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Neck Circumference as a New Anthropometric Indicator for Prediction of Metabolic Syndrome in Arab Women

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ABSTRACT

Background: Neck circumference has been associated with obesity-related metabolic and cardiovascular abnormality in several studies. This study designed to evaluate the potency of neck circumference for identifying cardiometabolic risk factors, and determining the neck circumference cutoff value for the prediction of metabolic syndrome (MetS).
Methods: This cross-sectional study involving 623 women aged 18-70 years, International Diabetes Federation (IDF) guidelines was used to diagnose metabolic syndrome among participants. The main indicators were neck circumference, waist circumference, body mass index, total body fat percentage, blood pressure, total cholesterol, lipoproteins (HDLc, LDLc), triglycerides, plasma glucose, and homeostasis model assessment-estimated insulin resistance (HOMA-IR) levels.
Results: Neck circumference was independently associated with all cardiometabolic risk factors (P <0.001), except LDLc. Fully adjusted odds ratio (95% confidence interval [CI]) values for incremental increases in neck circumference in women were reported for raised fasting glucose levels, 1.70 (1.48–2.94); raised blood pressure, 1.29 (1.15–1.45); high triglycerides, 1.25 (1.13–1.38); insulin resistance, 1.20 (1.02–1.40); and low HDLc, 1.14 (1.02–1.40). Women in the largest neck circumference quartile were 13 times more likely [13.39 (6.35 - 28.23)] to have MetS than the lowest neck circumference quartile after adjusting for confounding factors (P <0.01). Finally, the appropriate neck circumference to predict ≥ 3 cardiometabolic risk factors in Saudi women is 35 cm. This cutoff value was associated with the risk of metabolic syndrome in participants with both high and normal body mass index and waist circumference values.
Conclusion: Neck circumference is independently and cumulatively associated with cardiometabolic risk factors in adult Saudi women.

Keywords: Obesity; Metabolic risk; Neck circumference; Cutoff, Saudis

INTRODUCTION

Obesity is well known as a cause of metabolic abnormalities. The distribution of excess adipose tissue may be considered to be more important than the total fat in conferring metabolic and cardiovascular risk [1]. The correlation between upper body fat distribution and increased cardiovascular disease risk, has long been recognized, when neck skinfold[2] or neck circumference (NC) [3] was used as an index of such an adverse risk profile. Moreover, free fatty acid release from the upper body subcutaneous fat adipose (SAT) is known to be larger than that released from the lower body subcutaneous fat or from the visceral adipose tissue, suggesting that this fat depot may play a considerable role in risk factor

pathogenesis [4]. Raised free fatty acid concentrations are associated with insulin resistance, increased very low-density lipoprotein cholesterol production, and endothelial cell dysfunction [5]. The strong correlation between SAT and cardiometabolic risk factors has been shown by the results of some [6, 7] but not all studies [8]. Waist circumference (WC) is reported as a cardiometabolic predictor in literature, with some drawbacks. For individuals with a body mass index (BMI) ≥35, WC adds little to the predictive power of the disease risk classification of BMI [9]. WC accuracy is limited in some situations, including pregnancy, medical conditions where there is distension of the abdomen (as in ascites), or reduction of the abdomen (as with abdominal liposuction or tummy tuck [abdominoplasty]). The main limitation of the WC measure is the huge inter-ethnic variations with certain ethnic groups and for children and young people. Special threshold for WC is being recommended for several different populations and ethnic groups. However, the risk associated with particular WC will differ according to different populations [10]. This is especially relevant in a country without a local cutoff level, such as in Saudi Arabia (KSA). Several studies have illustrated that NC may be a strong independent correlate of metabolic risk factors than BMI and WC [11, 12]. However, NC has also been presented in another study as a simple, time-saving, and cost effective measure to assess overweight and obesity in busy primary care practices [13]. The available up to date cutoff points of NC for determining subjects with overweight, obesity, and metabolic and cardiovascular disease risks are presented in the following table. The main goals of this study were to examine the usefulness of NC in identifying overweight, obesity, and to test NC application in predicting cardiometabolic risk in Saudi adult women. The generated data aim to aid in providing standardized assessment tools to determine accurate prevalence, treatment protocols, and achieve control of obesity and its associated consequences in KSA and in the entire Gulf Cooperation Council (GCC) countries.

MATERIALS AND METHODS

Study Sample

This cross-sectional survey study was carried out between September 2014 and April 2016 in King Khalid University Hospital (KKUH) and primary health care centers in Riyadh, KSA. We undertook an a priori power calculation to determine the sample size required to detect a small effect size (0.1) with a two-tailed, α = .05 and power of 80%. The analysis indicated a sample size of 600 would be sufficient. This number was adjusted upwards to account for a possible 5% dropout rate. Of the 630 women initially selected, seven women didn't show up at the second visit (laboratory). Accordingly, the final sample size was 623.

Study recruitment was restricted to Saudi women aged 18-70 years. We excluded women who were pregnant, breastfeeding or had thyroid disorders, organ failure, organ transplant, or cancer. Participants were selected by systematic random sampling from the patient list in each center. The women who agreed to participate were scheduled for another visit to perform blood test, the biochemical analysis, within 1 week. And they instructed to fast for 10-12 h. Informed consent was gained at the time of data collection after we provided a full explanation of the study.

Ethical approval for this study was given by the University of Maryland College Park Institutional Review Board (IRB) (No. 411873-4) and the Ethics Committee of KSU, in Riyadh, KSA (No. 429679/67/4). All procedures were performed in accordance with the 1964 Declaration of Helsinki and its later amendments.

Data collection

Data were collected using a pre-coded interview questionnaire that solicited the following information: socio-

demographics, medical history, dietary habits and practices, and physical activity and lifestyle.

Anthropometric and clinical measures

Anthropometric data were taken using standardized procedures and equipment. The height was recorded to the nearest 0.5 cm. The weight was recorded to the nearest 0.1 Kg, and measured without shoes and with light clothing. BMI was calculated by the equation:

BMI = weight in Kg / (height in meters)^2

According to the World Health Organization's (WHO) BMI categorization, participants were classified into: normal weight (≤24.99 kg/m2), over-weight (25 kg/m2 to 29.99 kg/m2), and obese (≥30 kg/m2) [14].

All circumferences were measured using a non-stretch measuring tape, to the nearest 0.5 cm. NC was measured at the middle of the neck, between the mid-cervical spine and mid-anterior neck, while the subject standing upright with their face in the Frankfort horizontal plane, and the shoulders relaxed, but not hunched [13,15]. WC was measured at the mid-point between the highest point of the iliac crest and the last floating rib. Hip circumference was measured at the largest point of the hips. Waist-to-hip ratio (WHR) was calculated by dividing the waist circumference (cm) by the hip circumference (cm). The WHO and IDF recommended that different WC cutoff points should be used to define central obesity among different ethnic groups, and that the Europid standards should be used in our Eastern Mediterranean region until specific national data become available. WC cutoff points categorized as: >80 cm (31.5 in) [16]. Body fat percentage (fat%) was assessed using a dual-energy X-ray absorptiometry (DEXA) scan (model: Prodigy Advance, GE healthcare, Madison, WI, USA).

Blood pressure (BP) was measured using the right arm, while participant was resting comfortably for 5 minutes in the seated position with back support. Standardized mercury sphygmomanometers (Diplomat Presameter 660/360; Rudolf Riester GmbH, Jungingen, Germany) were used.

Biochemical measures

An overnight fasting (10–12 h) blood sample was collected from all subjects. Samples were analyzed and stored at the Biomarkers Research Program (BRP), College of Science, KSU. All blood and serum samples were stored at −20°C until analysis. Fasting plasma glucose and serum lipids (total cholesterol, triglycerides (TG), and high-density lipoprotein cholesterol (HDLc) were analyzed using the hexokinase and colorimetric methods, (Konelab, Thermo Fisher Scientific, Vantaa, Finland), respectively. Low-density lipoprotein cholesterol (LDLc) was calculated using the Friedewald formula [17].

LDL = [Total Cholesterol] - [HDLc] - ([TG]/2.2)

Fasting serum insulin was determined by the electrochemiluminescence method (COBAS-E-411; Roche Diagnostics, Mannheim, Germany). Insulin resistance, was defined by the homeostasis model assessment insulin index (HOMA-IR), and calculated using the following equation [18]:

HOMA-IR = Fasting insulin (µU/mL) X fasting plasma glucose (mmol/L) /22.5

Cardiometabolic risk factors definition

According to the IDF definition guidelines [19], the following thresholds were considered cardiometabolic risk: hypertriglyceridemia (TG ≥1.7 mmol/L), low HDLc (1.29 mmol/L or specific treatment for this lipid abnormality), hyperglycemia (fasting plasma glucose ≥5.6 mmol/L or previously diagnosed type 2 diabetes), hypertension (systolic BP ≥130 mmHg, diastolic BP ≥85 mmHg or treatment for previously diagnosed

hypertension), and central obesity (WC ≥80 cm). Insulin resistance was defined as HOMA-IR >75th percentile.

Metabolic syndrome was defined as per (IDF, National Heart, Lung and Blood Institute [NHLBI], American Heart Association [AHA], International. Atherosclerosis Society [I AS], and International Association for the Study of Obesity [IASO]) harmonized definition guidelines [16] as the presence of any three or more of the previously defined risk factors: (1) raised TG, (2) reduced HDLc, (3) raised fasting plasma glucose, (4) raised BP, and (5) central obesity.

Statistical Analysis

Continuous data were presented as mean ± standard deviation (SD) or median (25th -75th) percentiles for variables, following Gaussian and non-Gaussian distributions as appropriate. Graphs, Kolmogorov-Smirnov test, as well as skewness and kurtoses (≤0.8) were performed to determine the distribution of variables. If the data were not normally distributed, the continuous variables were log transformed or SQRT transformed, where it was appropriate. The means± standard deviations (SD), and median (25th -75th) percentiles were used to describe continuous data, following Gaussian and non-Gaussian distributions as appropriate. All analyses involving insulin measures (insulin and HOMA-IR) were restricted to subjects without diabetes.

Multiple binary logistic regression analysis was performed, with cardiometabolic risk factors as dependent variables and the NC as an independent variable, controlling for covariates. Then subjects were classified into quartiles (Q1–Q4), with Q1 (<25th percentile) as the reference. Multivariate logistic regression analysis was used to calculate odds ratios (ORs) and 95% confidence intervals (CI) for cardiometabolic risks according to the NC quartiles after adjusting for covariates. The following variables were included in the analysis: age (y), physical activity and lifestyle, dietary habits and practice, menopausal status (premenopausal vs. postmenopausal), and current estrogen use (no vs. yes).

The receiver operating characteristic curve (ROC) analysis was performed to determine the cutoff values of NC for predicting metabolic syndrome. The optimal cutoff points were determined using the shortest distance between any point on the curve and the top left corner on the y-axis. The distance on ROC curve values were calculated as the square root of [(1-sensitivity) 2 + (1-specificity) 2]. All tests were 2-sided, and p <0.05 was considered statistically significant. All statistical analyses were implemented using IBM SPSS 22.0 (IBM Corp., Armonk, NY, USA).

RESULTS

The participants' clinical and biochemical characteristics are shown in Table 1. The mean age was 47±10.7 years and mean NC was 36.7±2.8.

Table 1. Clinical and biochemical characteristics of the study subjects

Parameters **Continuous characteristics**	**N**	**Mean ± SD**
Age in years	616	47.3 ± 10.6
Height cm	623	154.2 ± 6.1
Wight kg	623	77.3 ± 15.3
BMI (kg/m^2)	623	32.5 ± 6.2
Hip circumference (cm)	619	109.9 ± 12.1
Waist Hip Ratio (WHR)	616	0.90 ± 0.1
Waist circumference (cm)	623	98.9 ± 13.0
Neck circumference (cm)	614	36.3 ± 2.6
Fat%%	527	46.9 ± 5.1
Systolic BP (mmHg)	620	124.3 ± 17.7
Diastolic BP (mmHg)	618	74.8 ± 10.8
Total cholesterol (mmol/L)	616	5.0 ± 0.9
TG¥ (mmol/L)	608	1.5 (1.1–2.0)
Fasting glucose# (mmol/L)	607	5.9 (5.1– 8.4)
HDLc (mmol/L)	613	1.26 ± 0.3
LDLc (mmol/L)	606	3.42 ± 0.8
HOMA-IR¥❖ (mmol/L × μU/mL)	331	7.7 (4.8–11.6)
Insulin¥❖ (μU/mL)	331	1.9 (1.2–3.1)

Data Represent Mean ±SD for Gaussian Variables and Median (25th -75th) percentiles for Non Gaussian variables. ❖Excluding diabetes subjects.log# and SQRT¥.

Neck Circumference Contribution to the Prediction of Cardiometabolic Conditions

Elevated NC was associated with increased ORs of metabolic syndrome and with all cardiometabolic risk factors (all

P<0.0001), except for LDLc. After further adjustment for BMI, WC, and fat%, NC remained an independent predictor of all binary cardiometabolic risk factors (all P<0.05) (Table 2 and Figure 1).

Table 2. Multiple binary logistic regression analysis, using each cardiovascular disease risk as the dependent variable and neck circumference the independent variable

Dependent Variables		OR(95% CI)	P-Value
Hypertension			
	Model 1	1.38(1.25–1.52)	0.000
	Model 2	1.32(1.18–1.46)	0.000
	Model 3	1.29(1.15–1.45)	0.000
	Model 4	1.29(1.15–1.45)	0.000
Elevated TG			
	Model 1	1.26(1.16–1.37)	0.000
	Model 2	1.27(1.16-1.40)	0.000
	Model 3	1.25(1.12-1.38)	0.000
	Model 4	1.25(1.13-1.38)	0.000
Elevated fasting glucose			
	Model 1	1.48(1.33–1.64)	0.000
	Model 2	1.62(1.43–1.84)	0.000
	Model 3	1.67(1.46–2.91)	0.000
	Model 4	1.70(1.48–2.94)	0.000
HOMA_IR >75th			
	Model 1	1.19(1.06–1.35)	0.004
	Model 2	1.21(1.04–1.39)	0.009
	Model 3	1.21(1.03–1.41)	0.017
	Model 4	1.20(1.02–1.40)	0.027
Reduced HDLc			
	Model 1	1.27 (1.08–1.27)	0.000
	Model 2	1.15(1.05–1.26)	0.002
	Model 3	1.13(1.02–1.24)	0.017
	Model 4	1.14(1.03–1.26)	0.012
Elevated LDLc			
	Model 1	1.11(1.02–1.19)	0.014
	Model 2	1.08(0.99–1.18)	0.101
	Model 3	1.06(0.96–1.16)	0.270
	Model 4	1.06(0.96–1.16)	0.268
Central obesity			
	Model 1	1.47(1.34–1.62)	0.000
	Model 1+(BMI, Fat%)	1.48(1.29–1.71)	0.000
Having two or more risks			
	Model 1	1.59(1.42–1.78)	0.000
	Model 2	1.59(1.40–1.81)	0.000
	Model 3	1.58(1.34–1.82)	0.000
	Model 4	1.61(1.40–1.85)	0.000
Metabolic Syndrome (harmonize)			
	Model 1	1.59(1.42–1.78)	0.000
	Model 2	1.59(1.40–1.81)	0.000
	Model 3	1.58(1.38–1.82)	0.000
	Model 4	1.61(1.40–1.85)	0.000
Metabolic Syndrome (IDF)			
	Model 1	1.61(1.44–1.81)	0.000
	Model 2	1.61(1.42–1.83)	0.000
	Model 3	1.59(1.39–1.83)	0.000
	Model 4	1.62(1.41–1.86)	0.000

Note:
Model 1: one dependent, one independent (NC) controlling for confounders (age, postmenopausal status, hormone use, dietary habits & practices, activity level & life style).
Model 2: one dependent, one independent (NC) controlling for confounders (age, postmenopausal status, hormone use, dietary habits & practices, activity level & life style, and BMI)
Model 3: one dependent, one independent (NC) controlling for confounders (age, postmenopausal status, hormone use, dietary habits & practices, activity level & life style, BMI, WC)
Model 4: one dependent, one independent (NC) controlling for confounders (age, postmenopausal status, and hormone use, dietary habits & practices, activity level & life style, BMI, WC and Fats)
OR, odds ratio; CI, confidence interval; TG, triglyceride; HOMA-IR, homeostasis model assessment-estimated insulin resistance; HDLc, high-density lipoprotein cholesterol; LDLc, low- density lipoprotein cholesterol; IDF, International Diabetes Federation.

Table 3 presents the dose-response effect of increasing NC on cardiometabolic risk. The ORs of metabolic syndrome or its components increased from the first (Q1) to the fourth quartile (Q4) of NC (P-trend, <0.001 for all). Compared with women in the lowest NC quartile, those in the highest quartile had ORs of 8.76 (95% CI: 5.13,

14.96) for hypertension; 15.28 (95% CI: 7.95, 29.36) for elevated fasting plasma glucose; 4.38 (95% CI: 2.67, 7.18) for elevated TG; 3.54 (95% CI: 2.08, 6.02) for reduced HDLc; 3.54 (95% CI: 2.08, 6.03) for elevated LDLc; 3.10 (95% CI: 1.63, 5.84) for elevated HOMA-IR; 6.34 (95% CI: 3.65, 11.01) for obesity; 27.01 (95% CI: 11.87, 61.46) for central obesity; 17.13 (95% CI: 8.38, 34.99) for having two or more cardiometabolic risks; and 17.98 (95% CI: 8.79, 36.78) for metabolic syndrome (all P<0.01) (Model 1). After adjustment for age, menopausal status, and hormone use (Model 2), same trends were found in the risk of the components of metabolic syndrome across increasing NC quartiles, except with the Q4 group for high HOMA-IR (all P< 0.01). Women in the highest NC quartile were 12 times more likely (95% CI: 5.67, 26.47) to have two or more metabolic risk factors compared to the lowest NC quartile. Moreover, women with the highest NC quartile were 13 times (95% CI: 6.35, 28.23) more likely to have metabolic syndrome compared to those with the lowest NC quartile, after adjusting for the listed confounders (all P<0.01).

Figure 1: Multiple binary logistic regression analysis of cardiovascular disease risk factors for neck circumference

	Female n=614	
OR1		1.19 (1.11–1.28)
Low HDLc		1.23 (1.10–1.38)
HOMA_IR>75th		1.31 (1.21–1.42)
High TG		1.41 (1.29–1.53)
High Blood Pressure		1.53 (1.39–1.68)
High Fasting Glucose		1.66 (1.50–1.84)
Having 2 or more risks		1.66 (1.49–1.84)
Metabolic Syndrome		
OR2		1.16 (1.08–1.26)
Low HDLc		1.19 (1.06–1.35)
HOMA_IR>75th		1.26 (1.16–1.37)
High TG		1.38 (1.25–1.52)
High Blood Pressure		1.48 (1.33–1.64)
High Fasting Glucose		1.60 (1.42–1.78)
Having 2 or more risks		1.59 (1.42–1.78)
Metabolic Syndrome		
OR3		1.14 (1.03–1.26)
Low HDLc		1.20 (1.02–1.40)
HOMA_IR>75th		1.25 (1.13–1.38)
High TG		1.29 (1.15–1.45)
High Blood Pressure		1.70 (1.48–1.94)
High Fasting Glucose		1.61 (1.40–1.84)
Having 2 or more risks		1.61 (1.10–1.85)
Metabolic Syndrome		
	OR (95% CI)	

Note: *OR1: unadjusted, OR2: adjusted for age, menopausal status, and hormonal use, eating index, activity index. OR3: adjusted for age, menopausal status, hormonal use, BMI, fat%, and WC. OR, odds ratio; CI, confidence interval; HDLc, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment-estimated insulin resistance; TG, triglyceride.*

Table 3. Logistic regression analysis of risk for metabolic syndrome and its components by quartile of neck circumference level.

	OR(95% CI)			
NC cm Women N (614)	Q1 <35 cm 144	Q2 35.0– 36.5 cm 172	Q3 36.6 –38 cm 171	Q4 >38 cm 127
		All P-trend<0.0001		
Hypertension				
Model 1	1	3.04(1.82–5.09)**	5.55(3.39–9.08)**	8.76(5.13–14.96)**
Model 2	1	2.39(1.38–4.12)**	4.77(2.82–8.07)**	6.76(3.78–12.08)**
High glucose				
Model 1	1	3.14(1.97–4.99)**	7.81(4.74–12.87)**	15.28(7.95–29.36)**
Model 2	1	2.47(1.51–4.05)**	6.85(4.05–11.57)**	11.51(5.81–22.77)**
High TG				
Model 1	1	1.79(1.11–2.89)*	2.63(1.67–4.14)**	4.38(2.67–7.18)**
Model 2	1	1.57(0.96–2.56)	2.30(1.44–3.66)**	3.37(2.02–5.65)**
Low HDLc				
Model 1	1	2.17(1.35–3.49)**	2.60(1.64– 4.13)**	3.54(2.08–6.02)**
Model 2	1	2.09(1.28–3.42)**	2.36(1.46– 3.81)**	3.28(1.87–5.75)**
High LDLc				
Model 1	1	2.17(1.35–3.49)**	2.60(1.64–4.13)**	3.54(2.08–6.03)**
Model 2	1	2.09(1.28–3.42)**	2.36(1.46–3.81)**	3.28(1.87–5.75)**
HOMA-IR >75th				
Model 1	1	2.98(1.62–5.50)**	3.29(1.83–5.93)**	3.10(1.63–5.84)**
Model 2	1	2.67(1.44–4.98)**	2.95(1.62–5.38)**	2.59(1.34–5.03)**
Obesity: BMI≥ 30				
Model 1	1	2.58(1.62–4.09)**	4.78(2.97–7.67)**	6.34(3.65–11.01)**
Model 2	1	2.68(1.67–4.31)**	4.83(2.97–7.88)**	6.57(3.69–11.70)**
Central-obesity: WC ≥ 92				
Model 1	1	5.37(3.25–8.85)**	10.07(5.89–17.23)**	27.01(11.87–61.46)**
Model 2	1	4.86(2.92–8.12)**	9.07(5.25–15.67)**	23.12(10.00–53.46)**
Having two risks or more				
Model 1	1	3.66(2.27–5.90)**	9.35(5.48–15.98)	17.13(8.38–34.99)**
Model 2	1	2.89(1.74–4.79)**	7.65(4.38–13.38)**	12.57(5.67–26.47)**

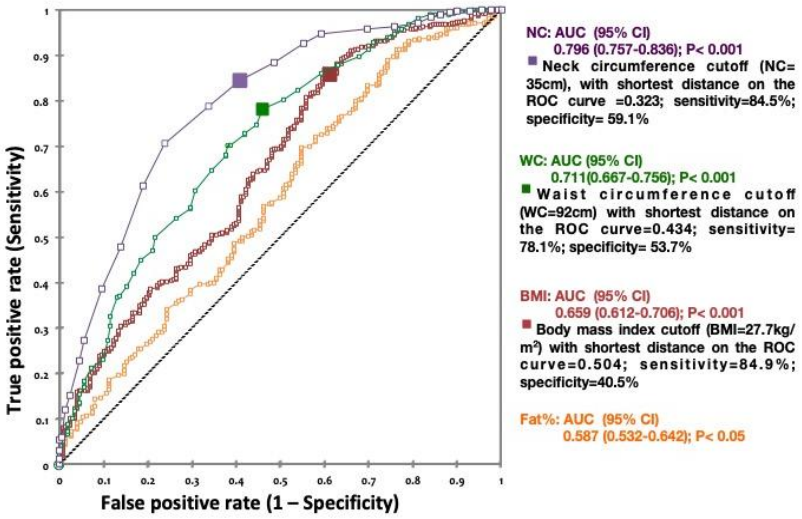
Metabolic Syndrome (harmonized)				
Model 1	1	3.84(2.38–6.20)**	9.82(5.74–16.80)**	17.98(8.79–36.78)**
Model 2	1	3.06(1.84–5.08)**	8.13(4.64–14.22)**	13.39(6.35–28.23)**
Metabolic Syndrome (IDF)				
Model 1	1	4.14(2.56–6.69)**	10.58(6.18–18.13)**	19.38(9.47–39.67)**
Model 2	1	3.30(1.98–5.49)**	8.83(5.04–15.49)**	14.55(6.89–30.72)**

*Model 1: Unadjusted. Model 2: Adjusted for age, postmenopausal status, hormone use, dietary habits & practices, activity level & life style. ** represented significant at 0.001 level.*
OR, odds ratio; CI, confidence interval; NC, neck circumference; N, number; Q, quartile; TG, triglyceride; LDLc, low- density lipoprotein cholesterol; HDLc, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment-estimated insulin resistance; BMI, body mass index; WC, waist circumference; IDF, International Diabetes Federation.

Optimal Cutoff Points to Predict Cardiometabolic Risks

Receiver operating characteristic (ROC) curves were used to determine the efficacy of NC as a screening measure for correctly identifying subjects with cardiometabolic risks and to select appropriate cutoff points for NC. The ROC curves are presented in Figure 2. For metabolic syndrome, NC showed the largest area under the curve compared with WC, BMI, and fat% as follows: 0.796 (0.757–0.836), 0.711 (0.667–0.756), 0.659 (0.612–0.706), and 0.587 (0.532–0.642), respectively, for NC, WC, BMI, and fat% (all P<0.001, except for fat%, where P<0.01). According to the ROC curve analysis, the optimal NC cutoff value with the shortest distance on the ROC curve from the perfect predictor was for NC=35 cm, distance in ROC curve=0.323. The accuracy, sensitivity, and specificity of this cutoff value were 77%, 84.5%, and 59.1%, respectively. We determined that WC=92 cm, with the shortest distance in ROC curve=0.434, was our optimal WC cutoff point. This cutoff point had sensitivity and accuracy of 78.1% and 70.7%, respectively; the specificity was 53.7%. Therefore, the appropriate NC and WC cutoffs to predict metabolic syndrome in the Saudi women were determined as 35 cm and 92 cm, respectively. Furthermore, 27.7 kg/m2 emerged as the optimal cutoff point for BMI with the shortest distance in ROC curve for predicting the presence of three or more metabolic risk factors. The distance in ROC curve=0.504, while the sensitivity and specificity were 84.9% and 40.5%, respectively (Figure 2).

Figure 2 ROC curve for NC, WC, BMI, and Fat% to predict the presence of three or more metabolic syndrome risk factors based on IDF definition in women



Note: NC, neck circumference; WC, waist circumference; BMI, body mass index; fat%, body fat percentage; AUR, area under the curve; CL, confidence interval.

Prevalence of Metabolic Syndrome

After dividing the subjects according to NC dichotomized by the cutoff of 35 cm,

the prevalence of metabolic syndrome, obesity, and central obesity were all significantly higher in the group with the higher cutoff (≥35 cm) than those with the lower cutoff (<35 cm) (Table 4).

Table 4. Comparison of the prevalence of metabolic syndrome and obesity by neck circumference cutoff point

	NC < 35 cm	NC ≥ 35 cm
N	144	470
Neck circumference (mean ± SD)	32.6(1.8)	37.5(1.6)***
Waist circumference (mean ± SD)	88.3(11.4)	102.8(10.8)***
Metabolic syndrome (%)	50(34.7)	381(81.2)***
Metabolic syndrome-IDF (%)	49(34)	379(80.8)***
Having 2 or more risks (%)	52(36.1)	381(81.2)***
Obesity (%)	56(38.9)	349(74.3)***
Central obesity (%)	120(83.3)	467(99.4)***

*NC, neck circumference; n, number; SD, standard deviation; IDF, international Diabetes Federation. Continuous data were reported as means ± standard deviation and categorical data were reported as n (%). ***p-values = 0.000 between groups with higher and lower cutoff points of NC.*

Then we checked the combined effects of NC (<35 cm vs. ≥35 cm) and WC (<92 cm vs. ≥92 cm) or BMI (<27.7 kg/m2 vs. ≥27.7 kg/m2) in predicting metabolic syndrome using a stratified analysis. In women with high NC values, the ORs (95% CI) of metabolic syndrome for those with high WC or BMI were 8.41 (4.91–14.38) and 12.5 (6.6–23.7), respectively (all P<0.001), which were much greater than for the women with low NC values (1.19–2.7). A high NC value was associated with a significantly greater risk of metabolic syndrome, even in subjects with normal WC or BMI. In addition, the combined effects between NC (<35 cm vs. ≥35 cm) and WC (<80 cm vs. ≥80 cm) groups in predicting metabolic syndrome revealed very high OR, 61.1 (95% CI, 7.9–470.9) of metabolic syndrome for the group with high NC and high WC. It is interesting to discover that only 3 women with a small WC had a large NC (Figure 3).

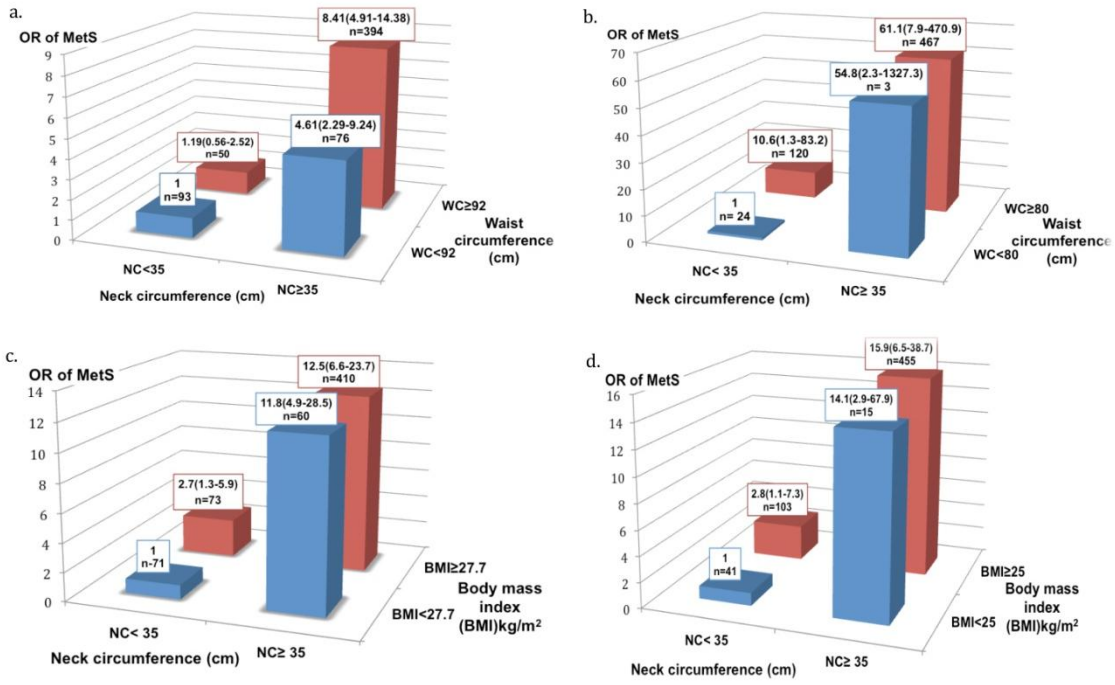


Figure 3 Age adjusted ORs of metabolic syndrome according to joint classification of neck circumference and other anthropometric indices

OR, odds ratio; MetS, metabolic syndrome

DISCUSSION

Prediction of Cardiometabolic Risks

In our study, adjustment for age, sex, menopausal status, hormonal use, lifestyle, BMI, and WC did not change the strength of the associations between NC and cardiometabolic risks. This finding suggests that the effects of higher NC in women are less likely to be mediated by these factors. The regression analysis results indicated that elevated NC increased the risk of developing insulin resistance, hypertrigly-

ceridemia, hypertension, central obesity, metabolic syndrome, and hyperglycemia 1.2; 1.2; 1.3; 1.5; 1.6; and 1.7 times, respectively. Several studies have demonstrated similar results, showing that, even after controlling for BMI and WC, NC remained a significant predictor of metabolic syndrome components 1.3 to 1.9 times [20, 15]. In our study, for women in the fourth quartile (NC >38 cm) there was association with increased OR for all metabolic syndrome components. We observed an extremely elevated risk, as much as 23-fold, 13-fold, and 11-fold, with central obesity, metabolic syndrome, and hyperglycemia, respectively. In addition, Laakso et al. reported that women with NC in the highest quintile showed about a fivefold increased risk of elevated fasting glucose and a threefold increased OR of hypertension after adjustment for BMI [21]. Other studies established that NC in the highest quartile added seven-fold, eight-fold, or 17 fold risks to the insulin resistance, obesity, and metabolic syndrome compared with that in the lowest quartile [22].

Neck Circumference Cutoff Points

The overall performance of NC, with an AUC of 0.796, in predicting metabolic syndrome using the IDF criteria was better than the performance of other anthropometric indices: WC (0.667); BMI (0.659); and fat% (0.587). Few studies have compared the predictive power of NC with those of other anthropometric indices. Yan et al. found that NC and WC shared the same predictive power (NC AUC =0.73, WC AUC =0.74) in women [26, 27]. However, in Zhou et al.'s study, NC had a significantly large AUC (0.703), but was relatively lower than those for WHR (0.766); WC (0.764); and BMI (0.723) [23]. For women, in this study, the optimal cutoff point to predict metabolic syndrome was 35 cm. The optimal cutoff point reported in this study falls within the range of 33-36 cm reported in the literature of NC studies [11, 23, 24, 25, 26, 27, 28]. Some studies considered NC =35 cm as the optimal cutoff value for the prediction of metabolic syndrome development [24, 25, 26].

We suggest that a WC value of 92 cm is more appropriate for defining central obesity and predicting the presence of two or more metabolic risk factors in Saudi women. This value differs from the recommended thresholds for American (88 cm) and European (80 cm) women by 4 and 12 cm, respectively [19]. However, our finding concurs with the results from previous studies in the Arabian Gulf region, in which the optimal WC cutoff for metabolic syndrome in Qatari and Iranian women were determined [29, 30]. Other studies showed that the optimal WC cutoff points for Omani and Iraqi women were 84.5 cm and 99 cm, respectively [31, 32].

Differences in the definitions of metabolic syndrome and in body sizes could explain the discrepancies in the optimal cutoffs of NC and WC among different populations. As a result, ethnic-specific cutoff values of NC and WC are required for the prediction of cardiometabolic abnormalities [19, 23, 27]. Neck circumference is an excellent independent cardiometabolic predictor, which exceeded other anthropometric indices in this study on Saudi women. WC, BMI, and fat% have denoted lower prediction power. WC could underestimate the real cardiovascular risk in subjects with small stature, which may be important in many populations, such as our Arab sample [33, 34]. Another reason might be the different settings of studied populations, since our study included subjects in their late middle ages to older adults, as our inclusion criteria included subjects aged 18-70 years [26, 27]. For individuals with a BMI ≥ 35, WC adds little to the predictive power of the disease risk classification of BMI [9]. Aging women tend to gain weight and have less estrogen protecting them against cardiovascular diseases [35]. Fat distribution changes with aging; and women develop a more central distribution (android shape) [35]. These findings imply that associations between

WC and cardiometabolic risks might have been mediated by obesity (BMI, fat%) and aging in our sample. Consequently, ethnic-specific cutoff points of NC should be required for the prediction of metabolic syndrome [23, 25, 26, 27], particularly for Saudi women. Lastly, although NC shows a strong association with both central obesity and metabolic syndrome, the consideration of NC as a screening test is a reasonable approach. Women with NC < 35 cm do not require additional evaluation. Women with a NC above this level require an extensive assessment of their metabolic and cardiovascular risk.

Our study has its limitations; the cross-sectional nature of this study prevents causal inferences. In this study, DEXA scan, which is a valid and widely used method, was used to assess body composition. However, other reference methods such as computed tomography (CT) scan, could be used to better quantify the upper body fat in future study. Our study was conducted in one city, limiting the generalization of our findings to all Saudi women. However, given the significant and consistent associations detected in our study and similar findings from different populations in other studies, NC shows promise as an alternative marker for the metabolic and cardiovascular risks associated with central or visceral adiposity.

CONCLUSIONS

Our findings showed NC as a stronger independent predictor of metabolic and cardiovascular risks than BMI and WC. Furthermore, for Saudi women, the appropriate NC that predicts three or more metabolic risk factors was 35 cm. Metabolic syndrome, obesity, and central obesity were more prevalent in women with an NC ≥35 cm. Larger NC was associated with greater risk of metabolic syndrome, even in women with normal WC or BMI. The current study reaffirms the importance of appropriately assessing the upper body obesity in screening for metabolic syndrome. And it provides practical guidance in identifying individuals with metabolic syndrome.

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