29.11-30.85) for those who do not have it.

The anthropometrical, clinical and biochemical characteristics of the studied adults, according to the presence or absence of HW phenotype, as well as their body composition is presented in table I. Higher averages were observed in all cardiometabolic risk factors analyzed in the group with the HW phenotype. Lower HDL values were only verified in these groups (Table I).

Figures 1 and 2 present the prevalence of cardiometabolic changes in participants according to gender and the presence or absence of the HW phenotype. The prevalence of high LDL cholesterol plasma concentrations, total cholesterol and RCP, along with that of changes in carbohydrates metabolism ($p < 0.001$) and blood pressure were higher in individuals who presented the HW phenotype in both genders ($p \leq 0,001$). It

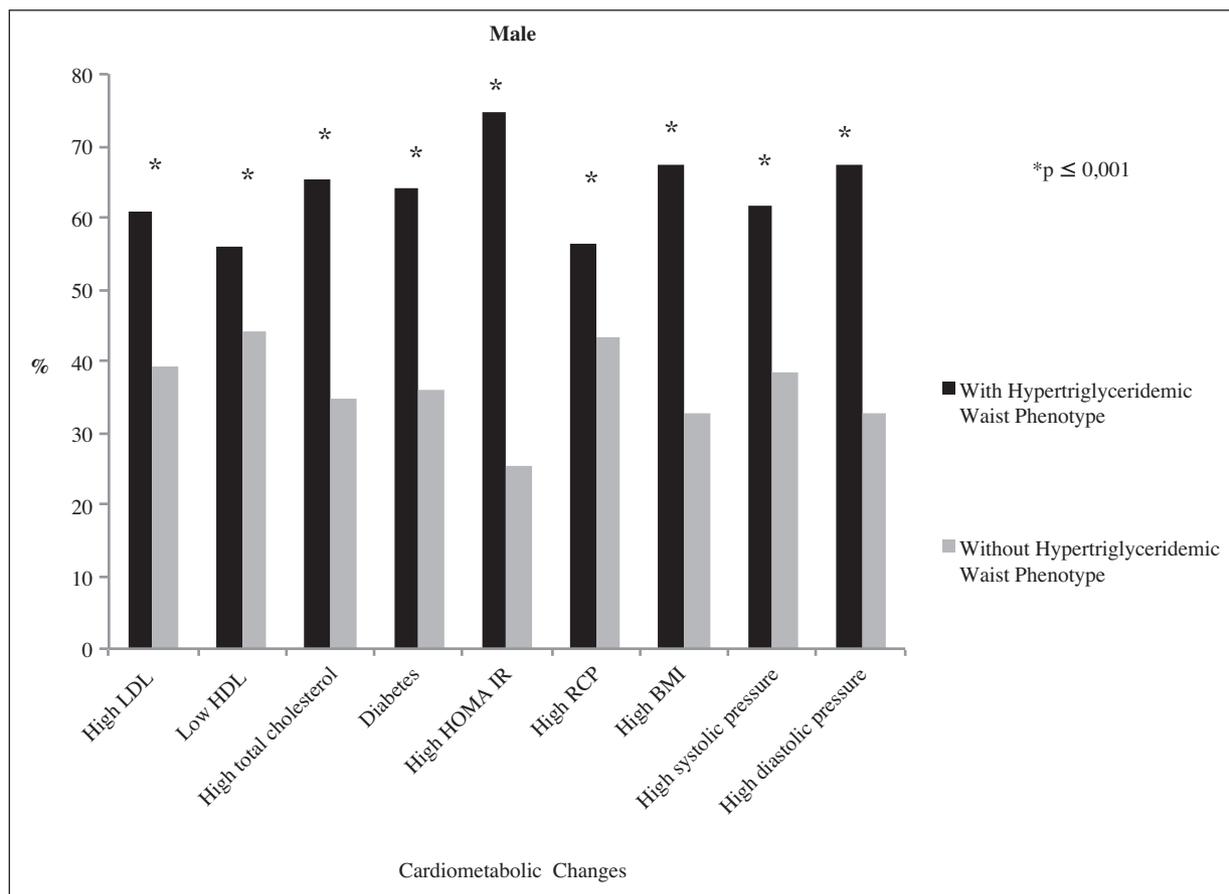


Fig. 1.—Prevalence of cardiometabolic changes in male individuals, according to the presence of the Hypertriglyceridemic Waist (HW) phenotype.

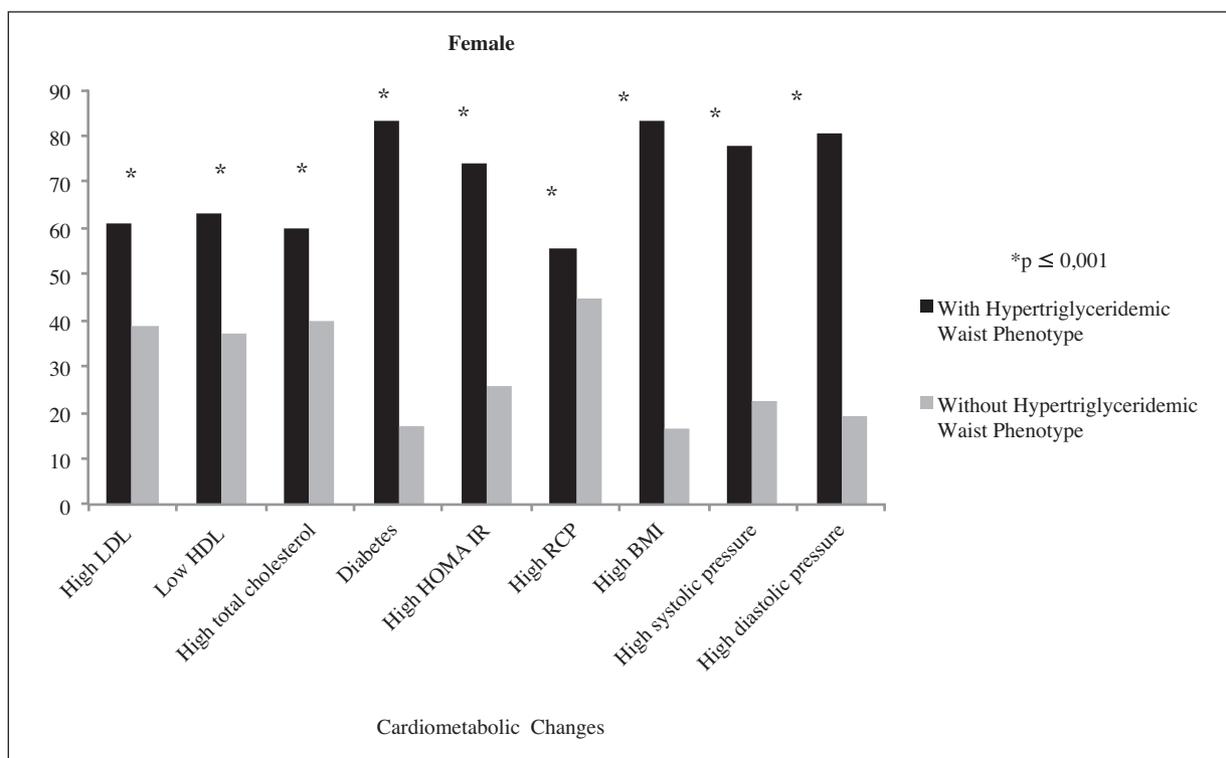


Fig. 2.—Prevalence of cardiometabolic changes in female individuals according to the presence of the Hypertriglyceridemic Waist (HW) phenotype.

was also found in individuals with higher prevalence of low HDL plasma concentrations ($p \leq 0,001$).

The probability of having a coronary event in 10 years, according to Framingham score calculations as well as to the presence or absence of the hypertriglyceridemic waist phenotype or just to one of its changed components is presented in the Kernel's estimate density graph (Fig. 3). It was observed that individuals who had the HW phenotype showed higher probability of developing a cardiovascular event within 10 years than those who did not have it. Besides, participants who did not have the HW phenotype or those with only one of its changed components were concentrated in the low cardiovascular risk classification, according to the herein mentioned risk score.

Discussion

The findings of the present study demonstrate that participants who have the HW phenotype show different changes in cardiometabolic markers; whereas the individuals who do not have the phenotype showed factors considered to be protectors against cardiovascular diseases, such as higher mean values of HDL cholesterol. It has been assumed that high WC associated with fasting hypertriglyceridemia would indicate the presence of visceral obesity and of dysfunctional highly lipolytic adipose deposit that together, behave

like a cardiovascular risk factor, regardless of other factors such as age, gender and LDL cholesterol plasma concentrations^{9,23}.

It is believed that high TGL serum concentrations are associated with small dense LDL cholesterol particles in the plasma and high apolipoprotein B concentrations. On the other hand, high WC is associated with the raise of visceral adiposity; and it can be linked to metabolic changes such as hyperinsulinemia. The alteration group formed by hyperinsulinemia, hyperapoproteinemia B and high plasma concentrations of small dense LDL cholesterol is called the atherogenic metabolic triad; and it is possibly identified in individuals with HW phenotype^{8,9}.

The present study verified that the participants who had the HW phenotype also had higher levels of total cholesterol, LDL-cholesterol, VLDL-cholesterol, BMI and higher body fat percentage than those who did not have the referred phenotype. However, lower HDL cholesterol values were observed in the same individuals. It is known that dyslipidemia is among the metabolic changes mostly associated with obesity worldwide². Highly unfavorable lipid profile has been verified among HW phenotype individuals, it is characterized by high concentrations of total cholesterol, LDL-cholesterol, VLDL-cholesterol - especially the more atherogenic one, small dense particles, and low HDL cholesterol concentrations closely related to the higher cardiovascular risk in these individuals^{2,8,24}.

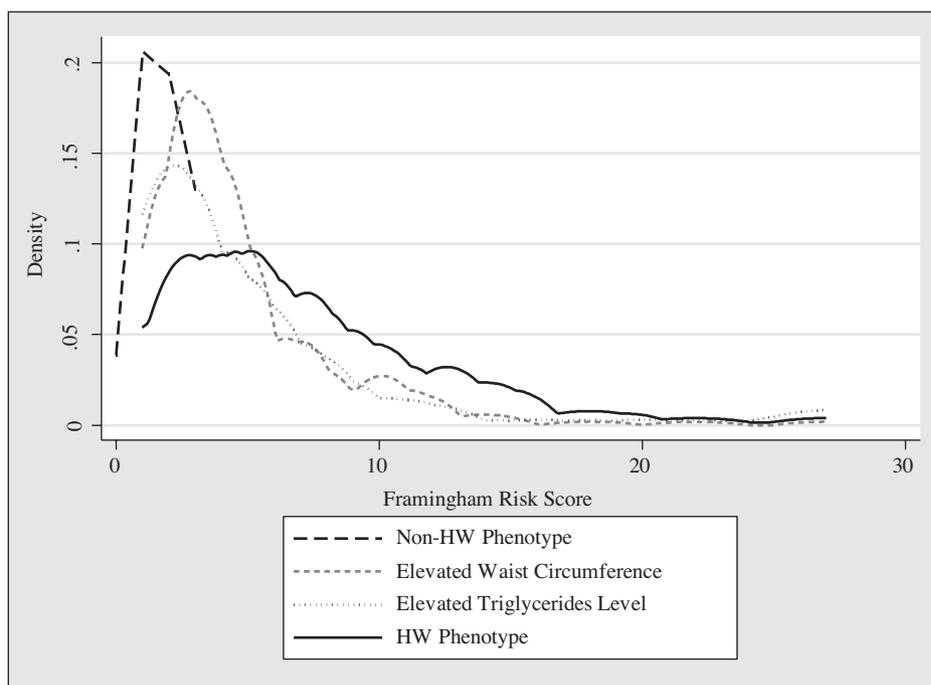


Fig. 3.—Risk probability of coronary event in 10 years, according to the Framingham score as well as to the presence or absence of the hypertriglyceridemic waist phenotype or to at least one of its changed components.

In addition, a recent study has stated that individuals who have a hypertriglyceridemic waist also showed higher corporal adiposity index and atherogenic lipid profile when they were compared to those who did not share the same feature²⁵. Similarly, a study conducted with diabetic volunteers to verify the ability of the HW phenotype to predict visceral adiposity observed that BMI values and the visceral fat deposits, evaluated by abdominal computer tomography, were higher among individuals who had the HW phenotype in comparison to individuals who had only one of its components and to individuals with TGL and WC within the normal range²⁶. Higher glycemia, fasting insulinemia values and higher HOMA IR index were observed in the presence of the HW phenotype. It is believed that metabolic changes associated with this phenotype, such as visceral obesity and insulin resistance, can influence the interaction between cardiovascular risk and hyperglycemia^{4,27}. Therefore, it was certified in a study with 1036 non-diabetic 70-year-old men that the presence of the HW phenotype would increase in approximately 4 times the risk of developing diabetes mellitus²⁸.

It is believed that visceral obesity in the hypertriglyceridemic waist may be related to the release of pro-inflammatory cytokines that can act on the skeletal muscle and peripheral adipose tissue. It may induce insulin action resistance and consequent dysfunction in carbohydrate metabolism^{3,4}. Furthermore, the action of these cytokines can result in endothelial dysfunction, atherosclerosis, vascular remodeling and subsequent systemic hypertension²⁹ and, therefore, it is an important risk factor for cardiovascular disease. These data may explain the findings of the current study, which found

higher values of systolic and diastolic blood pressure in participants with hypertriglyceridemic waist.

The CRP stands out among the proinflammatory cytokines associated with inflammatory subclinical condition and hypertriglyceridemic waist³⁰. Higher values in the concentration of this protein in individuals with HW phenotype were verified in comparison to those in the absence of it. Similarly, it was observed, in a study conducted in China involving 3289 men between 50-70 years of age, that 2 cm CW increase and the 20 mg/dl TGL concentrations were able to increase plasma concentrations of inflammatory cytokines, including CRP³¹. Thus, it is possible that the presence of hypertriglyceridemic waist favors the release of various pro-inflammatory adipokines that contribute to the development of subclinical inflammation and to the increase of cardiometabolic risk³⁰.

Moreover, besides the aforementioned metabolic changes, higher values of uric acid have been found in individuals who had the hypertriglyceridemic waist. It is now known that the enzymes involved in the production of uric acid may be related to intracellular oxidative stress such as muscle cells of the vessels and adipocytes - which can trigger harmful effects as stimulation of platelet aggregation, inhibition of nitric oxide production and proinflammatory activity³². Thus, hyperuricemia has been linked to the increased risk of developing metabolic syndrome, high blood pressure and coronary artery disease³².

Over the past few years, a shift in the focus given to the approach of cardiovascular diseases has been observed in order to prevent rather than just treat them⁷. The use of tools to identify risk has been addressed in clinical practice since the Framingham Study in the

40's and further the development of the Framingham score cardiovascular risk²¹. In the Framingham risk score, points are granted to items such as age, HDL plasma concentrations and total cholesterol, systolic blood pressure levels, smoking and diabetes presence to obtain, at the end of the sum, the risk estimation of having a cardiovascular event within 10 years^{7,21}. It was observed higher Framingham score in the presence of HW phenotype in this study. It could ultimately suggest that the HW phenotype could predict the cardiovascular risk by indicating the presence of atherogenic metabolic triad, thus enabling the tracking of asymptomatic individuals with increased risk of developing cardiovascular event in the future.

Finally, it is noteworthy that the HW phenotype can be considered an important cardiovascular risk marker. Therefore, its use in clinical practice should be encouraged to allow the early identification of cardiometabolic risk and the establishment of strategies for health promotion and preventing cardiovascular diseases, mainly because it is a simple and inexpensive asset. Thus, the current subject should continue to be addressed and longitudinal studies might be of great contribution.

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Conflict of Interest

None of the authors has any conflict of interest to declare.

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