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Neck circumference, cardiometabolic risk, and Framingham risk score: Population-based study

Circunferência do pescoço, risco cardiometabólico e escore de risco de Framingham: estudo de base populacional

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A B S T R A C T

Objective

To investigate the association of the neck circumference with cardiometabolic risk factors and the Framingham risk score.

Methods

The study was a cross-sectional population-based one with 948 adults (522 women) aged 20–59 years. Sociodemographic, anthropometric, body composition, behavioral, biochemical, and hemodynamic factors were evaluated. The association between neck circumference, anthropometric variables, body composition and cardiometabolic risk factors was evaluated by multiple linear regression, adjusted for sociodemographic and behavioral factors.

Results

Are presented as β coefficients, standard errors, and 95% confidence intervals with a 0.05 significance level. The neck circumference was positively associated with triglycerides, insulin resistance index, uric acid, systolic and

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diastolic blood pressure, C-reactive protein, waist circumference, body mass index and total body fat estimated by dual energy X-ray absorptiometry. The neck circumference and high-density lipoprotein cholesterol were negatively associated, even after adjustment for sociodemographic and behavioral factors. Individuals with a neck circumference below the cut-off point to predicting cardiometabolic risks, 39.5cm for men and 33.3cm for women, had lower probability of having a coronary event in 10 years compared to those with a neck circumference above the cut-off point.

Conclusion

Neck circumference is an alternative measure to estimate body fat and as an additional marker to screen for cardiovascular risk diseases.

Keywords: Anthropometry. Insulin resistance. Neck. Obesity. Risks.

RESUMO

Objetivo

Investigar a associação da circunferência do pescoço com fatores de risco cardiometabólico e escore de risco de Framinghan.

Métodos

Estudo transversal de base populacional com 948 adultos (522 mulheres), de 20 a 59 anos. Fatores sociodemográficos, antropométricos, de composição corporal, comportamentais, bioquímicos e hemodinâmicos foram mensurados. Associação entre circunferência do pescoço, variáveis antropométricas, de composição corporal e fatores de risco cardiometabólico foi avaliada por regressão linear múltipla, ajustada por fatores sociodemográficos e comportamentais.

Resultados

Foram apresentados como coeficientes β, erros-padrão e intervalos de confiança de 95% com nível de significância de 0,05. Circunferência do pescoço associou-se positivamente com triglicerídeos, índice de resistência a insulina, ácido úrico, pressão arterial sistólica e diastólica, proteína C-reativa, circunferência da cintura, índice de massa corporal e gordura corporal total estimada pela absorciometria por dupla emissão de raios-X. Circunferência do pescoço e lipoproteinas de alta densidade colesterol apresentaram associação negativa. Estas associações permaneceram significativas mesmo após ajuste por fatores sociodemográficos e comportamentais. Indivíduos com circunferência do pescoço abaixo do ponto de corte para predição de risco cardiometabólico (39,5cm para homens e 33,3cm para mulheres), apresentaram menor probabilidade de evento coronariano em 10 anos que aqueles com circunferência do pescoço acima do ponto de corte.

Conclusão

A circunferência do pescoço é uma alternativa para estimar a gordura corporal, podendo ser usado como instrumento adicional de triagem durante a avaliação de pacientes assintomáticos com risco cardiovascular.

Palavras-chave: *Antropometria. Resistência à insulina. Pescoço. Obesidade. Risco.*

INTRODUCTION

Obesity is a public health problem associated with cardiovascular diseases, the prevalence of which is increasing worldwide [1]. Family Budget Surveys, carried out by the *Instituto Brasileiro de Geografia e Estatística* (IBGE, Brazilian Institute of Geography and Statistics) in 2008/2009, confirmed this trend, with obesity affecting 12.5% of men and 16.9% of women [2]. In the United States, this prevalence was even higher in 2009/2010, affecting 35.5% of men and 35.8% of adult women [3-5]. Excess fat, especially in the upper body, is associated with lipid profile changes, increased blood pressure and hyperinsulinemia, factors that increase the Cardiovascular Disease (CVD) risks [6-8].

The accumulation of body fat can be quantified by standard gold methods such as computed tomography and nuclear magnetic resonance, allowing an assessment of the different fat deposits. However, these measures are expensive and inaccessible to large sections of the population and health services [9]. An alternative is the evaluation of body fat by indirect methods, using anthropometric measures that are parameters of easy measurement and low cost, which is important in the context of public health in Brazil [1,7,10-12]. Some anthropometric markers, such as waist circumference and Body Mass Index (BMI), are already accepted from the cardiometabolic risk viewpoints. Others, such as neck circumference, still need further studies to be considered an additional new indicator [1]. The neck circumference estimates the accumulation of fat in the upper body segment which is lipolytically more active than that of the lower body fat. This could lead to insulin resistance, atherosclerosis, and endothelial dysfunction [12,13].

Cardiovascular disease, including coronary heart disease, can be prevented by the control of systemic arterial hypertension, dyslipidemia, smoking, diabetes, and obesity, and it has a great impact on public health. The Framingham risk score was devised to estimate the development of coronary disease risks ten years later [14].

It is of great interest to evaluate the cardiometabolic risk factors with new anthropometric indicators and to associate them to CVD. In this regard, neck circumference may be useful in the screening of asymptomatic patients at high risk of cardiovascular events. However, population studies investigating neck circumference as a predictor of cardiometabolic risk and coronary events are few.

The aim of this study was to investigate the association of neck circumference with cardiometabolic risk factors, other anthropometric measurements, and body composition, and to evaluate it as a cardiovascular risk predictor using the Framingham risk score.

METHODS

A cross-sectional, population-based study was conducted in the urban area of the *Viçosa* municipality, *Minas Gerais*, Brazil. *Viçosa* is a university city with 72,220 inhabitants and a human development index of 0.7752. Data from 948 volunteers, aged 20 to 59 years, were collected between 2012 and 2014, selected by probabilistic sampling, by clusters and in a double stage: census tract and domicile. The sector numbers were determined according to the recommendations for municipalities with characteristics similar to those of *Viçosa* [15].

The data collection was commenced at home. Subsequently, the volunteers attended the laboratory for anthropometric measurements, body composition assessments, laboratory tests and blood pressure measurement.

Pregnant women, bedridden individuals, amputees, those for whom it was difficult to obtain certain measurements, anatomical deformities in the neck and/or with cognitive/intellectual limitations to answer the questionnaire, were excluded.

The study was approved by the Ethics Committee in Research on Human Subjects (nº 008/2012) of the *Universidade Federal de Viçosa* in 02/04/2012. The subjects provided Informed Written Consent.

Weight, height, neck circumference and waist circumference were the anthropometric data that were collected. Body weight was measured using a Tanita scale (Arlington Heights, Illinois, United States), model Ironman BC–554® (precision of 100g) with the individual without shoes and wearing light clothes. Height was measured with a wall stadiometer (0.5cm scale accuracy) with the individual barefoot and in the orthostatic position [16]. Body Mass Index (BMI=weight/height^2) was calculated using the following cut-off points to classify individuals: low weight (BMI <18); eutrophic (BMI ≥18.0 and <25); overweight (BMI ≥25 and <30) and obese (BMI ≥30) [17].

The neck circumference was measured thrice by a single examiner, with the individual standing, head in the Frankfurt position,

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with an inelastic tape measure just below the prominence of the larynx. The mean of these measurements was calculated [18].

Waist circumference was also measured by a single examiner thrice with the subject standing. Measurements were taken with a 1.5mm inelastic metric tape at the midpoint between the iliac crest and the last rib. The mean of these measurements was calculated. The site and cut-off points for classification were 90cm for men and 80cm for women using the Harmonized Criteria for Metabolic Syndrome [19].

Blood pressure was measured twice, after five and twenty minutes of rest, with the Omron HEM–742INT IntelliSense® Automatic Blood Pressure Monitor (Omron Healthcare, Inc., Shanghai, China).

The total body fat composition was quantified using Dual-Energy X-Ray Absorptiometry (DXA) by a specialist technician using the DPX-IQ #5781 device (Lunar Radiation, Madison, Wisconsin). The instrument was calibrated daily [17]. The examination lasted about twelve minutes with the individual lying supine on a table where the source and detector passed through the body at a relatively slow speed of 1cm/s emitting X-ray and doing the mapping.

Venous blood samples were collected after 12-hour fasting to determine: total cholesterol and its Hight Density Lipoprotein (HDL) and Low Density Lipoprotein (LDL) fractions, after precipitation; triglycerides by enzymatic methods; uric acid by the enzymatic calorimetric method; C-Reactive Protein (CRP) by immunoturbidimetric test; glucose oxidase and plasma insulin by the Enzyme Linked Immuno Sorbent Assay method to calculate the insulin resistance index Homeostatic Model Assessment-Insulin Resistance (HOMA-IR) [20,21].

The behavioral variables assessed with a questionnaire were: smoking (non-smokers, current smokers and ex-smokers); alcoholic beverages, categorized by the number of doses consumed in a normal week (none, one to seven, eight to fourteen, fifteen doses or more); physical activity (physically active ≥150 minutes/week, physically inactive <150 minutes/week), measured from the analysis of domain 4 of the International Physical Activity Questionnaire [22], and number of school years (≤ four, five to eight, nine to twelve and ≥ thirteen years).

The Framingham risk score was determined from the sum of the positive and negative scores of the variables age, sex, Systolic Blood Pressure (SBP), total cholesterol *ratio* and HDL fraction, smoking, and diagnosis of diabetes results. Subsequently, this score was converted into a risk estimate of developing coronary disease in a 10–year period [23,24]. The Framingham risk score was calculated according to the presence or absence of increased neck circumference.

The data were tabulated in duplicate, using the program EpiData (Odense, Dermark) and checked by the module "data compare". Statistical analyses were performed using the Stata (Stata Corporation, College Station, Texas, United States) 13.1 statistical program with the survey (svy) command set, since conventional estimators could underestimate the point estimate variance. The svy commands set considered the complex sampling design. Sample weights were calculated for the variables gender, age, and schooling to minimize differences in the sociodemographic composition of the sample related to the total adult population of the municipality according to the census distribution of 2010 [2].

Receiver Operator Characteristic curves were developed and the area under the curve calculated to obtain the optimum neck circumference cut-off point to predict cardiometabolic risk according to the gender.

Normality was tested using the Kolmogorov-Smirnov test. The variables without normal distribution (triglycerides, CRP, and HOMA-IR) underwent log transformation. The association between neck circumference (main independent variable) and biochemical variables (glucose, HDL, LDL, triglycerides, uric acid, CRP, HOMA-IR), hemodynamic (SBP, diastolic blood pressure), anthropometric (waist circumference, BMI) and body composition, which were the dependent variables, was tested with linear regression models. Three model blocks were constructed: the first associating the neck circumference with each one of the dependent variables, the second model was adjusted for the variables gender and age, and the third for the variables gender, age, schooling, smoking, alcohol consumption and physical activity, since epidemiologically these variables are possible confounding factors. We chose not to adjust neck circumference with anthropometric variables due to the strong correlation between them.

The residuals of the adjusted models presented a linear distribution along the values, showing that the linear regression model was adequate. The standardized residual charts and predicted values showed that the former were uniformly distributed around the mean.

The results are presented as mean values, β coefficients, standard errors and 95% Confidence Intervals (95%CI) with a 0.05 significance level.

The Framingham risk score was calculated for participants according to the presence or absence of increased neck circumference. The variables sex, age, SBP, total cholesterol, HDL cholesterol, smoking and diabetes *Mellitus* diagnosis received points which were added to estimate the risk of coronary disease development in a 10–year period [12,24,25]. The Kernel density plot was obtained to assess the probability of a coronary event according to the presence or absence of increased neck circumference.

RESULTS

A total of 948 subjects were included, 426 men (44.93%), averaging 36.44 years (95%CI=33.80–39.08) and 522 women (55.06%), averaging 40.06 years (95%CI=38.10–42.03). The men presented with greater waist circumference, neck circumference, uric acid and SBP values than women. However, women had higher HDL cholesterol levels (Table 1).

The regression models, adjusted for age and sex, were positively associated with neck circumference and Triglycerides, HOMA-IR, uric acid, SBP, diastolic blood pressure, CRP, waist circumference, BMI and DXA. The association between neck circumference and HDL cholesterol, after adjusting for age and sex, was negative. In this block, the increase of one centimeter in neck circumference was associated with a decrease in HDL cholesterol level of 1.41mg/dL, and an increase of one centimeter in neck circumference was associated with the mean increase in waist circumference by 3.06cm and fat (estimated by DXA) by 1.47% (Model 1, Table 2). In the model zero, the association of neck circumference with total body fat estimated by DXA was negative, but after adjusting the models 1 and 2 with sociodemographic and behavioral variables, the association became positive. This shows that the result found in model zero can be explained by the confounding factors. The associations remained significant, even after adjusting for age, gender, schooling, smoking, alcohol consumption and physical activity (Model 2, Table 2). The LDL cholesterol variable was significantly associated in the zero model, but the significance was no longer present after adjusting for sociodemographic and behavioral variables (Table 2).

The receiver operator characteristic curve, stratified by gender, showed a neck circumference cut-off point of 39.5cm for men and 33.3cm for women as a cardiometabolic risk predictor (data not shown). According to the Kernel probability graph, individuals with a neck circumference below the cut-off as a predictor of cardiometabolic risk are less likely to have a coronary event risk in 10 years than those with a neck circumference above the cut-off point (Figure 1).

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Table 1. Demographic, biochemical, hemodynamic, behavioral, and anthropometric characteristics in adults (N=948). *Viçosa* (MG), Brazil (2012–2014).

Parameters	Men		Women	
	Mean	95%CI	Mean	95%CI
Age (years)	36.44	33.80–39.08	40.06	38.10–42.03
Height (m)*	1.73	1.72–1.75	1.59	1.58–1.61
Weight (kg)*	80.10	76.39–83.81	65.15	63.70–66.60
Body mass index (kg/m^2)	25.66	24.91–26.41	25.55	24.73–26.37
Waist circumference (m)*	87.47	85.37–89.56	80.62	78.60–82.64
Neck circumference (m)*	38.63	38.27–38.99	33.11	32.73–33.50
Glucose (mg/dL)	86.65	84.82–87.48	86.13	82.81–89.44
HDL (mg/dL)*	43.82	42.25–45.40	54.50	52.48–56.52
SBP (mmHg)*	123.29	121.24–125.35	117.04	114.30–119.77
DBP (mmHg)	77.69	75.97–79.41	76.22	74.46–77.97
Triglycerides (mmHg)	141.60	122.50–160.70	122.23	113.95–130.50
HOMA-IR	1.77	1.51–2.02	2.08	1.85–2.32
Uric acid (mg/dL)*	4.76	4.58–4.95	3.47	3.31–3.63
Physical activity (min)	134.19	89.72–178.67	79.40	57.75–101.05
Smoking (%)				
Non-smoking	61.47	52.01–70.14	69.14	62.59–75.00
Ex-smoker	24.83	16.65–35.32	21.01	16.16–26.85
Smoker	13.69	10.26–18.05	9.84	6.74–14.16

Note: *Significant difference between the sexes (p<0.05).
HDL: High-Density Lipoprotein; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HOMA-IR: Insulin Resistance Index; 95%CI: 95% Confidence Interval.

DISCUSSION

The association of neck circumference with cardiometabolic risk factors, except LDL cholesterol, remained significant even after adjusting for sociodemographic and behavioral variables. These findings are consistent with a Brazilian population-based study, where increased neck circumference was associated with increased blood pressure, triglycerides, and insulin resistance [15], and with other studies that found a positive association with anthropometric markers such as increased BMI and waist circumference [18,26]. In fact, this association was also observed in the pediatric population [11]. The neck circumference is an additional indicator of cardiometabolic risk and may replace BMI and waist circumference [5].

Research on body composition and CVD risks emphasizes the importance of fat distribution in the upper or lower body segment or in visceral or subcutaneous compartments. Obesity in the upper body segment, which is estimated by neck circumference, is associated with adverse metabolic outcomes such as insulin resistance, diabetes, hypertension, and elevated triglycerides, whereas individuals with fat accumulation in the lower body segment tend to have a lower incidence of these problems [27,28].

The positive association of neck circumference with waist circumference and BMI, anthropometric cardiometabolic risk measures that are easy to obtain, indicates that it is a good predictor of fat deposition pathogenicity. A study with adult individuals comparing neck circumference and waist circumference and

Table 2. Multiple linear regression for the association between neck circumference, cardiometabolic risk factors, anthropometric and body composition variables in adults (N=948). *Viçosa* (MG), Brazil (2012–2014).

Dependent variables	Model 0	Model 1	Model 2
HDL (mg/dL)			
β ± SE	-1.73 ±0.13	-1.41 ± 0.14	-1.37 ±0.14
95%CI	(-2.00; -1.46)	(-1.70; -1.12)	(-1.67; -1.07)
R^2	0.187	0.194	0.202
LDL (mg/dL)			
β ± SE	0.36 ± 0.28	0.43 ± 0.50	0.49 ± 0.49
95%CI	(-0.20; 0.94)	(-0.58; 1.45)	(-0.51; 1.50)
R^2	0.002	0.134	0.143
Triglycerides (mg/dL)			
β ± SE	0.04 ± 0.01	0.05 ±0.01	0.050 ± 0.01
IC95%	(0.03; 0.05)	(0.03; 0.06)	(0.03; 0.06)
R^2	0.077	0.162	0.180
HOMA-IR			
β ± SE	0.04 ± 0.01	0.12 ± 0.12	0.12 ± 0.01
95%CI	(0.02; 0.05)	(0.09; 0.15)	(0.09; 0.14)
R^2	0.055	0.238	0.238
Uric acid (mg/dL)			
β ± SE	0.19 ± 0.01	0.13 ± 0.02	0.13 ± 0.02
95%CI	(0.16; 0.21)	(0.10; 0.17)	(0.10; 0.16)
R^2	0.323	0.346	0.369
SBP (mmHg)			
β ± SE	1.60 ± 0.15	1.58 ± 0.22	1.46 ± 0.22
95%CI	(1.29; 1.93)	(1.12; 2.03)	(1.00; 1.92)
R^2	0.146	0.254	0.251
DBP (mmHg)			
β ± SE	0.70 ± 0.12	0.80 ± 0.12	0.77 ± 0.12
95%CI	(0.46; 0.95)	(0.44; 1.16)	(0.44; 1.09)
R^2	0.064	0.199	0.211
C-Reactive Protein (mg/dL)			
β ± SE	0.005 ± 0.01	0.096 ± 0.02	0.093 ± 0.02
95%CI	(-0.01; 0.02)	(0.06; 0.12)	(0.06; 0.12)
R^2	0.000	0.086	0.090
Waist circumference (cm)			
β ± SE	2.14 ± 0.09	3.06± 0.17	3.02 ± 0.16
95%CI	(1.95; 2.32)	(2.71; 3.41)	(2.68; 3.36)
R^2	0.460	0.637	0.643
Body Mass Index (kg/m²)			
β ± SE	0.66 ± 0.05	1.32 ± 0.09	1.30 ± 0.08
95%CI	(0.55; 0.77)	(1.14; 1.50)	(1.12; 1.47)
R^2	0.265	0.551	0.558
DXA (% total body fat)			
β ± SE	-0.36 ± 0.07	1.47 ± 0.12	1.46 ± 0.12
95%CI	(-0.50; -0.22)	(1.21; 1.72)	(1.20; 1.71)
R^2	0.019	0.553	0.562

Note: The results are presented as β coefficient, 95%CI and R^2 coefficient. Model 0: neck circumference (cm). The only independent variable considered in the analyses; Model 1: neck circumference (cm), adjusted for age and sex; Model 2: Neck circumference (cm) adjusted for age, sex, schooling, smoking, beverage consumption and physical activity; Logarithmic transformation applied to HOMA-IR, triglycerides and CRP variable SE: Standar Error; 95%CI: 95% Confidence Interval; HDL: High-Density Lipoprotein; LDL: Low Density Lipoprotein; HOMA-IR: Homeostatic Model Assessment Insulin Resistance Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; DXA: Dual Energy X-Ray Absorptiometry.

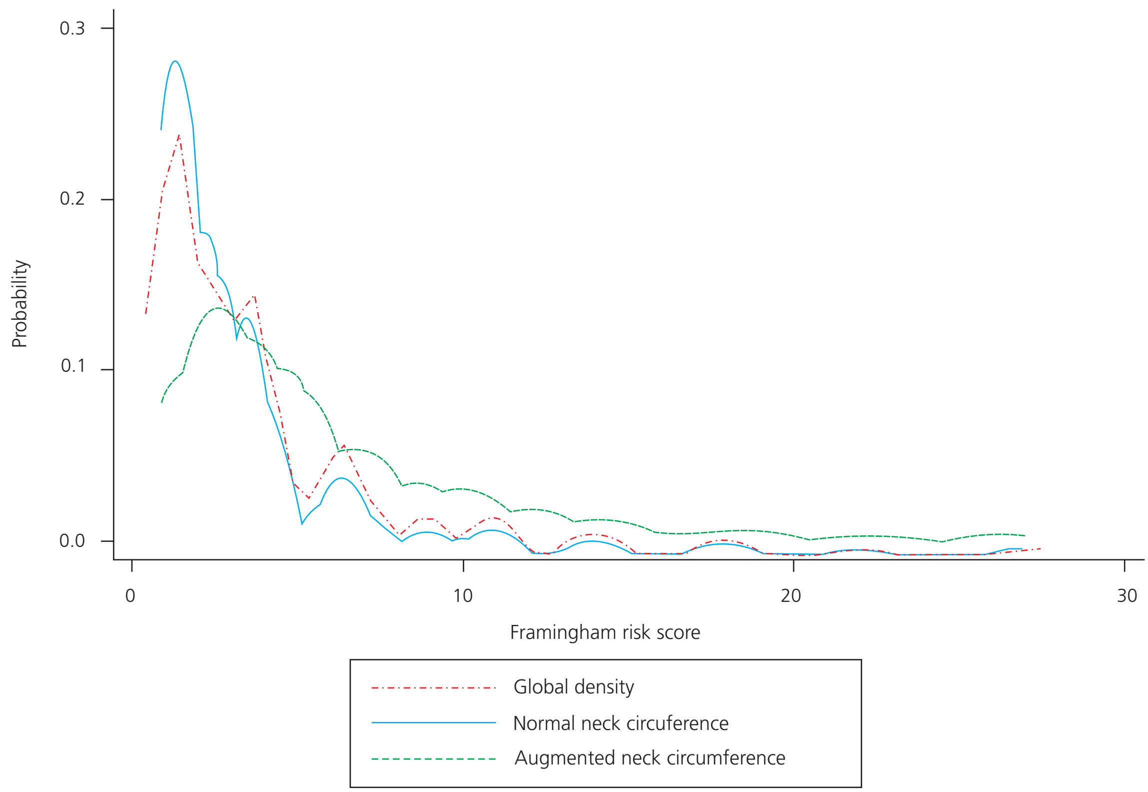

Figure 1. Kernel probability graph. Probability of risk of coronary events in 10 years. Neck circumference (men ≥39.5cm and women ≥33.3cm) and normal neck circumference (men <39.5cm and women <33.3cm).

their associations with cardiometabolic risk factors, showed that neck circumference is similar to waist circumference in predicting these factors, but easier to measure [29]. It is useful in situations such as ascite presence, hernia, pregnancy or in individuals who have undergone abdominoplasty, where waist circumference becomes an inappropriate parameter [10,12].

The mechanism of increased cardiometabolic risks related to neck circumference is not well understood; however, the lipolytic activity of upper body subcutaneous fat may explain this association. This fat compartment would be responsible for a greater release of free fatty acids than the visceral fat, particularly in obese individuals, leading to insulin resistance, hypertriglyceridemia, oxidative stress, vascular injury, and development of arterial hypertension [5,9,12,28,30,31]. These metabolic abnormalities, related to fat accumulation in the upper body segment, makes neck circumference as a possible indicator of atherogenic dyslipidemia.

Overweight and obesity are evaluated with different techniques, from standard gold methods such as computed tomography, magnetic resonance and DXA, which are expensive and often inaccessible, to anthropometric measurements such as waist circumference, BMI, and neck circumference, which are simple and at low cost, but less reliable than the imaging methods for a large section of the population [1,7,10,11]. The positive association of neck circumference with total body fat estimated by the DXA, after adjusting for sociodemographic and behavioral factors, reinforces the use of this measure as a cardiometabolic risk predictor.

Individuals with neck circumference above the cut-off point established by the Receiver Operator Characteristic curve, for both sexes (data not shown), presented a higher Framingham risk score, that is, a higher probability of a coronary event in the next 10 years. Thus, the increase in neck circumference may be a coronary risk indicator for atherogenesis, and thus allow for tracking of asymptomatic individuals. There are no studies directly associating neck circumference with this risk score, though a Framingham Heart Study cohort showed that neck circumference and cardiometabolic risk factors were associated, being stronger in women; however, it did not show neck circumference causality with CVD and coronary disease risks [28]. This finding may be due to the short follow-up period of the individuals to evaluate the coronary disease outcome. However, a Brazilian case-control study reported an association between increased neck circumference and coronary artery disease, where the neck circumference above the 90th percentile increased the chance of coronary artery disease two-fold, and it was an independent cardiovascular disease predictor [32].

This is the second Brazilian population-based study evaluating neck circumference as a cardiometabolic risk indicator, and the first one associating neck circumference cut-off points with coronary artery disease. It was a cross-sectional study, with no causal information. Thus, neck circumference is an indirect fat assessment tool of the upper body segment and not a direct imaging method; however, it is possible to explore associations between the variables studied in a representative sample of an adult population.

CONCLUSION

Increased neck circumference was associated with cardiometabolic risk factors, anthropometric variables, and body composition, even after adjusting for confounding variables. Individuals with neck circumference below the established cutoff points are less likely to have a coronary event in 10 years than those with neck circumference above the cutoff points. Therefore, it is recommended to use this anthropometric parameter as an additional screening tool for asymptomatic adults with cardiovascular risk.

CONTRIBUTORS

VV ZANUNCIO contributed to writing, drafting, statistical analysis, article review. MC PESSOA contributed to in writing and article review. PF PEREIRA contributed to analysis and interpretation of the data. GZ LONG contributed to guiding the research project, elaboration of the article ideas, statistical analysis and article review.

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