


NECK CIRCUMFERENCE AS AN ADIPOSITY INDICATOR AND PREDICTOR OF CARDIOMETABOLIC RISK IN ADOLESCENTS

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ABSTRACT

Objective: To investigate the association between neck circumference (NC) with the central and total adiposity, as well as cardiometabolic risk factors in adolescents. Design: A sectional study included 476 students (53% boys) from 10 to 19 years old of Brazilian population. Weight, height, neck and waist circumferences were measured following standard protocols and total body fat, trunk and android fat were obtained by dual-energy X-ray absorptiometry. Glicidic and lipidic profile, uric acid and arterial pressure have been assessed, and life style characteristics were self-reported. The adolescents were classified according to the presence of insulin resistance (IR) and metabolic syndrome (MetS).

Results: The NC presented positive association with total fat body, trunk and android ($p < 0.05$). The relation between NC with homeostasis model assessment-insulin resistance, uric acid and systolic arterial pressure remained the same when the sample was

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categorized by the nutritional status (eutrophic vs overweight) and by the the occurrence of abdominal obesity (normal vs obese). The NC values were higher ($p<0.05$) in the groups which had ≥ 3 risk factors compared to the ones with 0 to 2 factors. The NC with cutoff point 28.8 and 29.9 cm for girls, as well as 31.7 and 30.4 cm for boys was capable of predicting in both genders the IR and the MetS, respectively ($AUC>0.5$; $p<0.05$). **Conclusion:** The NC can be an alternate instrument of obesity and cardiometabolic risk trial in adolescents.

Keywords: Neck circumference. Central obesity. Cardiovascular risk factors. Metabolic syndrome. Adolescents.

INTRODUCTION

Adolescence constitutes a period of life, from 10 to 19 years old, in which the transition from childhood to the adult life occurs. This stage of life starts with body changes of puberty, and it is characterized by intense biological and psychosocial transformations (WHO, 2005). These changes, sometimes come with conflicts and difficulties, which can be an aggravating or inciting obesity factor (Lamounier *et al.*, 2010), especially when associated with inappropriate eating habits (Chaves *et al.*, 2013) and low frequency of physical activity (Giugliano e Carneiro, 2004). In Brazil, the number of overweight adolescents changed from 3.7% to 21.7% between boys and from 7.6% para 19.4% between girls between 1974-1975 and 2008-2009 (IBGE, 2009).

The adiposity excess in adolescence, especially the abdominal adipose tissue, tends to maintain in the adult phase (Spolidoro *et al.*, 2013) and it is associated to various metabolic alterations, such as insulin resistance, diabetes, high arterial pressure, dyslipidemia, hyperuricemia and subclinical inflammation (Pereira *et al.*, 2012; Staiano *et al.*, 2014). With the obesity increase and the risk factors manifestation for cardiovascular diseases during adolescence, the demand for instruments capable of evaluating and better define obesity and the comorbidity associated risks has also increased.

The body mass index (BMI) is one of the most used feature to evaluate the nutritional status in epidemiological studies, although it is known that there are limitations of this index compared to the localized body fat evaluation (Brambilla *et al.*, 2013). The waist circumference in relation to waist/height ratio (WHR) are used as indicators of central fat and seem to be good predictors of cardiovascular risk factors in adolescents (Pereira *et al.*, 2012; Brambilla *et al.*, 2013). In recent years, the neck circumference (NC) was also introduced as an instrument for obesity trial in young and adults (Nafiu *et al.*, 2010; Li *et al.*, 2014). The NC has been associated with various cardiovascular risk factors in adults (Ben-Noun *et al.*, 2001; Preis *et al.*, 2010; Stabe *et al.*, 2013) children and adolescents (Androutsos *et al.*, 2012; Guo *et al.*, 2012; Kurtoglu *et al.*, 2012) and it has the advantage of being a constant measure throughout the day (Nafiu *et al.*, 2010; Hingorjo *et al.*, 2012).

Since the anthropometric evaluation is a low cost practice, and the early obesity identification and associated comorbidities is important, this study aimed to investigate the association of NC with total and central adiposity, as well as the cardiometabolic risk in adolescents.

METHODS

RESEARCH DESIGN AND STUDIED POPULATION

This cross-sectional epidemiological study was carried out with adolescents from 10 to 19 years old, both genders selected by simple random sampling in all private and public schools in the urban and rural areas of Viçosa, Minas Gerais, Brazil. Inclusion criteria were: not taking regular medicines that could modify glucose, the lipid metabolism and or pressure levels, not having neck deformities, not participate in any reduction or weight control program, not being pregnant or have already been pregnant, not being diagnosed with infections, acute inflammations, Thyroid disease and or other non-communicable chronic diseases.

The sample size has been calculated based on a tool called StatCalc from the program Epi Info, version 6.04 using a specific formula designed to cross-sectional studies, considering the total population of adolescents 11.898 in the municipality of Viçosa (IBGE, 2010), expected prevalence of 50%, since the study considers as outcome the multiple cardiovascular risk factors, acceptable variability of 5% and confidence level 95%. We was added 20% to control the possible confounding factors, totalizing minimum sample of 446 adolescents.

The students were selected among those who delivered the informed consent signed by themselves and by parents or guardians, respecting the proportion of students at each age, in each school. When a participant refused or gave up participating in any of the study phases, another student was selected to substitute him/her. The study was approved by the Human Research Ethics Committee of the Federal University of Viçosa (#0140/2010).

The data collection occurred between 7:00 and 9:30h at the Nutrition Sector and at the Clinical Analysis Laboratory, located at the Health Division Department at Federal University of Viçosa, by qualified previously trained professionals, from January 2010 to march 2012.

ANTHROPOMETRIC EVALUATION

Weight and height have been measured through international standardized techniques (Lohman, 1988), electronic digital scale (LC 200PP, Marte®, São Paulo, SP, Brazil) and portable stadiometer (Altuxata®, Belo Horizonte, MG, Brazil) have been used, with these measurements BMI has been calculated and used to classify the nutritional

status, according to the World Health Organization (WHO, 2013). The NC has been measured at the midpoint between the backbone and the anterior neck, except when the individual had a protrusion in the thyroid cartilage (Adam's apple), in this situation the NC was measured below it (Ben-Noun *et al.*, 2001). The waist circumference was measured at the midpoint between the last rib and the iliac crest in the end of a normal expiration (Lohman T., 1988). All the measurements were taken in the horizontal plane, the adolescents were standing and looking at the horizon, the measurements were carried out in duplicate by a single examiner trained (the average values have been calculated), variations of 0.5 cm were acceptable, a 2 meter flexible inelastic tape measure has been used (Cardiomed®, São Luis, MA, Brazil). The WHtR was assessed through the division between the waist circumference (cm) by the height (cm). The abdominal obesity was considered if $WHtR \geq 0.50$ (Brambilla *et al.*, 2013).

BODY COMPOSITION EVALUATION

Body composition was assessed using dual-energy X-ray absorptiometry (DXA; Lunar Prodigy Advance DXA System - analysis version: 13.31, GE Healthcare, Madison, WI, USA). All evaluations were carried out by the same technician using standard procedures described in the Hologic User's Manual. Total body fat (kg), and truncal (kg) and android adiposity (kg) were assessed by scanning the whole body. Truncal and android fat were determined by analyzing the regions of interest using the manufacturer's software, which demarked the superior margin of the trunk with a horizontal line below the chin. The lateral part of the ribs represented the vertical boundaries, and the inferior margins were formed by oblique lines passing through the femoral heads. The android region was defined as the lower boundary at the pelvis cut and the upper boundary above the pelvis cut at 20% of the distance between the pelvis and the neck cuts (Foo *et al.*, 2013).

BIOCHEMICAL AND BLOOD PRESSURE EVALUATION

After 12 hours of fasting, blood samples were collected from the antecubital vein, and serum was separated by centrifugation at $2,225 \times g$ for 15 minutes at room temperature (2–3 Sigma, Sigma Laborzentrifuzen, Osterodeam Harz, Germany).

Blood glucose was measured using the glucose oxidase method with a Cobas Mira Plus analyzer (Roche Diagnostics, GmbH, Montclair, NJ, USA). Fasting hyperglycemia was

defined as ≥ 100 mg/dL. The fasting insulin was dosed by the electrochemiluminescence method.

High density lipoprotein cholesterol (HDL) and triglycerides have been measured by the enzymatic colorimetric method with automation by the *Cobas Mira Plus (Roche Corp.)* equipment and the low density lipoprotein cholesterol (LDL) was measured by the *Friedewald's* formula for triglycerides results below 400 mg/dL (Friedewald et al., 1972). The lipid profile classification was done according to the Expert Panel and integrated guide for cardiovascular health and risk decreasing in children and adolescents (NHLBI, 2012). The results were considered abnormal when: LDL ≥ 130 mg/dL, HDL < 40 mg/dL e triglycerides ≥ 130 mg/dL.

The uric acid was measured by the enzymatic colorimetric method with automation by the *Cobas Mira Plus (Roche Corp.)* and the results considered high concentration were > 5.5 mg/dL (Loeffler et al., 2012).

Blood pressure has been measured after a minimum 15 minute rest period, using an automatically inflation blood pressure monitor (Omron® Model HEM-741 CINT, Quioto, KYT, Japan) and a long enough cuff to fit the arm perimeter. The measure has been measured three times on the arm that had higher blood pressure, with 1 minute interval between them, and the last two measures were used. The high blood pressure levels were described as systolic blood pressure (SBP) and diastolic (DBP) \geq percentile 90 for age, gender and height (NHLBI, 2012).

INSULIN RESISTANCE DEFINITION AND METABOLIC SYNDROME

The insulin resistance (IR) has been calculated by the mathematical model Homeostasis Model Assessment – Insulin Resistance (HOMA-IR), using the insulin dosage and fasting blood glucose: $HOMA-IR = [(fasting\ insulin\ (\mu U/mL) \times fasting\ glycemia\ [mmol/L])/22.5]$ (Mathews et al., 1985). The results of HOMA-IR ≥ 3.16 were considered as presence of IR.

For the metabolic syndrome (MetS) diagnosis the definition suggested by De Ferranti *et al.* (2004) was used, it is based in the presence of three criteria: waist circumference $>$ percentile 75 according to population gender and age; HDL < 50 mg/dL (except for boys from 15 to 19 years old, in which < 45 mg/dL were used; triglycerides ≥ 100 mg/dL; SBP/DBP $>$ percentile 90 for gender, age and height and fasting glucose ≥ 100 mg/dL. It should be noted that de Ferranti *et al.* (2004), criteria suggests

fasting glucose ≥ 110 , but we opted to use the most recent recommendation of American Diabetes Association (ADA, 2006).

LIFE STYLE

The pattern of physical activity were assessed using the International Physical Activity Questionnaire short form, validated for this population group (Guedes *et al.*, 2005) as a way to classify the sedentary adolescents in irregularly active, active and very active.

Considering that the prevalence of sedentary lifestyle was low in this population, it was chosen to join the sedentary individuals and the irregularly active in the “insufficient active” group and the active and very active individuals in the “physically active” group. The adolescents were also questioned about habits like cigarette smoking and drinking alcoholic beverages.

STATISTICAL ANALYSIS

The results are presented in means \pm standard deviations for the continuous variables with normal or symmetric distribution, in median (the first quartile and the third quartile) for those with asymmetric distribution and in frequency [N(%)] for the categorical variables. The test Shapiro-Wilk, graphical methods (ex: histograms) and the asymmetry coefficient (Skewness >1 : asymmetric) were used to evaluate the variables for normality. The Student's t-test and the U Mann-Whitney test were used for the comparison of anthropometric, corporal composition and cardiometabolic parameters between genders, for variables with parametrical and non-parametrical distribution, respectively. The life style variables frequencies have been compared between genders, using the chi-square test (χ^2).

The correlation between NC and the anthropometric, corporal composition, biochemical and blood pressure variables have been obtained by the Pearson correlation coefficient or Spearman for variables with parametrical and non-parametrical distribution, respectively.

It was used the multiple linear regression analysis to evaluate the association between NC (independent variable) with total adiposity (kg), truncal (kg) and android (kg) (dependent variables). The models were adjusted by gender, age (log), alcohol consumption, smoking habits and physical activity practice. The linear regression was used to investigate the association between NC and the cardiovascular risk parameters: HOMA-IR (log), HDL (log), LDL, triglycerides, uric acid, SBP and DBP. Models without adjustment

have been developed (model 0), adjustment by gender and age (years) (model 1) and adjustment by gender, age, alcohol consumption, smoking habits and physical activity practice (model 2). The results are presented as coefficient $b \pm$ standard error with its confidence interval 95%. The presence of linearity and multicollinearity were evaluated by graphic methods (scatter plots) and tests (variance inflation factor). The residues were tested for normality and homoscedasticity using the Breusch-Pagan /Cook-Weisberg test and graphic methods (scatter plots e histograms).

The Receiver Operating Characteristic (ROC) curves were elaborated and the area under the curve, sensibility, specificity and the optimum cut-off (highest sum between sensibility and specificity) of NC were obtained to predict RI and MetS in each gender.

The data base was elaborated with double digitation, at *Microsoft Office Excel 2007* and for the statistics analysis the programs *STATA*, version 11.0 e *Med Calc*, version 9.3 were used. The significance level in the study was $P < 0.05$.

RESULTS

The demographic, life style, anthropometric and body composition characteristics are presented in Table 1. The participants of both genders presented homogeneous age distribution ($p = 0.295$). In relation to life style, sedentariness was more frequent between the female participants ($p = 0.042$), while the smoking tends to be more frequent in the male gender ($p = 0.056$). The other parameters didn't differ between genders ($p > 0.05$).

The NC average for female and male were, respectively: 29.9 (2.1) cm e 31.4 (3.4) cm; being higher for boys ($p < 0.001$). The total body fat, truncal and android were higher between girls ($p < 0.001$). They also presented a higher frequency of hyperinsulinemia and insulin resistance, while between boys the HDL levels and hyperuricemia were more frequent. The girls presented higher insulinemia, HOMA-IR, HDL, triglycerides and DBP levels. The boys presented higher glucose, uric acid and SBP levels (Table 1).

Table 1 Demographic characteristics, lifestyle, clinical, anthropometric and body composition

Variables	Female	Male	P value
N (%)	222 (47)	254 (53)	
Demographic			
Age	12.2 (10.9-14.2)	12.4 (11.0-14.3)	0.295
Lifestyle			
Insufficient physical activity	69 (31)	58 (23)	0.042
Smoking	8 (3.6)	18 (7.1)	0.056

Consumption of alcohol	19 (8.6)	36 (14.2)	0.095
<i>Anthropometry</i>			
Weight (kg)	44.8 (10.2)	47.1 (15.4)	0.809
Height (cm)	152.3 (9.8)	155.4 (13.6)	0.067
BMI (kg/m ²)	19.2 (3.2)	19.0 (3.8)	0.330
Waist (cm)	70 (9.0)	69.3 (10.7)	0.244
WHR	0.45 (0.42-0.48)	0.43 (0.41-0.47)	0.116
NC (cm)	29.9 (2.1)	31.4 (3.4)	0.001
<i>Body Composition</i>			
Body fat (kg)	11.2 (8-15.5)	6.5 (4.3-11)	0.001
Truncal fat (kg)	3.1 (2.1-4.8)	1.7 (1.1-3.7)	0.001
Android fat (kg)	0.3 (0.2-0.5)	0.2 (0.1-0.4)	0.001
<i>Clinics</i>			
Prevalence N(%)			
Overweigh/obesity	47 (21.2)	56 (22.1)	0.817
Abdominal obesity	45 (20.3)	35 (13.8)	0.059
Metabolic Syndrome	19 (8.6)	19 (7.5)	0.665
Insulin resistance	34 (15.3)	16 (6.3)	0.001
Low HDL	25 (11.3)	53 (20.9)	0.005
High LDL	21 (9.5)	21 (8.3)	0.647
Hypertriglyceridemia	21 (9.5)	17 (6.7)	0.267
Hyperuricemia	0 (0)	15 (5.9)	0.001
Hypertension	6 (2.7)	9 (3.5)	0.600
Glycemia (mg/dL)	84.3 (7.2)	86.3 (6.9)	0.003
Insulinemia (mcU/mL)	9.2 (6.6-13)	6.5 (4.7-9.3)	0.001
HOMA-IR	1.9 (1.3-2.8)	1.4 (0.9-2.0)	0.001
HDL (mg/dL)	51 (44-59)	48 (41-58)	0.009
LDL (mg/dL)	95.7 (25.8)	94.7 (23.2)	0.696
Triglycerides (mg/dL)	66 (51-92)	63 (50-84)	0.106
Uric acid (mg/dL)	2.9 (0.7)	3.3 (1.1)	0.006
SBP (mmHg)	97.3 (10)	99.8 (12.1)	0.004
DBP (mmHg)	61.4 (7.3)	58.9 (7.2)	0.001

BMI: Body Mass Index; WHtR: Waist/height ratio; NC: Neck circumference; HOMA-IR: Homeostatic Model Assessment Insulin Resistance; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure. The dates were presented through mean and standard deviation (SD), median (percentile 25-percentile75) or N (%) according the characteristics of the variable. U Mann-Whitney test for variables with asymmetric distribution and Student's t-test for variables with symmetric distribution. Chi-squared test for to analyze categorical variables.

The NC presented correlations that varied from 0.38-0.81 with the total and central adiposity indicators, as body total fat, truncal and android. The NC has also correlated positively with HOMA-IR, insulinemia, uric acid, SBP and DBP, with amplitudes that vary from 0.28-0.74; and negatively with HDL, in both genders. Besides that, in the male gender the NC has also presented positive correlation with triglycerides (Table 2).

Table 2 Correlation coefficient of the neck circumference with age, anthropometric parameter, body composition and cardiometabolic risk factors

Parameters	Female (r)	Male (r)
Age	0.48**	0.71**
BMI (kg/m ²) ^a	0.72**	0.80**
Waist (cm) ^a	0.70**	0.81**
WHR ^b	0.46**	0.38**
Body fat (kg) ^b	0.68**	0.58**
Truncal fat (kg) ^b	0.66**	0.63**
Android fat (kg) ^b	0.57**	0.66**
Insulinemia (mcU/mL) ^b	0.39**	0.43**
HOMA-IR ^b	0.34**	0.40**
HDL (mg/dL) ^b	-0.19**	-0.28**
LDL (mg/dL) ^a	-0.04	-0.09
Triglycerides (mg/dL) ^b	0.04	0.22**
Uric acid (mg/dL) ^a	0.28**	0.68**
SBP (mg/dL) ^a	0.60**	0.74**
DBP (mg/dL) ^a	0.39**	0.35**

r, correlation coefficient; BMI, Body Mass Index; WHtR, Waist/height ratio; HOMA-IR, Homeostatic Model Assessment- Insulin Resistance; LDL, Low Density Lipoprotein; HDL, High Density Lipoprotein; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure. ^aPearson or ^bSpearman correlation coefficient. * p<0.05, **p<0.01

The multiple linear regression analysis indicated that NC is a good predictor of truncal, android and total body fat in adolescents, no matter the gender or how old they are, even after the adjustment for smoking habits, alcohol consumption and physical activity (Table 3).

Table 3 Results of multiple linear regression models to evaluate the association between neck circumference and total, truncal and android body fat

Dependent Variable	b±SE	CI 95%	R ²	P value
Total body fat (kg)	0.072±0.004	0.064; 0.080	0.496	< 0.001
Truncal fat (kg)	0.091±0.005	0.081; 0.101	0.487	<0.001
Android fat (kg)	0.102±0.006	0.090; 0.114	0.445	<0.001

The results were presented in b (coefficient) ± SE (standard error), CI (Confidence Interval 95%), R² (determination coefficient) and P value.

Model adjusted for age, sex, smoking, alcohol consumption and physical activity practice.

Logarithmic transformation was applied to variables with skewed distribution (age, total body fat, truncal and android).

The linear regression models between NC and the cardiometabolic risk factors, adjusted by gender and age, indicated positive association of NC with HOMA-IR, triglycerides, uric acid, SBP and DBP and negative with HDL (Table 4). Indeed, NC was a

better predictor of acid uric and blood pressure, every increase of 1cm at the NC was related to the increase of 0.2 mg/dL in the acid uric concentration, to the increase of 2.4 mmHg at SBP and 0.8 mmHg at DBP. These associations remained significant at the same direction even after the smoking cigarette, alcohol consumption and physical activity practice adjustment. When the analysis was done for each gender separately, only the relation with triglycerides didn't remain significant for the female gender.

Table 4 Results of linear regression models to evaluate the association between neck circumference (cm) and cardiometabolic risk parameters

Dependent Variable		Model 0	Model 1	Model 2
HOMA-IR	b ±SE	0.024±0.003	0.047±0.004	0.0457±0.005
	CI 95%	0.017; 0.032	0.037; 0.056	0.036; 0.055
	R ²	0.083	0.232	0.235
	P	<0.001	<0.001	<0.001
HDL (mg/dL)	b ±SE	-0.009±0.001	-0.011 ±0.002	-0.010± 0.002
	CI 95%	-0.012; -0.058	-0.015; -0.006	-0.014; -0.006
	R ²	0.065	0.068	0.069
	P	<0.001	<0.001	<0.001
LDL (mg/dL)	b ± SE	-0.572± 0.380	-0.328± 0.518	-0.219± 0.527
	IC 95%	-1.312 ; 0.174	-1.347; 0.691	-1.255; 0.815
	R ²	0,004	-0.0004	-0.004
	P	0.132	0.426	0.692
TG (mg/dL)	b ±SE	0.008±0.003	0.015±0.003	0.014 ±0.003
	IC 95%	0.003; 0.014	0.007; 0.023	0.007±0.022
	R ²	0.017	0.035	0,041
	P	=0.0034	=0.0002	=0,0002
UA (mg/dL)	b ±SE	0.199±0.118	0.187±0.016	0.184±0.016
	IC 95%	0.176; 0.222	0.155; 0.219	0.152; 0,217
	R ²	0.374	0.372	0.371
	P	<0.001	<0.001	<0.001
SBP (mmHg)	b ±SE	2.618±0.127	2.361±0.171	2.374± 0.174
	IC 95%	0.429; 0.862	2.024; 2.698	2.032; 2.716
	R ²	0.472	0.482	0.480
	P	<0.001	<0.001	<0.001
DBP (mmHg)	b ±SE	0.645±0.110	0.812±0,146	0.811± 0.148
	IC 95%	0.429; 0.862	0.524 ; 1.098	0.519; 1.102
	R ²	0.067	0.118	0.113
	P	<0.001	<0.001	<0.001

HOMA-IR, Homeostatic Model Assessment-Insulin Resistance; LDL, Low Density Lipoprotein; HDL, High Density Lipoprotein; UA, Uric Acid; TG, Triglycerides; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure. The results were presented in b (coefficient) ± SE (standard error), CI (Confidence Interval 95%), R² (determination coefficient) and P value.

Model 0: neck circumference (cm) was the only independent variable included in the model.

Model 1: neck circumference (cm), age and gender adjusted.

Model 2: model 1, additionally adjusted for smoking, alcohol consumption and physical activity practice. Logarithmic transformation was applied to variables with skewed distribution (HOMA-IR, HDL, triglycerides and age).

Because of the multicollinearity between anthropometric indicators and as a way to evaluate the independent NC effect, the analysis of this perimeter as an adiposity predictor has been stratified by the nutritional status classification (overweight/obesity; BMI Z-score $\geq +1$ or normal: BMI Z-score $< +1$) and abdominal obesity (WHtR ≥ 0.50 or WHtR < 0.50). In all the stratifications of BMI and WHtR, the NC was positively associated with HOMA-IR, uric acid and SBP. Besides that, the NC maintained positive association to DBP and triglycerides and negative with HDL in the groups with appropriate BMI and normal WHtR (table 5).

Table 5 Results of linear regression models to evaluate the association between neck circumference (cm) and cardiometabolic risk parameters, according to the classification of nutritional status and abdominal obesity

Dependent variable		BMI Z-score $\geq +1$	BMI Z-score-z $< +1$	WHtR ≥ 0.50	WHtR < 0.50
HOMA-IR	b \pm SE	0.039 \pm 0.012	0.030 \pm 0.006	0.048 \pm 0.012	0.031 \pm 0.006
	CI 95%	0.015; 0.064	0.017; 0.043	0.024; 0.071	0.019; 0.043
	R ²	0,134	0.174	0.140	0.171
	P	0.0028	<0.001	0.0084	<0.001
HDL (mg/dL)	b \pm SE	-0.002 \pm 0.005	-0.008 \pm 0.003	-0.006 \pm 0.004	-0.008 \pm 0.003
	IC 95%	-0.012; 0.008	-0.014 \pm 0.002	-0.016; 0.003	-0.013; -0.002
	R ²	-0.02	0,038	-0.044	0.048
	P	0.687	0.0025	0.8511	0.0003
LDL (mg/dL)	b \pm SE	-0.425 \pm 1.405	-1.143 \pm 0.735	-0.245 \pm 1.385	-1.197 \pm 0.660
	CI 95%	-3.214; 2.364	-2.589; 0.308	-3.006; 2.516	-2.496; 0.102
	R ²	-0.006	0.001	-0.002	0.015
	P	0.5001	0.3903	0.4514	0.0682
TG (mg/dL)	b \pm SE	0.010 \pm 0.0117	0.006 \pm 0.005	0.010 \pm 0.011	0.005 \pm 0.005
	CI 95%	-0.013; 0.033	-0.004; 0.0165	-0.011; 0.032	-0.004 \pm 0.015
	R ²	-0.048	0.026	-0.055	0.021
	P	0.9702	0.0144	0.9337	0.0282
UA (mg/dL)	b \pm SE	0.149 \pm 0.049	0.162 \pm 0.021	0.172 \pm 0.045	0.184 \pm 0.021
	CI 95%	0.0507; 0.247	0.120; 0.205	0.081; 0.263	0.143; 0.224
	R ²	0.388	0.339	0.354	0.352
	P	<0.001	<0.001	<0.001	<0.001
SBP (mmHg)	b \pm SE	2.608 \pm 0.418	2.033 \pm 0.249	2.793 \pm 0.389	2.062 \pm 0.227
	CI 95%	1.778; 3.438	1.543; 2.522	2.016; 3.570	1.616; 2.508
	R ²	0.496	0.444	0.527	0.446
	P	<0.001	<0.001	<0.001	<0.001
DBP (mmHg)	b \pm SE	0.663 \pm 0.350	0.574 \pm 0.211	0.458 \pm 0.318	0.613 \pm 0.192

CI 95%	-0.032; 1.359	0.160; 0.989	-0.176; 1.093	0.234; 0.991
R ²	0.057	0.115	0.058	0.099
P	0.0671	<0.001	0.1070	<0.001

BMI, body mass index, WHtR, waist/height ratio; HOMA-IR, Homeostatic Model Assessment-Insulin Resistance; LDL, Low Density Lipoprotein; HDL, High Density Lipoprotein; UA, Uric Acid; TG, Triglycerides; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure. The results were presented in b (coefficient) ± SE (standard error), CI (Confidence Interval 95%), R² (determination coefficient) and P value. Models adjusted for age, gender, smoking, alcohol consumption and physical activity practice. Logarithmic transformation was applied to variables with skewed distribution (HOMA-IR, HDL, triglycerides and age).

The NC distribution according to the cardiometabolic risk factor numbers was analyzed (risk factors: HDL, triglycerides, blood pressure, HOMA-IR and uric acid). There was an increase of this perimeter related to the increase of risk factor numbers. The NC averages were higher ($p < 0.05$) in the group with ≥ 3 risk factors when compared to those with 0 to 2 factors (data not shown in tables).

In the ROC analysis, to predict IR, on the female gender, the NC presented sensibility 94.1 and specificity 36.2. On the male gender, the sensibility was 87.7 and specificity 64.3. The cutoff point with better equilibrium between sensibility and specificity was NC > 28.8 cm for girls and > 31.7 cm for boys (Figure 1). In relation to MetS, on the female gender, the sensibility was 89.5 and specificity 55.2. On the male gender, the sensibility was 94.7 and specificity 49.4. The cutoff point with better equilibrium between sensibility and specificity was NC > 29.9 cm for girls and > 30.4 for boys (Figure 2). For both genders and risk markers, the areas below curve were ≥ 0.5 .

Fig. 1 Receiver Operating Characteristic (ROC) curve of the neck circumference for predicting insulin resistance in females (a) and males (b). NC, neck circumference; AUC, Area under curve.

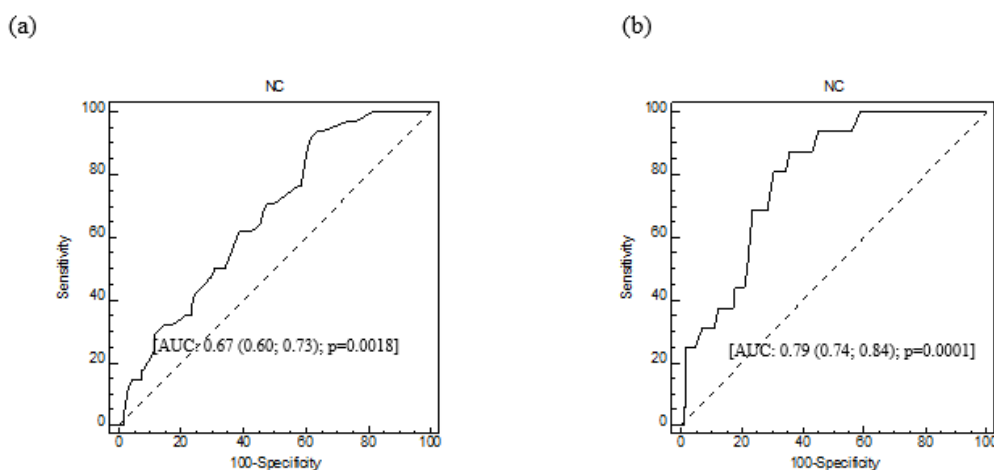
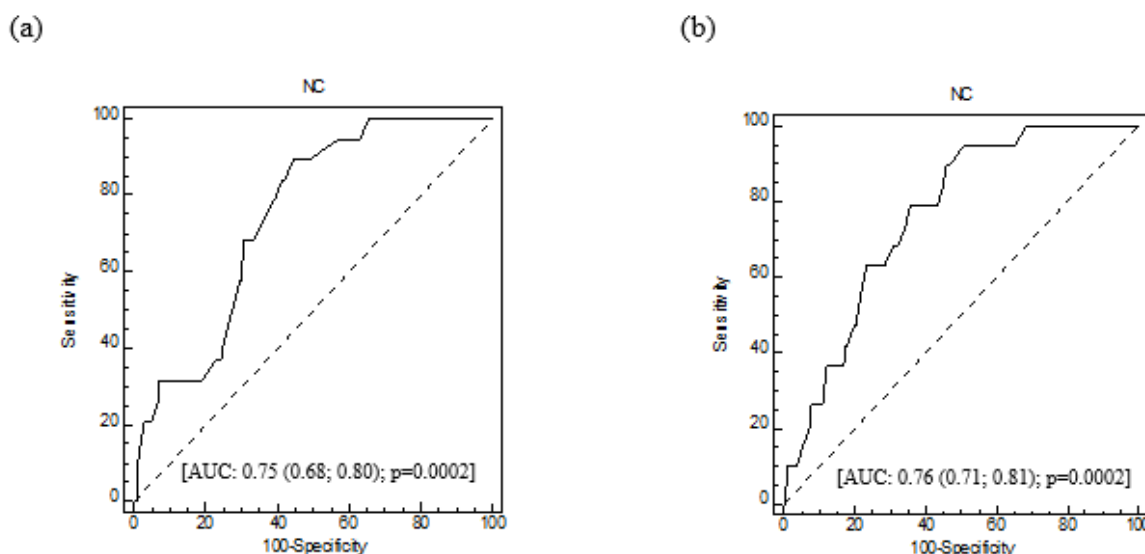


Fig. 2 Receiver Operating Characteristic (ROC) curve of the neck circumference for predicting metabolic syndrome in females (a) and males (b). NC, neck circumference; AUC, Area under curve.



DISCUSSION

It is known that the fat accumulation on the upper part of the body, more than the total body fat, is associated to metabolic disorders and cardiovascular risk factors (Kurtoglu *et al.*, 2012). The waist circumference has been considered an anthropometric indicator of better performance. More recently, the NC has been suggested as an alternate measurement to the waist circumference, because it is not influenced by the abdominal distension level after eating, nor even by the respiratory movements and for being at the same time a simple, trustful and practical parameter, besides presenting a good interobserver reliability (Nafiu *et al.*, 2010; Androutsos *et al.*, 2012; Kurtoglu *et al.*, 2012).

In this study, higher NC have been observed on the male gender, which is in agreement with previous studies in adult (Stabe *et al.*, 2013) and young (5 to 18 years old) (Guo *et al.*, 2012). A study with 5.841 children and adolescents (6 to 18 years) from Turkey it was observed that until 12 years old, there are no differences between genders on NC, but from this age on the NC is higher on boys, which can be a result of the increase of subcutaneous adipose tissue on the upper part of the body in boys and an increase of this adipose tissue on the bottom part of the girl's body (Mazicioglu *et al.*, 2010). However, Androutsos *et al.* (2012) hasn't observed difference on NC between genders, possibly due to the studied age range, that was, 9 to 13 years old.

This study has revealed that NC is a good predictor of truncal, android and total adiposity in adolescents of both genders through multiple linear regression analysis (R^2

from 0.44 to 0.49). The high correlations ($0.70 < r < 0.81$) observed between NC with BMI and waist circumference reinforce that NC can be a reliable obesity measurement. The obtained results are in accordance with those described in the literature, since the significant correlation between the fat area neck and visceral adipose tissue was described in adults and elderly Chinese people, of both genders (Li *et al.*, 2014). In another adult evaluation, the correlation between NC and adipose visceral tissue ($r=0.63$ men; $r=0.74$ women) and BMI ($r=0.79$ men; $r=0.80$ women) was observed (Preis *et al.*, 2010). In children and adolescents, the NC has presented positive correlation with age, BMI and waist circumference in boys and girls, and it was capable of identifying individuals with high BMI (Nafiu *et al.*, 2010). When the NC was used to evaluate the overweight and obesity trial in childhood and adolescence it was observed similar capacity to the waist circumference (Hatipoglu *et al.*, 2010). It is important to point out that the central obesity has a positive association with the obstructive sleep syndrome or apnea, since the NC constitutes a good indicator of this adiposity, it can be used in the trial of individuals with sleep disorders (Mazicioglu *et al.*, 2010).

The subcutaneous fat on the upper part of the body is a unique fat deposit that can be easily evaluated and seems to be an important cardiometabolic risk predictor. The analysis of this risk can lead to a better understanding of the differential effects of adiposity in men and women (Preis *et al.*, 2010). At the present study, the NC has been associated with established cardiometabolic risk factors, such as insulin, HOMA-IR, triglycerides (only in boys), HDL and blood pressure in adolescents. The NC was associated with uric acid, an emerging cardiometabolic risk. These associations remained significant even after the adjustment by demographic and life style characteristics. When the analysis were stratified by gender, the triglycerides association in girls didn't remain significant. When the models were stratified by category of BMI and WHtR, the association of NC with HOMA-IR, uric acid and SBP remained significant. The association of NC with the lipid profile seems to be dependent on the body fat accumulation. These results confirm that the NC is useful to evaluate the cardiometabolic risk, it has been shown previously with adults (Preis *et al.*, 2010; Stabe *et al.*, 2013) as well as in children and adolescents (Androutsos *et al.*, 2012; Guo *et al.*, 2012; Kurtoglu *et al.*, 2012).

The free fatty acid excess that comes from the subcutaneous fat, in the upper part of the body, can be one of the mechanisms that explain the relation between NC and the cardiometabolic risk (Preis *et al.*, 2010). This location contributes with the major part of free

fatty acid release in the systemic circulation, in large quantity can lead to IR, high blood pressure and dyslipidemia (mainly characterized by hypertriglyceridemia, low HDL levels and high LDL levels small and dense more atherogenic) that benefits the vascular damage and the atherosclerotic plaques (Jensen *et al.*, 2008).

In the Framingham Heart Study conducted with 3.307 (48% women) adults, the NC was associated with high insulin levels, HOMA-IR, triglycerides and the SBP; and with low HDL concentration, even after adjustment by gender, visceral adipose tissue and BMI (Preis *et al.*, 2010). In another study with adults, the NC was predictor of dyslipidemia atherogenic (hypertriglyceridemia and low HDL concentration) and hyperuricemia, independently of BMI and the waist circumference (Vallianou *et al.*, 2013). The results of the present study about the relation between NC and the cardiometabolic risk factors have been similar to the ones found by Androutsos *et al.* (2012) studying 324 children and adolescents from 9 to 13 years old in Greece.

It is known that the International Federation of Diabetes focus on the importance of the diagnosis and treatment of the MetS in children and adolescents to prevent cardiovascular diseases. The clinical elements to diagnose the MetS include alteration in three of the following components: waist circumference, HDL, triglycerides, blood pressure and glucose (Zimmet *et al.*, 2007). In the present study the NC presented correlation from moderate to strong with all the MetS components in adolescents, except with HDL in which the correlation was considered low for both genders. Indeed, the NC cutoff point identified with a better equilibrium between the sensibility and specificity for the IR diagnosis was 28.8 cm for girls and 31.7 cm for boys, while to predict the MetS was 29.9 cm for girls and 30.4 cm for boys. Kurtoglu *et al.* (2012) identified NC of 35 cm and 36 cm for girls and boys, respectively as a great cutoff point to identify MetS in adolescents from 10 to 18 years old.

In practice, a trial population instrument should be sensible, which results in a lower number of false negative, even if it has a higher number of false positive, due to the specificity loss. However, an ambulatory instrument to evaluate the risks to health should have equilibrium between the two parameters, since the specificity helps in the rationalization of the health resources (Barbosa *et al.*, 2006). The cutoff points obtained in this study indicate high sensibility, but low specificity, which suggests the use of it for a population study and its limitation as an isolated measurement in the clinical assistance.

The major strength of the present study is that the study sample was composed by adolescents of all ages and also of all weight categories, thus broadening the applicability of the findings. The overweight prevalence in our population was very similar to the one observed in the adolescents population of Brazil, according to the last Family Budgets Survey (IBGE, 2009). The limitations of this study includes the transversal delineating cut that does not allow to establish the relation between cause and effect of the results and the relative sample size that did not permit a layered analysis for adolescence stage, even though the models have been adjusted by age.

Further research is needed to examine the NC relation with the cardiometabolic risk factors in a longitudinal design, as well as cutoff points in different population and in both sexes, once they may present a distinct behavior depending on gender and age group.

CONCLUSION

In this study, the NC has shown to be a good total and central adiposity indicator, independent of gender and age. Besides that, the NC was a predictor for values of HOMA-IR, uric acid, SBP in adolescents, no matter the presence of overweight or central obesity. The association of NC with the lipid profile seems to be dependent of the body fat accumulation. Together, our results show that the NC is an additional simple instrument, that has low cost and it is sensible for the trial of cardiometabolic risk factors in adolescents, especially in epidemiological studies.

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