Waist, neck circumferences, waist-to-hip ratio: Which is the best cardiometabolic risk marker in women with severe obesity? The SOON cohort

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Abstract

A centralized deposit of adiposity increases the risk of cardiometabolic diseases. Several anthropometric markers can be used to characterize fat distribution. In the case of severe obesity, several markers, such as hip and waist circumference, are prone to measurement error. Conversely, neck circumference is easy to obtain. The aim was to determine the best surrogate marker of obesity-related cardiometabolic diseases from: body mass index (BMI), waist, hip and neck circumferences and waist-to-hip ratio.

Methods

Data from women (n = 305, aged 43 [34; 53] years-old, BMI 44.2 [40.8; 48.2] kg/m^2) included in the Severe Obesity Outcome Network (SOON) cohort were analyzed (i) to evaluate collinearity between the different anthropometric markers, (ii) to compare the association of markers with hypertension, type 2 diabetes, obstructive sleep apnea syndrome (OSAS) and other cardiometabolic risks.

Results

Hip, waist and neck circumferences correlated with BMI with respectively less collinearity (r = 0.70, r = 0.59 and r = 0.37, respectively, p<0.001) whereas waist-to-hip ratio was not correlated (r = 0.11, p = 0.072). Waist and neck circumferences were significantly associated with hypertension, type 2 diabetes and OSAS in univariate logistic regressions, waist-to-hip ratio with hypertension and type 2 diabetes. Hip circumference was inversely correlated with type 2 diabetes (OR 0.970 (95CI: 0.948; 0.991) p = 0.006). BMI was only linked to OSAS (OR 1.092 (95CI: 1.043; 1.143) p<0.001). Neck circumference was the only marker significantly associated with all cardiometabolic risk markers (HOMA-IR, apnea-hypopnea index, Log Triglycerides/HDL-c, alanin-aminotransferase, aspartate-aminotransferase, gamma-glutamyl transpeptidase).

Conclusions

Neck circumference appears the most appropriate anthropometric marker to identify the fat distribution associated with high cardiometabolic risk in women with severe obesity.

Introduction

Obesity affects physical, psychological and social well-being. Although there is a relationship between obesity and cardiometabolic diseases, the risk of developing such diseases is variable. In the 1950's studies showed that obesity-related cardiovascular and metabolic comorbidities were associated with a centralized deposit of adiposity [1]. Excess visceral fat is associated with a loss of the capacity to stock excessive calories within subcutaneous adipose tissue, inducing an ectopic fat deposition in the liver, muscles, heart etc. that leads to metabolic syndrome and cardiometabolic diseases [2]. Patients with a central obesity distribution have therefore a higher risk of hypertension, type 2 diabetes, obstructive sleep apnea syndrome (OSAS) and non-alcoholic fatty liver diseases (NAFLD). The risk of cardiovascular diseases is also high [3]. Conversely, obese patients with peripheral or subcutaneous adiposity are usually "metabolically healthy", and even protected against metabolic diseases because subcutaneous adiposity is both a marker of, and a contributor to, a high level of insulin sensitivity [4, 5].

Waist circumference and waist-to-hip ratio are well established as useful indicators of visceral fat accumulation. These simple anthropometric measurements can detect subjects at risk in the primary care setting. However, waist circumference increases with increasing body weight. Progressively higher median waist values are associated with increasing body mass index (BMI), although for any given BMI value, the variation in waist circumference is considerable. Thus it is difficult to define a single cut-off value for abdominal obesity across a large range of BMIs [6]. Waist-to-hip ratio is not limited in the same way since the collinearity of waist and hip circumferences with BMI is neutralized by dividing one by the other [7]. However, the measurement of waist and hip circumference in patients with severe obesity is hampered by technical issues. The measurement of waist circumference is often complicated by the lumbar lordosis and measurement of hip circumference is difficult due to the abdominal fat apron. Neck circumference is used as an anthropometric marker to detect patients at risk of sleep apnea syndrome [8]; however, this marker also appears to be associated with metabolic disorders [9, 10].

The aim of this study was to compare the level of association of different anthropometric markers with cardiometabolic diseases and cardiometabolic risk markers in women with severe obesity. We sought to determine which of the following parameters was the best surrogate to identify women with a high risk of obesity related diseases: BMI, waist, hip and neck circumferences, and waist-to-hip ratio. In addition, we assessed whether waist-to-height and neck-to-height ratios improved the results obtained with waist and neck circumferences, respectively.

Materials and methods

The severe obesity outcome network (SOON) cohort recruited adult patients volunteering for bariatric surgery from the 1st of September 2013, at the Grenoble Alpes University Hospital, France. The population studied was mainly of Caucasian people living in France. Inclusion criteria were based on French recommendations; adults aged 18–65 years-old with class III

obesity (body mass index (BMI) $\geq$40 kg/m^2) or class II obesity (40>BMI $\geq$35 kg/m^2) with at least one obesity-related complication (type 2 diabetes, hypertension, OSAS or nonalcoholic steatohepatitis). Exclusion criteria were contraindications to bariatric surgery: pregnancy, psychotic disease and alcohol or drug addictions. The present work analyzed the data from the 305 women included by September 2016. The present study was reviewed and approved by an institutional review board (ethics committee: "Comité de protection des personnes Sud-Est V", IRB 6705) before the study began. All patients signed informed consent for their inclusion. The SOON cohort is registered on clinical trials (NCT02264431).

Study design

Observational, transversal study.

Anthropometric measures

Height, weight, and hip, waist and neck circumference were measured according to standardized procedures at the greater trochanter, iliac crest, and cricoid, respectively [11]. Circumferences were measured with the participant in a standing position using a non-extensible, flexible anthropometric tape.

Plasma, glucose/insulin homeostasis profile

Women were considered to have type 2 diabetes either based on current medication for diabetes or by HbA1c > 6.5%, fasting plasma glucose above 7 mmol/L over two separate analyses, or according to the results of a 75g oral glucose tolerance test (OGTT) with fasting glucose $\geq$7 mmol/L or 120 min OGTT-glucose $\geq$11.1 mmol/L [12]. Insulin resistance was assessed with HOMA-IR index, based on fasting plasma and insulin levels [13].

Plasma lipid/lipoprotein profile

Plasma HDL-cholesterol, triglycerides, VLDL-cholesterol and LDL-cholesterol were determined according to standardized procedures [14, 15].

Blood pressure

Hypertension was determined either by current use of anti-hypertensive drugs or by a mean systolic blood pressure above 140 mmHg and/or a diastolic blood pressure above 90 mmHg found during three blood pressure measurements taken 3 min apart on the non-dominant arm, with an appropriate-sized cuff after the patient had been sitting for 5 min [16].

Sleep apnea syndrome

OSAS was determined either by current use of continuous positive airway pressure therapy or an oral mandibular advancement device, or by the results of nocturnal polygraphy. The recordings were scored according to standardized methods, described in the American Academy of Sleep Medicine (AASM) Manual for Scoring Sleep and Associated Events [17]. Patients with an apnea+hypopnea index (AHI) >30 apnea + hypopnea events per hour were considered to have severe OSAS.

Functional liver tests

Functional liver enzymes, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gammaglutamyl transpeptidase (GT) were evaluated.

Statistical analysis

Descriptive data are reported as medians [interquartile range] for continuous variables and as numbers (%) for qualitative variables.

Univariate correlations were analyzed using non-parametric Spearman tests to assess collinearity between anthropometric markers. A weighted local regression line (LOESS) was added on graphic representations.

Univariate logistic regressions were performed to address the relationship between anthropometric markers and obesity related diseases (Type 2 diabetes, hypertension, OSAS). The linearity of each variable was tested using a generalized additive model (proc GAM in SAS). One outlier for waist-to-hip ratio conducted to perform a sensitivity analysis for logistic regressions involving waist-to-hip ratio. Multiple logistic regressions were then performed including age, tobacco, alcohol consumption and the presence of depression as covariates in the models.

Univariate correlations were performed using non-parametric Spearman tests to measure the relationship between anthropometric markers and continuous cardiometabolic risk markers (log TG/HDL, HOMA-IR, AST, ALT, GT, AHI).

Models were performed with imputed data according to the FCS logistic regression method, using 10 data sets to deal with missing data (less than 10% in all cases). For patients previously diagnosed and treated for severe OSAS, AHI was missing. Imputation of data for AHI in these patients was performed using the subpopulation of women who were found to have OSAS on nocturnal polygraphy.

The significance level was set at $p < 0.05$. All analyses were performed with the SAS statistical package version 9.4 (SAS Institute, Cary, NC, USA).

Results

The characteristics of the women included are reported in Table 1. In these mainly middle-aged women, the prevalence of obesity-related diseases was 26.6% for type 2 diabetes, 28.0% for hypertension and 29.9% for severe OSAS.

Collinearity among anthropometric markers

Waist and hip circumferences were highly collinear with BMI ($r = 0.59$ $p < 0.001$ and $r = 0.70$ $p < 0.001$, respectively). Neck circumference and BMI were collinear but with a smaller r coefficient ($r = 0.37$ $p < 0.001$), whereas waist-to-hip ratio was unrelated to BMI ($r = 0.11$ $p = 0.072$). Waist-to-height and neck-to-height ratios demonstrated similar results to waist and neck circumferences, respectively ($r = 0.61$, $p < 0.001$ and $r = 0.37$, $p < 0.001$, respectively).

Waist circumference and waist-to-hip ratio were also collinear with hip circumference ($r = 0.37$ and $r = 0.53$, respectively, $p < 0.001$ for both). Neck circumference was the only anthropometric marker that was collinear with other markers of central adiposity ($r = 0.51$ with waist circumference and $r = 0.34$ with waist-to-hip ratio, $p < 0.001$) whereas it was unrelated to hip circumference ($r = 0.11$, $p = 0.084$), a marker of subcutaneous adiposity.

Association between anthropometric markers and obesity related diseases

Univariate logistic regressions are reported in Fig 1. Waist and neck circumferences were significantly associated with hypertension, type 2 diabetes and OSAS. Hip circumference was unrelated to hypertension or OSAS and inversely associated with type 2 diabetes. The logistic regressions with waist-to-hip ratio were influenced by an outlier waist-to-hip ratio of 1.99, due to an extremely large abdominal apron. A sensitivity analysis without this patient led to a significant association of waist-to-hip with hypertension and type 2 diabetes but not with OSAS.

Table 1. Patient characteristics.

	N = 305
Age (years)	43 [34; 53]
Female gender n (%)	305 (100.0)
Anthropometric markers	
Body weight (kg)	117 [107; 129]
BMI (kg/m2)	44.2 [40.8; 48.2]
Waist circumference (cm)	123 [115; 130.5]
Hip circumference (cm)	134 [125; 143]
Neck circumference (cm)	40.2 [38; 42]
Waist-to-hip ratio	0.91 [0.85; 0.98]
Neck-to-height	0.25 [0.23; 0.26]
Waist-to-height	0.76 [0.71; 0.81]
Obesity related diseases	
Hypertension n (%)	85 (28.0)
Systolic blood pressure (mmHg)	123 [116; 133]
Diastolic blood pressure (mmHg)	70 [63; 77]
Diabetes n (%)	81 (26.6)
HOMA-IR	3.6 [2.3; 6.4]
Sleep apnea syndrome	
Mild n (%)	102 (34.6)
Moderate n (%)	63 (21.4)
Severe n (%)	88 (29.8)
IAH 3% (event/h)	13.8 [7.1; 26]
Number of associated comorbidities*	
0 n (%)	145 (47.5)
1 n (%)	83 (27.2)
2 n (%)	60 (19.7)
3 n (%)	17 (5.6)
Lipid/lipoprotein profile	
Triglycerides (mmol/L)	1.5 [1.1; 2]
HDL-c (mmol/L)	1.2 [1; 1.4]
LDL-c (mmol/L)	2.9 [2.4; 3.6]
Log Tg/HDL-c	0.4 [0.1; 0.6]
Liver functional tests	
ALT (UI/L)	31 [23.5; 44]
AST (UI/L)	18 [14; 25]
GT (UI/L)	31 [19; 53]

Data are medians (IQR) for continuous variables and n (%) for qualitative variables. Abbreviations: BMI: body mass index; HOMA-IR: HOMA-Index Resistance; Tg: triglycerides; AHI: apnea-hypopnea index; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GT: gammaglutamyl transpeptidase.

*The comorbidities taken into account are hypertension, type 2 diabetes, severe sleep apnea syndrome.

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These results are reported in Fig 1. BMI was significantly associated with OSAS but not with hypertension or type 2 diabetes. The results for waist-to-height and neck-to-height ratios were similar to those for waist and neck circumferences: OR 1.077 (95CI: 1.035; 1.121), p<0.0001 and OR 1.221 (95CI: 1.073; 1.389), p = 0.002, respectively for association with hypertension; OR 1.054 (95CI: 1.015; 1.093), p = 0.006 and OR 1.179 (95CI: 1.044; 1.331), p = 0.008 for
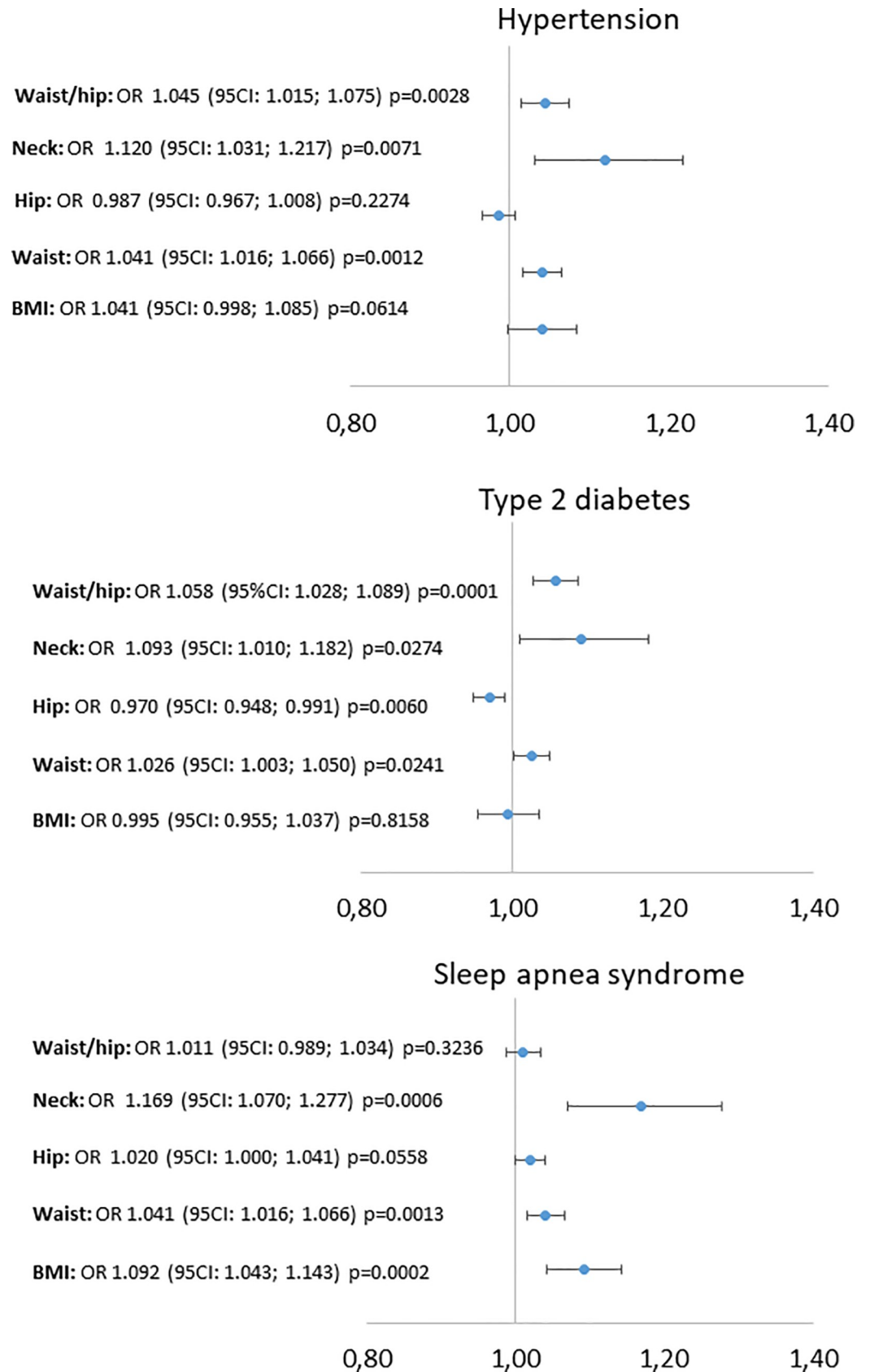
Hypertension

Waist/hip: OR 1.045 (95CI: 1.015; 1.075) p=0.0028

Neck: OR 1.120 (95CI: 1.031; 1.217) p=0.0071

Hip: OR 0.987 (95CI: 0.967; 1.008) p=0.2274

Waist: OR 1.041 (95CI: 1.016; 1.066) p=0.0012

BMI: OR 1.041 (95CI: 0.998; 1.085) p=0.0614

0,80   1,00   1,20   1,40

Type 2 diabetes

Waist/hip: OR 1.058 (95%CI: 1.028; 1.089) p=0.0001

Neck: OR 1.093 (95CI: 1.010; 1.182) p=0.0274

Hip: OR 0.970 (95CI: 0.948; 0.991) p=0.0060

Waist: OR 1.026 (95CI: 1.003; 1.050) p=0.0241

BMI: OR 0.995 (95CI: 0.955; 1.037) p=0.8158

0,80   1,00   1,20   1,40

Sleep apnea syndrome

Waist/hip: OR 1.011 (95CI: 0.989; 1.034) p=0.3236

Neck: OR 1.169 (95CI: 1.070; 1.277) p=0.0006

Hip: OR 1.020 (95CI: 1.000; 1.041) p=0.0558

Waist: OR 1.041 (95CI: 1.016; 1.066) p=0.0013

BMI: OR 1.092 (95CI: 1.043; 1.143) p=0.0002

0,80   1,00   1,20   1,40

association with diabetes; OR 1.058 (95CI: 1.017; 1.100), p = 0.003 and OR 1.223 (95CI: 1.072; 1.395) p = 0.008 for association with OSAS. The areas under the curve for these logistic regressions are reported in Table 2.

To test whether such associations were independent of potential covariates, multiple logistic regressions were then performed including age, tobacco, alcohol consumption and the presence of depression as covariates in the models. Results were essentially the same than in univariate logistic analyses. These models are reported in Table 3.

Correlations between anthropometric and cardiometabolic risk markers

Spearman correlations are reported in Table 4. Neck circumference (as well as neck-to-height ratio) was the only anthropometric marker that strongly correlated with all cardiometabolic risk parameters, particularly with functional liver enzymes, i.e. ALT, AST and GT. No significant correlation was found between the different anthropometric markers and the LDL-c levels.

Prevalence of obesity related diseases according to neck circumference

We reported the prevalence of hypertension, type 2 diabetes and severe OSAS according to the different anthropometric markers, divided into quintiles (Fig 2). The prevalence of hypertension progressively increased from 16 to 43%, type 2 diabetes from 13 to 33% and severe OSAS from 14 to 49% across increasing neck circumference quintiles.

Discussion

The present work studied women with class II or class III obesity who were volunteering for bariatric surgery. The results demonstrated that waist-to-hip ratio was the only anthropometric marker that was unrelated to BMI. The other markers were all collinear with BMI, although neck circumference was less strongly related than waist and hip circumferences. In addition, neck circumference was collinear with markers of central obesity (waist circumference and waist-to-hip ratio) but not with a marker of subcutaneous adiposity (hip circumference).

This study therefore showed that neck circumference was as valid as waist circumference and waist-to-hip ratio for the identification of women with a high cardiometabolic risk profile. Moreover, it is much easier to measure in routine clinical practice in women with severe obesity.

Reliability of anthropometric markers in the context of severe obesity

In the present work, hip circumference, a marker of subcutaneous adiposity, was not correlated with any metabolic markers and was inversely associated with type 2 diabetes. Previous

Table 2. Areas under the curve of univariate logistic regressions.

	Waist circ.	Hip circ.	Waist-to-hip	Neck circ.	Waist circ.-to-height	Neck circ.-to-height
Hypertension	0,77	0,74	0,78	0,76	0.78	0.76
Type 2 diabetes	0,67	0,67	0,72	0,66	0.68	0.67
OSAS	0,77	0,76	0,75	0,78	0.76	0.77

Abbreviation: OSAS: obstructive sleep apnea; Circ.: circumference.

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Table 3. Multivariable logistic regressions for obesity related diseases.

	B-estimate	Standard error	OR (95%CI)	P values
Hypertension				
BMI	0.0431	0.0223	1.044 (0.999;1.091)	0.0534
Neck circumference	0.1215	0.0446	1.129 (1.035; 1.232)	0.0064
Waist circumference	0.0407	0.0129	1.042 (1.015; 1.068)	0.0017
Hip circumference	-0.0103	0.0109	0.990 (0.969; 1.011)	0.3450
Waist/hip raio	0.0385	0.0154	1.039 (1.008; 1.071)	0.0123
Neck circ./height	0.2019	0.0691	1.224 (1.069; 1.401)	0.0035
Waist circ./height	0.0718	0.0212	1.074 (1.031; 1.120)	0.0007
Type 2 diabetes				
BMI	-0.00046	0.0221	1.000 (0.957; 1.044)	0.9836
Neck circumference	0.0856	0.0429	1.089 (1.001; 1.185)	0.0462
Waist circumference	0.0260	0.0122	1.026 (1.002; 1.051)	0.0330
Hip circumference	-0.0278	0.0117	0.973 (0.951; 0.995)	0.0171
Waist/hip raio	0.0505	0.0150	1.052 (1.021; 1.083)	0.0008
Neck circ./height	0.1475	0.0664	1.159 (1.018; 1.320)	0.0263
Waist circ./height	0.0495	0.0201	1.051 (1.010; 1.093)	0.0139
Obstructive sleep apnea syndrome				
BMI	0.0843	0.0239	1.088 (1.038; 1.140)	0.0004
Neck circumference	0.2015	0.0483	1.223 (1.113; 1.345)	<0.0001
Waist circumference	0.0433	0.0131	1.044 (1.018; 1.071)	0.0009
Hip circumference	0.0170	0.0107	1.017 (0.996; 1.039)	0.1137
Waist/hip raio	0.0140	0.0123	1.014 (0.990; 1.039)	0.2556
Neck circ./height	0.2480	0.0714	1.281 (1.114; 1.474)	0.0005
Waist circ./height	0.0589	0.0210	1.061 (1.018; 1.105)	0.0050

Abbreviations: Circ: circumference; BMI: body mass index; CI: confidence interval. Multiple logistic regressions were performed including age, tobacco, alcohol consumption and the presence of depression as covariates in the models.

Table 4. Univariate Spearman correlations between anthropometric parameters and cardiometabolic risk markers.

	BMI	Neck circ.	Waist circ.	Hip circ.	Waist/hip	Neck circ./height	Waist circ./height
HOMA-IR	r = 0.07	**r = 0.34**	**r = 0.30**	**r = 0.14**	**r = 0.37**	**r = 0.34**	**r = 0.32**
	p = 0.230	**p<0.001**	**p<0.001**	**p = 0.018**	**p<0.001**	**p<0.001**	**p<0.001**
AHI	**r = 0.16**	**r = 0.23**	r = 0.11	r = 0.05	r = 0.05	**r = 0.29**	**r = 0.18**
	p = 0.010	**p<0.001**	p = 0.079	p = 0.448	p = 0.431	**p<0.001**	**p = 0.003**
Log Tg/HDL	r = 0.00	**r = 0.24**	**r = 0.14**	r = 0.08	**r = 0.22**	**r = 0.22**	**r = 0.15**
	p = 0.966	**p<0.001**	**p = 0.018**	p = 0.167	**p<0.001**	**p<0.001**	**p = 0.008**
ALT	r = 0.05	**r = 0.24**	r = 0.08	**r = 0.21**	**r = 0.28**	**r = 0.24**	r = 0.09
	p = 0.351	**p<0.001**	p = 0.147	**p<0.001**	**p<0.001**	**p<0.001**	p = 0.123
AST	r = 0.06	**r = 0.14**	r = 0.07	**r = 0.19**	**r = 0.26**	**r = 0.17**	r = 0.10
	p = 0.315	**p<0.001**	p = 0.212	**p = 0.001**	**p<0.001**	**p = 0.040**	p = 0.092
GGT	r = 0.04	**r = 0.36**	**r = 0.17**	r = 0.04	**r = 0.18**	**r = 0.34**	**r = 0.17**
	p = 0.450	**p<0.001**	**p = 0.003**	p = 0.515	**p = 0.002**	**p<0.001**	**p = 0.004**

Abbreviations: Circ: circumference; BMI: body mass index; HOMA-IR: HOMA-Index Resistance; Tg: triglycerides; AHI: apnea-hypopnea index; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gammaglutamyl transpeptidase.
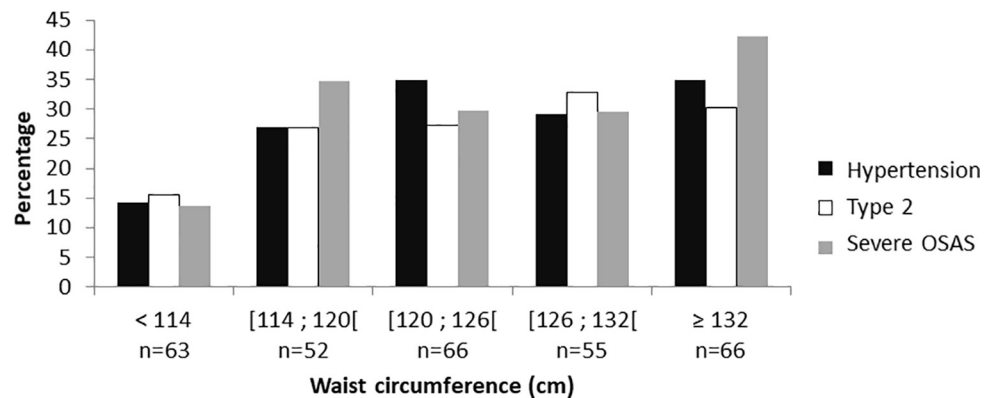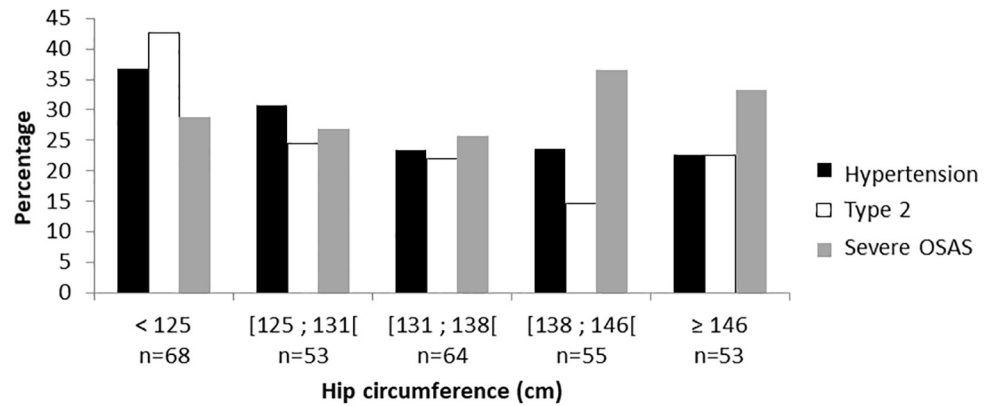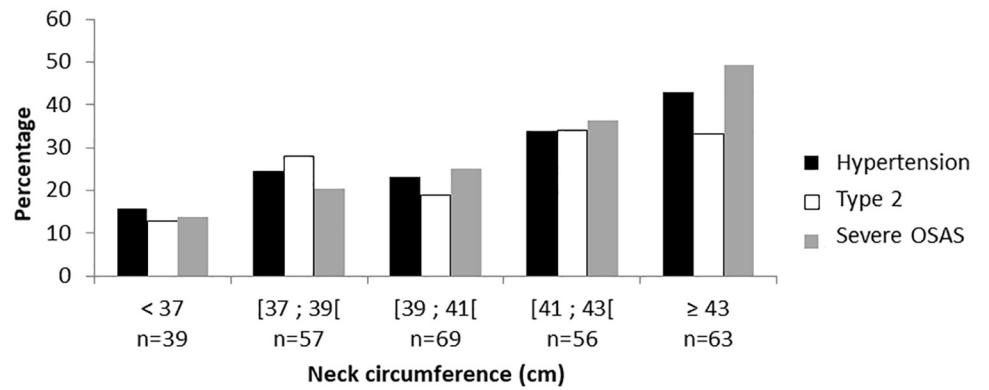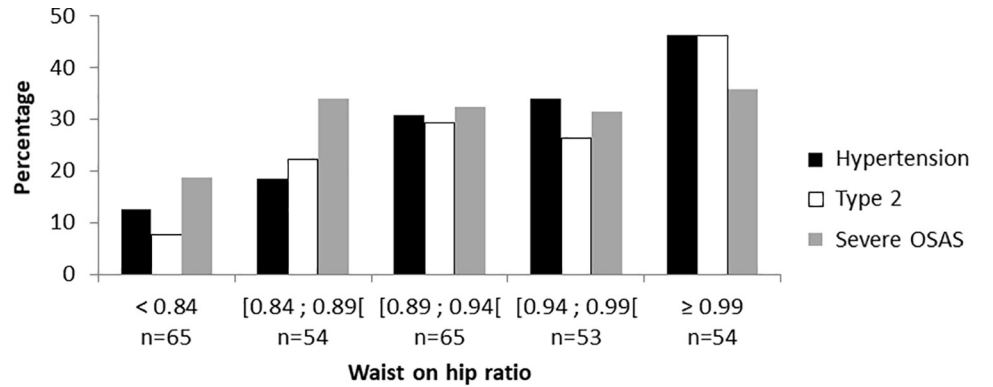
Fig 2. Prevalence of obesity related diseases according to quintiles of anthropometric markers. Abbreviation: OSAS: Obstructive sleep apnea syndrome.

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studies have shown that hip circumference was inversely associated with the risk of incident type 2 diabetes in men and women [18]. Subcutaneous adipose tissue, measured by abdominal computed tomography, was also found to be inversely correlated with type 2 diabetes [4]. An increase in hip circumference reflects an expansion in low body subcutaneous adipose tissue. This subcutaneous fat depot is diametrically opposed to visceral fat. In epidemiological studies, it has been associated with a lower cardiac risk factor burden [19] and lower risk of incident cardiovascular diseases [20] and cancer [21]. This low body subcutaneous fat may impart a protective effect by acting as a metabolic buffer to the influx of dietary lipids and protecting other tissues from the lipotoxicity caused by lipid overflow and ectopic fat deposition [5]. In addition, human obese visceral and subcutaneous adipose tissues secretomes are clearly distinct. Visceral fat secretome leads to a low-grade inflammation profile whereas subcutaneous secretome favors insulin sensitivity [22].

Waist circumference has been shown to be a less reliable marker of metabolic abnormalities in men [23] and women [24] with severe obesity, compared to those with lower or normal BMI scores. This could be attributed to the contribution of abdominal subcutaneous adipose tissue, which appears to be protective for metabolic conditions [25]. However, other studies have also found the well-known relationship between waist circumference and cardiometabolic risk profile in patients with severe obesity [26, 27]. The present work confirmed that in women with severe obesity, waist circumference was associated with hypertension, type 2 diabetes and OSAS, as well as with HOMA-IR and Log TG/HDL, both markers of insulin resistance.

Waist-to-hip ratio and waist circumference, were associated with an increased risk of cardiovascular mortality in women from the Nurses' Health Study prospective cohort [28], as well as in other cohorts of women [29]. In the present study, waist-to-hip ratio in women with severe obesity was a reliable marker for the identification of hypertension, type 2 diabetes (but not OSAS) and other cardiometabolic risk markers. The stronger reliability of this measure over waist circumference alone could be related to the neutralization of abdominal subcutaneous adiposity by the hip circumference denominator, which adjusts waist circumference for subcutaneous adiposity [30]. For the same reason, waist-to-hip ratio is unaffected by increases in BMI, across large ranges of BMI, as confirmed by the present results. However, these results need to be considered according to the ease and accuracy of the physical measurements. It is common clinical experience that waist and hip measurements are subject to errors in patients with severe obesity. This was underlined in our cohort by the outlier data for the patient who had a very high waist-to-hip ratio (1.99) because of a very large abdominal apron. Neck circumference could therefore be a clinically relevant anthropometric marker of central obesity in patients with severe obesity.

Previous evidence regarding neck circumference

Neck circumference was first identified as a risk marker for OSAS through its use as an index of upper airway restriction by fat deposits in the neck [31]. It has been identified as a relevant tool for clinical screening for OSAS through the STOP-BANG questionnaire [32], which was found to be the most sensitive for the detection of OSAS [8]. In addition, neck circumference was found to be correlated with the visceral adipose tissue, measured by computed tomography in 3307 men (r = 0.63, p<0.001) and women (r = 0.74, p<0.001) in the Framingham health study [33]. Neck circumference was found to be linked with cardiometabolic risk factors

after correction for BMI and visceral fat. In other cross-sectional studies, neck circumference was also associated with atherogenic dyslipidemia [34], inflammatory markers (PAI-1) [35], insulin resistance [36], coronary artery disease [37], carotid wall intima-media thickness [38] and NAFLD [39, 40].

Prospective studies have shown that changes in neck circumference are associated with changes in blood pressure [41] and incident type 2 diabetes [42, 43]. Finally, in a cohort of 12,151 patients with a high risk of cardiovascular disease, higher values of neck circumference predicted a higher incidence of fatal and non-fatal cardiovascular events [44].

Thus, neck circumference appears to be a relevant anthropometric marker for the identification of patients with a high cardiometabolic risk associated with central adiposity. Only two previous studies have addressed the question of the relevance of this marker in the context of severe obesity. Assyov et al. [45] found that neck circumference was superior to waist circumference for the identification of a high-risk cardiometabolic profile in 205 men and women with a mean BMI of 36.9 (6.2) kg/m^2. A cut-off neck circumference value of 37 cm in women was 74% sensitive and 62% specific to identify a risk of type 2 diabetes. Cizza et al. [46] found that neck circumference was associated with metabolic syndrome and OSAS in 102 men and women with a mean BMI of 38.6 (6.5) kg/m^2, who were identified as short sleepers (<6.5h/night).

Finally, we assessed whether waist-to-height and neck-to-height ratios yielded better results than waist and neck circumferences based on the hypothesis that dividing by height would reduce the variability. Waist-to-height ratio was previously used as a marker of central adiposity in childhood obesity [47]. We found similar results for waist-to-height ratio as for waist circumference, as previously demonstrated in adult women [48]. Accordingly, neck-to-height ratio was previously used in children [49] and adults [50], mainly to screen for sleep apnea. Similarly to our results, neck-to-height ratio did not improve the association observed with neck circumference.

Study strengths and limitations

The present study sought the easiest and most clinically relevant anthropometric marker for the identification of a high-risk profile for cardiometabolic diseases in women with severe obesity. The study sample was large and the cardiometabolic characteristics of the women were well-characterized. The results are limited by the cross-sectional design of the study, thus it was not possible to determine if anthropometric markers were good predictors of incident metabolic diseases and cardiovascular events in this population, as has been demonstrated in subjects with lower BMIs. The sex ratio of obese patients volunteering for bariatric surgery is largely in favor of women (76% in our cohort). Thus, too few men were included in our cohort to allow the same analyses to be performed in men. However, it would be of interest to study whether the present results are extendable to men in future work. Finally, the population studied was mainly Caucasian thus the results cannot be extrapolated to other ethnicities.

Conclusion

The present work showed that waist-to-hip ratio and neck circumference have low collinearity with BMI in women with severe obesity. Both markers demonstrated significant associations with prevalent hypertension and type 2 diabetes. Neck circumference was also linked to OSAS. Both were collinear with all other markers of cardiometabolic risk, in particular functional liver tests. Because of the ease of measurement of neck circumference in routine clinical practice, we propose neck circumference to be the best anthropometric marker in women with severe obesity. Further investigation regarding the ability of neck circumference to predict

incident cardiometabolic diseases in this population should be carried out. Future studies should evaluate whether a reduction in neck circumference after bariatric surgery is a good marker of cardiometabolic improvement.

Supporting information

S1 Database.
(XLS)

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References

1. Heady JA, Morris JN and Raffle PA. Physique of London busmen; epidemiology of uniforms. Lancet. 1956 271:569–70. PMID: 13368467

2. Despres JP and Lemieux I. Abdominal obesity and metabolic syndrome. Nature. 2006 444:881–7. https://doi.org/10.1038/nature05488 PMID: 17167477

3. Sperling LS, Mechanick JI, Neeland IJ, Herrick CJ, Despres JP, Ndumele CE, et al. The CardioMeta-bolic Health Alliance: Working Toward a New Care Model for the Metabolic Syndrome. J Am Coll Cardiol. 2015 66:1050–67. https://doi.org/10.1016/j.jacc.2015.06.1328 PMID: 26314534

4. Smith JD, Borel AL, Nazare JA, Haffner SM, Balkau B, Ross R, et al. Visceral Adipose Tissue Indicates the Severity of Cardiometabolic Risk in Patients with and without Type 2 Diabetes: Results from the INSPIRE ME IAA Study. J Clin Endocrinol Metab. 2012.

5. Neeland IJ, Poirier P and Despres JP. Cardiovascular and Metabolic Heterogeneity of Obesity: Clinical Challenges and Implications for Management. Circulation. 2018 137:1391–1406. https://doi.org/10.1161/CIRCULATIONAHA.117.029617 PMID: 29581366

6. Despres JP. Excess visceral adipose tissue/ectopic fat the missing link in the obesity paradox? J Am Coll Cardiol. 2011 57:1887–9. https://doi.org/10.1016/j.jacc.2010.10.063 PMID: 21545945

7. Picon PX, Leitao CB, Gerchman F, Azevedo MJ, Silveiro SP, Gross JL, et al. [Waist measure and waist-to-hip ratio and identification of clinical conditions of cardiovascular risk: multicentric study in type 2 diabetes mellitus patients]. Arq Bras Endocrinol Metabol. 2007 51:443–9. PMID: 17546244

8. Chiu HY, Chen PY, Chuang LP, Chen NH, Tu YK, Hsieh YJ, et al. Diagnostic accuracy of the Berlin questionnaire, STOP-BANG, STOP, and Epworth sleepiness scale in detecting obstructive sleep apnea: A bivariate meta-analysis. Sleep Med Rev. 2016.

9. Onat A, Hergenc G, Yuksel H, Can G, Ayhan E, Kaya Z, et al. Neck circumference as a measure of central obesity: associations with metabolic syndrome and obstructive sleep apnea syndrome beyond waist circumference. Clin Nutr. 2009 28:46–51. https://doi.org/10.1016/j.clnu.2008.10.006 PMID: 19010573

10. Ahbab S, Ataoglu HE, Tuna M, Karasulu L, Cetin F, Temiz LU, et al. Neck circumference, metabolic syndrome and obstructive sleep apnea syndrome; evaluation of possible linkage. Med Sci Monit. 2013 19:111–7. https://doi.org/10.12659/MSM.883776 PMID: 23403781

11. MJ Marfell-Jones AS, JH de Ridder. International standards for anthropometric assessment. Wellington, New Zealand; 2012.

12. Nathan DM, Davidson MB, DeFronzo RA, Heine RJ, Henry RR, Pratley R, et al. Impaired fasting glucose and impaired glucose tolerance: implications for care. Diabetes Care. 2007 30:753–9. https://doi.org/10.2337/dc07-9920 PMID: 17327355

13. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF and Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985 28:412–9. PMID: 3899825

14. Burstein M and Samaille J. [On a rapid determination of the cholesterol bound to the serum alpha- and beta-lipoproteins.]. Clin Chim Acta. 1960 5:609. PMID: 13806309

15. Friedewald WT, Levy RI and Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972 18:499–502. PMID: 4337382

16. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014 311:507–20. https://doi.org/10.1001/jama.2013.284427 PMID: 24352797

17. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med. 2012 8:597–619. https://doi.org/10.5664/jcsm.2172 PMID: 23066376

18. Snijder MB, Dekker JM, Visser M, Bouter LM, Stehouwer CD, Kostense PJ, et al. Associations of hip and thigh circumferences independent of waist circumference with the incidence of type 2 diabetes: the Hoorn Study. Am J Clin Nutr. 2003 77:1192–7. https://doi.org/10.1093/ajcn/77.5.1192 PMID: 12716671

19. Manolopoulos KN, Karpe F and Frayn KN. Gluteofemoral body fat as a determinant of metabolic health. Int J Obes (Lond). 2010 34:949–59.

20. Neeland IJ, Turer AT, Ayers CR, Berry JD, Rohatgi A, Das SR, et al. Body fat distribution and incident cardiovascular disease in obese adults. J Am Coll Cardiol. 2015 65:2150–1. https://doi.org/10.1016/j.jacc.2015.01.061 PMID: 25975481

21. Gupta A, Pandey A, Ayers C, Beg MS, Lakoski SG, Vega GL, et al. An Analysis of Individual Body Fat Depots and Risk of Developing Cancer: Insights From the Dallas Heart Study. Mayo Clin Proc. 2017 92:536–543. https://doi.org/10.1016/j.mayocp.2016.12.023 PMID: 28291590

22. Roca-Rivada A, Bravo SB, Perez-Sotelo D, Alonso J, Castro AI, Baamonde I, et al. CILAIR-Based Secretome Analysis of Obese Visceral and Subcutaneous Adipose Tissues Reveals Distinctive ECM Remodeling and Inflammation Mediators. Sci Rep. 2015 5:12214. https://doi.org/10.1038/srep12214 PMID: 26198096

23. Lemieux I, Drapeau V, Richard D, Bergeron J, Marceau P, Biron S, et al. Waist girth does not predict metabolic complications in severely obese men. Diabetes Care. 2006 29:1417–9. https://doi.org/10.2337/dc06-0441 PMID: 16732038

24. Drapeau V, Lemieux I, Richard D, Bergeron J, Tremblay A, Biron S, et al. Waist circumference is useless to assess the prevalence of metabolic abnormalities in severely obese women. Obes Surg. 2007 17:905–9. PMID: 17894150

25. Porter SA, Massaro JM, Hoffmann U, Vasan RS, O'Donnel CJ and Fox CS. Abdominal subcutaneous adipose tissue: a protective fat depot? Diabetes Care. 2009 32:1068–75. https://doi.org/10.2337/dc08-2280 PMID: 19244087

26. Perea V, Jimenez A, Flores L, Ortega E, Coves MJ and Vidal J. Anthropometric indexes outperform bioelectrical impedance analysis-derived estimates of body composition in identification of metabolic abnormalities in morbid obesity. Surg Obes Relat Dis. 2013 9:648–52. https://doi.org/10.1016/j.soard.2012.05.010 PMID: 22867555

27. Zazai R, Wilms B, Ernst B, Thurnheer M and Schultes B. Waist circumference and related anthropometric indices are associated with metabolic traits in severely obese subjects. Obes Surg. 2014 24:777–82. https://doi.org/10.1007/s11695-013-1141-6 PMID: 24338435

28. Zhang C, Rexrode KM, van Dam RM, Li TY and Hu FB. Abdominal obesity and the risk of all-cause, cardiovascular, and cancer mortality: sixteen years of follow-up in US women. Circulation. 2008 117:1658–67. https://doi.org/10.1161/CIRCULATIONAHA.107.739714 PMID: 18362231

29. Lapidus L, Bengtsson C, Larsson B, Pennert K, Rybo E and Sjostrom L. Distribution of adipose tissue and risk of cardiovascular disease and death: a 12 year follow up of participants in the population study of women in Gothenburg, Sweden. Br Med J (Clin Res Ed). 1984 289:1257–61.

30. Dalton M, Cameron AJ, Zimmet PZ, Shaw JE, Jolley D, Dunstan DW, et al. Waist circumference, waist-hip ratio and body mass index and their correlation with cardiovascular disease risk factors in Australian adults. J Intern Med. 2003 254:555–63. PMID: 14641796

31. Davies RJ and Stradling JR. The relationship between neck circumference, radiographic pharyngeal anatomy, and the obstructive sleep apnoea syndrome. Eur Respir J. 1990 3:509–14. PMID: 2376247

32. Chung F, Abdullah HR and Liao P. STOP-Bang Questionnaire: A Practical Approach to Screen for Obstructive Sleep Apnea. Chest. 2016 149:631–8. https://doi.org/10.1378/chest.15-0903 PMID: 26378880

33. Preis SR, Massaro JM, Hoffmann U, D'Agostino RB, Sr., Levy D, Robins SJ, et al. Neck circumference as a novel measure of cardiometabolic risk: the Framingham Heart study. J Clin Endocrinol Metab. 2010 95:3701–10. https://doi.org/10.1210/jc.2009-1779 PMID: 20484490

34. Vallianou NG, Evangelopoulos AA, Bountziouka V, Vogiatzakis ED, Bonou MS, Barbetseas J, et al. Neck circumference is correlated with triglycerides and inversely related with HDL cholesterol beyond BMI and waist circumference. Diabetes Metab Res Rev. 2013 29:90–7. https://doi.org/10.1002/dmrr.2369 PMID: 23135790

35. Jamar G, Pisani LP, Oyama LM, Belote C, Masquio DC, Furuya VA, et al. Is the neck circumference an emergent predictor for inflammatory status in obese adults? Int J Clin Pract. 2013 67:217–24. https://doi.org/10.1111/ijcp.12041 PMID: 23409690

36. Liang J, Teng F, Li Y, Liu X, Zou C, Wang Y, et al. neck circumference and insulin resistance in Chinese adults: the Cardiometabolic Risk in Chinese (CRC) Study. Diabetes Care. 2013 36:e145–6. https://doi.org/10.2337/dc13-1114 PMID: 23970724

37. Zen V, Fuchs FD, Wainstein MV, Goncalves SC, Biavatti K, Riedner CE, et al. Neck circumference and central obesity are independent predictors of coronary artery disease in patients undergoing coronary angiography. Am J Cardiovasc Dis. 2012 2:323–30. PMID: 23173107

38. Rosenquist KJ, Massaro JM, Pencina KM, D'Agostino RB, Beiser A, O'Connor GT, et al. Neck circumference, carotid wall intima-media thickness, and incident stroke. Diabetes Care. 2013 36:e153–4. https://doi.org/10.2337/dc13-0379 PMID: 23970728

39. Li Q, Wang N, Han B, Chen Y, Zhu C, Chen Y, et al. Neck circumference as an independent indicator to non-alcoholic fatty liver disease in non-obese men. Nutr Metab (Lond). 2015 12:63.

40. Huang BX, Zhu MF, Wu T, Zhou JY, Liu Y, Chen XL, et al. Neck circumference, along with other anthropometric indices, has an independent and additional contribution in predicting fatty liver disease. PLoS One. 2015 10:e0118071. https://doi.org/10.1371/journal.pone.0118071 PMID: 25679378

41. Ben-Noun LL and Laor A. Relationship between changes in neck circumference and changes in blood pressure. Am J Hypertens. 2004 17:409–14. https://doi.org/10.1016/j.amjhyper.2004.02.005 PMID: 15110899

42. Preis SR, Pencina MJ, D'Agostino RB, Sr., Meigs JB, Vasan RS and Fox CS. Neck circumference and the development of cardiovascular disease risk factors in the Framingham Heart Study. Diabetes Care. 2013 36:e3. https://doi.org/10.2337/dc12-0738 PMID: 23264305

43. Cho NH, Oh TJ, Kim KM, Choi SH, Lee JH, Park KS, et al. Neck Circumference and Incidence of Diabetes Mellitus over 10 Years in the Korean Genome and Epidemiology Study (KoGES). Sci Rep. 2015 5:18565. https://doi.org/10.1038/srep18565 PMID: 26681338

44. Dai Y, Wan X, Li X, Jin E and Li X. Neck circumference and future cardiovascular events in a high-risk population—A prospective cohort study. Lipids Health Dis. 2016 15:46. https://doi.org/10.1186/s12944-016-0218-3 PMID: 26946432

45. Assyov Y, Gateva A, Tsakova A and Kamenov Z. A comparison of the clinical usefulness of neck circumference and waist circumference in individuals with severe obesity. Endocr Res. 2017 42:6–14. https://doi.org/10.3109/07435800.2016.1155598 PMID: 27050332

46. Cizza G, de Jonge L, Piaggi P, Mattingly M, Zhao X, Lucassen E, et al. Neck circumference is a predictor of metabolic syndrome and obstructive sleep apnea in short-sleeping obese men and women. Metab Syndr Relat Disord. 2014 12:231–41. https://doi.org/10.1089/met.2013.0093 PMID: 24571423

47. Zhou D, Yang M, Yuan ZP, Zhang DD, Liang L, Wang CL, et al. Waist-to-Height Ratio: a simple, effective and practical screening tool for childhood obesity and metabolic syndrome. Prev Med. 2014 67:35–40. https://doi.org/10.1016/j.ypmed.2014.06.025 PMID: 24967955

48. Hajian-Tilaki K, Heidari B, Hajian-Tilaki A, Firouzjahi A and Bagherzadeh M. The discriminatory performance of body mass index, waist circumference, waist-to-hip ratio and waist-to-height ratio for detection of metabolic syndrome and their optimal cutoffs among Iranian adults. J Res Health Sci. 2014 14:276–81. PMID: 25503283

49. de Sousa Caixeta JA, Saramago AM, de Cacia Pradella-Hallinan ML, Moreira GA, Tufik S and Fujita RR. Waist-to-height ratio distinguish obstructive sleep apnea from primary snoring in obese children. Sleep Breath. 2015 19:231–7. https://doi.org/10.1007/s11325-014-1001-1 PMID: 24809293

50. Banhiran W, Junlapan A, Assanasen P and Chongkolwatana C. Physical predictors for moderate to severe obstructive sleep apnea in snoring patients. Sleep Breath. 2014 18:151–8. https://doi.org/10.1007/s11325-013-0863-y PMID: 23703693