Association Between Neck Circumference And Metabolic Syndrome In Women With Polycystic Ovary Syndrome

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Research

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Abstract

Objective: To explore the correlation of neck circumference (NC) with metabolic syndrome (MetS) and metabolic risk factors, and assess the predictive value of NC for MetS in women with polycystic ovary syndrome (PCOS).

Methods: This is a cross-sectional study recruited 633 women diagnosed with PCOS from January 2018 to June 2021. Anthropometric parameters, neck circumference, blood pressure, reproductive hormones, glycemic and lipid profile were measured in all subjects. The definition of MetS adopted in this study was the International Diabetes Federation (IDF) criteria.

Results: Of the 633 subjects, MetS was diagnosed in 177 women (28.0%). PCOS women with larger NC had significantly greater values of body weight, body mass index (BMI), waist circumference (WC), hip circumference (HC), waist to hip ratio (WHR), systolic blood pressure, diastolic blood pressure, fasting blood glucose, fasting insulin, homeostasis model assessment of insulin resistance (HOMA-IR), homeostasis model assessment of β cell function (HOMA-β), triglyceride and high-density lipoprotein cholesterol. The prevalence of MetS, hypertention, obesity, central obesity, hyperglycemia and dyslipidaemia was also significantly higher in women with larger NC. Additionally, logistic regression analysis showed that women in the highest quartile of NC had the highest prevalence of MetS (RR=7.14, 95%CI: 1.82-28.01) after adjusting for confounding factors. Furthermore, NC was able to identify MetS in women with PCOS and the optimal cutoff points were 33.0 cm (Youden index = 0.44). The area under the curve (AUC) in predicting MetS by NC was 0.813，which was significantly larger than HC while comparable with BMI and WHR.

Conclusions: Neck circumference was positively and independently correlated with the prevalence of MetS and showed a good predictive ability in women with PCOS. Therefore, NC could be recommended as a simple, stable and highly reproducible measuring method in the routine clinical assessment and long-term management of women with PCOS to screen those at high risk of MetS.

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrinopathies characterized by oligo-anovulation, hyperandrogenism and polycystic ovarian morphology, affecting 4%–21% women of reproductive age(1). PCOS not only leads to reproductive dysfunction in women of childbearing age, but is also closely related to the incidence and development of a variety of diseases, including impaired glucose tolerance, type 2 diabetes, obstructive sleep apnea syndrome, non-alcoholic fatty liver disease, cardiovascular and cerebrovascular diseases(2-4). Hitherto, the pathogenesis of metabolic changes in women with PCOS has not yet been fully elucidated, making it more difficult to perform intervention at a metabolic level.

The metabolic syndrome (MetS) is the constellation of metabolic abnormalities including obesity, glucose intolerance, dyslipidaemia, and hypertension, all of which are associated with increased risks of

cardiovascular diseases(5). It has been reported that the prevalence of metabolic syndrome in women with PCOS was almost threefold higher than women without PCOS(2). PCOS women with MetS have a lower cumulative live birth rate compared with women without MetS, which indicates a vicious cycle between abnormal metabolism and lowered female fecundity(6). The etiologies of MetS include central obesity and insulin resistance, of which the central obesity is one of the criteria for the diagnosis of metabolic syndrome(7). In the clinical practice, waist circumference has been used as an evaluation index for central obesity(8). However, it is not always feasible and accurate to measure waist circumference in the winter with heavy clothes or postprandially. Additionally, in order to make a definite diagnosis of MetS, patients need to undergo a series of examinations including blood drawing, blood pressure measurement and anthropometric measurement, which is time-consuming and requires professional personnel as well as specific equipments(9). Therefore, there is a need for a reliable, simple, and fast method to identify MetS early in clinical practice.

Neck circumference (NC) is a convenient anthropometric index which reflects the subcutaneous fat tissue of the upper body(10). Studies have demonstrated that larger NC is closely related to abnormal glyco-lipid metabolism and higher incidence of MetS(11). It has been reported that the optimal cutoff points of neck circumference for MetS in women of all ages range between 34.2 cm to 38.0 cm(11, 12). However, since women with PCOS are more susceptible to metabolic abnormalities, it is currently unclear whether those cutoff values are also applicable in women with PCOS. Therefore, we conducted this study aiming to explore the correlation of NC with MetS and metabolic risk factors and to assess the predictive value of NC for MetS in women with PCOS.

Patients And Methods

Participants

This is a retrospective cross-sectional study that initially enrolled 765 women with PCOS from January 2018 to June 2021 at the reproductive center of the First Affiliated Hospital of Wenzhou Medical University. The exclusion criteria were as follows: 1) patients with other causes of hyperandrogenemia, including congenital adrenal hyperplasia, androgen-secreting neoplasms, and Cushing's syndrome (n= 6); 2) patients with any medical intervention or diseases that could alter the neck circumference or affect glyco-lipid metabolism, including neck surgery (n= 7), neck malformation (n= 2), thyroid dysfunction (n= 11), tuberculosis (n= 3), malignant tumor (n= 2), and regular oral glucocorticoids (n= 2), oral contraceptives (n= 20) or any anti-diabetic treatment (n= 10); and 3) patients with incomplete information for anthropometric parameters or laboratory examination (n= 69). Finally, 633 (82.7%) women between 21 to 42 years of age were included for further analysis. This study was approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University (2021N07). Written informed consent for the whole procedure was obtained from all participating patients.

Definitions

The diagnostic criteria of PCOS include two out of three features according to the 2003 Rotterdam diagnostic criteria(13): 1) menstrual abnormalities: oligomenorrhea or amenorrhea; 2) clinical and/or biochemical hyperandrogenism: hirsutism (Ferriman-Galwey score > 6) or testosterone concentration > 2.81 nmol/L; 3) polycystic ovarian morphology under B-ultrasound: at least one ovary containing 12 or more peripheral follicles measuring 2–9 mm in diameter and/ or ovarian volume of at least 10 mL on transvaginal or abdominal ultrasound. The definition of MetS adopted in this study was promulgated by the International Diabetes Federation (IDF) — the IDF criteria. According to the IDF definition of MetS, at least three of the following factors should be included to diagnose the MetS: (1) central obesity based on waist circumference (WC ≥ 80 cm for women in a Chinese population)(14); (2) increased triglycerides (TG, ≥ 1.69 mmol/L); (3) decreased high-density lipoprotein (HDL, < 1.29 mmol/L for women); (4) high blood pressure (systolic blood pressure ≥ 130 or diastolic blood pressure ≥ 85 mmHg); (5) increased fasting blood glucose (≥ 5.60 mmol/L)(15). The prevalence was calculated as the number of patients diagnosed with MetS divided by the total number of PCOS patients recruited in the study. Obesity was defined as a body mass index (BMI) ≥ 25 kg/m^2 according to the Asian BMI criteria(16). Hyperglycemia was defined as fasting blood glucose (FBG) ≥5.6 mmol/L(15). Hypertension was diagnosed as systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, or use of any antihypertensive medication within 2 weeks(17). Dyslipidaemia was defined as total cholesterol (TC) ≥ 6.22 mmol/L or triglycerides (TG) ≥2.26 mmol/L or high-density lipoprotein (HDL) < 1.04 mmol/L, or low-density lipoprotein (LDL) ≥4.14 mmol/L, according to the National Cholesterol Education Program(18). Insulin resistance was estimated by the homeostasis model assessment of insulin resistance (HOMA-IR) index as follows: HOMA-IR= fasting blood glucose (FBG, mmol/L) x fasting insulin (FINS, mIU/L)/ 22.5. The β-cell function was estimated by the HOMA of β-cell function (HOMA-β) index as follows: HOMA-β= (20×FINS)/ (FBG-3.5). The prevalence of MetS was calculated as the number of patients diagnosed with MetS divided by the total number of PCOS patients recruited in the study.

Anthropometric and Laboratory Measurements

The anthropometric measurements include BMI, NC, WC, hip circumference (HC), waist to hip ratio (WHR), which were taken after an overnight fast with standing upright and shoulders relaxed position. Neck circumference was measured using a flexible tape at the level of the thyroid cartilage(19). BMI was calculated as the body weight in kilograms divided by the height in meters squared(20). WC was measured at the midpoint between the iliac crest and the lowest rib, and HC was measured at the level of maximum extension of the hip(8, 21). All the anthropometric measurements were completed by one nurse who had received training to ensure the reliability of data in our center. Blood pressure was measured with an electronic sphygmomanometer in the sitting position after 10 min rest. Fasting blood samples were collected after an overnight fast of at least 8 hours during the 2^{nd} to 5^{th} day of menstrual cycle to measure hormonal and metabolic parameters. All biochemical measurements were tested in the central laboratory of the First Affiliated Hospital of Wenzhou Medical University. Serum basal luteinizing hormone (LH), follicle stimulating hormone (FSH), estradiol (E2) and testosterone (T) were measured using an autoimmunoassay analyzer [Unicel Dxl 800, Beckman Coulter, USA]. Serum anti-mullerian

hormone (AMH) concentrations were analyzed using enzyme-linked immunosorbent assay [DSL,USA]. FBG, total cholesterol (TC), serum triglycerides (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were quantified by an autoanalyzer [AU 5800, Beckman, USA]. The intra-assay variation was less than 10% and the inter-assay variation was less than 15% for all detection methods.

Statistical analysis

The results were evaluated by using SPSS version 23.0 software (IBM Corporation) and MedCalc Application version 19.0.4 software. Patients enrolled were grouped into four frequency groups according to neck circumference. The value lied below the 25 percent of the bottom value was called quartile 1 and denoted by Q1.The other three quartiles were respectively denoted by Q2, Q3, and Q4. Demographic and biochemical variables with a skewed distribution were presented as the medians (interquartile ranges), otherwise were presented as mean ± standard deviation. Skewness and kurtosis tests for normality were performed and found that the level of basal LH, LH/FSH ratio, basal E2, basal T, AMH, FINS, HOMA-IR, HOMA-β, TG, and LDL did not follow normal distributions. *P* values for trends across quartiles were calculated by linear regression analysis for continuous variables. Data with skewed distributions were logarithmically transformed prior to linear regression analysis. Logistic regression analysis was performed to obtain the odds ratios and 95% confidence interval (CI) of NC for metabolic syndrome based on quartiles of NC. No variables were adjusted in model 1. Adjusted variables in model 2 included age, SBP, and DBP. In model 3, BMI, HC, LH/FSH ratio (log-transformmed), TG (log-transformmed), HDL and HOMA-IR (log-transformmed) were further adjusted. Logistic regression analysis was performed to obtain the prevalence ratios for each metabolic risk factors (hypertension, obesity, central obesity, hyperglycemia and dyslipidaemia) based on quartiles of NC after adjusting for relevant variables. Meanwhile, *P* values for trends across the quartiles were calculated by the Cochran–Mantel–Haenszel method. Receiver operating characteristic (ROC) curves were used to compare the predictive ability of NC, BMI, HC and WHR for MetS by calculating the area under the curve (AUC). The Youden index, defined as sensitivity + specificity − 1, was calculated to identify the optimal cutoff points. The specificity and sensitivity of NC, BMI, HC and WHR as well as the positive and negative predictive values were calculated for each cutoff point in the sample. All *P* values were two-sided and $P< 0.05$ was considered statistically significant.

Results

Baseline characteristics according to the quartiles of neck circumference in PCOS

The general demographic, anthropometric information and metabolic characteristics according to the quartiles of NC were described in Table 1. The quartile ranges of NC were < 31.0cm (n=200), 31.0-33.0 cm (n=189), 33.0 cm-35.0 cm (n=150), and > 35.0 cm (n=94). Subjects with larger NC showed elevated levels of BMI, NC, WC,HC,WHR, SBP, DBP, basal T, FBG, FINS, HOMA-IR, HOMA-β, TG, LDL, but lower levels of HDL. No significant differences were observed between the quartiles of age, the number of current smoker, LH/FSH ratio and the level of basal LH, basal FSH, basal E2, AMH and TC.

Percentages of MetS and metabolic risk factors across the quartiles of NC in PCOS

Of the 633 subjects, MetS was diagnosed in 177 women (28.0%). Hypertension was diagnosed in 32 women (5.1%). Obesity and central obesity were diagnosed in 210 (33.2%) and 311 women (49.1%), respectively. Hyperglycemia was found in 125 (19.8%) women. Dyslipidaemia was detected in 140 women (22.1%). The prevalence of MetS and the percentages of metabolic risk factors, including hypertension, obesity, central obesity, hyperglycemia, and dyslipidaemia were shown in Figure 1. The prevalence of MetS from Q1 to Q4 was 5.0%, 19.0%, 47.3% and 63.8%, respectively. More specifically, there exhibited a growing tendency in the percentage of hypertension, obesity, central obesity, hyperglycemia and dyslipidaemia consistent with the elevation of NC in PCOS.

Prevalence ratios for MetS based on the quartiles of NC in PCOS

The prevalence ratios for MetS and metabolic risk factors based on the quartiles of NC in PCOS were shown in Table 2. The prevalence ratio of MetS increased significantly, ranging from the lowest quartile of NC to the highest. Compared with the lowest quartile, women with PCOS in the highest quartile of NC showed the highest prevalence ratio of MetS (OR=33.53, 95% CI: 15.64-71.87). After adjusting for traditional confounding factors of age, SBP and DBP (model 2), the ORs for the prevalence of MetS, as compared with the lowest quartile, were 3.14 (95% CI, 1.47-6.70) for Q2, 11.29 (95% CI, 5.41-23.57) for Q3, and 15.99 (95% CI, 7.20-35.53) for Q4, respectively ($P_{\text{for trend}}$ <0.001). Following further adjustment for BMI, HC, LH/FSH ratio (log-transformmed), TG (log-transformmed), HDL and HOMA-IR (log-transformmed) (model 3), an 123%, 723%, and 894% increase in prevalence ratios for MetS was found in the second, third and fourth quartiles, respectively, compared with those in the first one ($P_{\text{for trend}}$<0.001).

Prevalence ratios for metabolic risk factors based on quartiles of NC in PCOS

The prevalence ratios for metabolic risk factors based on quartiles of NC were showed in Table 3. The prevalence ratio of hypertension, obesity and central obesity gradually increased, ranging from the lowest quartile of NC to the highest. Compared with the lowest quartile, PCOS women in the highest quartile of NC showed the highest prevalence ratio of hypertension (OR=6.34, 95%CI: 1.70-23.61), obesity (OR=54.74, 95%CI: 17.30-173.23) and central obesity (OR=15.48, 95%CI:

5.62-42.65).

The predictive ability of NC for MetS

The ROC curves constructed to compare the predictive values of NC and other anthropometric indices for MetS were shown in Figure 2. An NC of ≥33 cm were the best values of combined sensitivity and specificity in identifying MetS in women with PCOS. The AUC (95% CI) for NC was 0.81 (0.78–0.84), which was significantly larger than that for HC, with the AUC (95% CI) of 0.74 (0.70–0.77). The AUCs of NC in identifying MetS were higher than those of BMI and WHR. However, there were no significant differences between those AUCs (Supplementary Table 1).

The different cutoff points, sensitivities, specificities, positive and negative predictive values of NC, BMI, HC and WHR are shown in Table 4. The optimal cutoff points of NC, BMI, HC and WHR in predicting hyperuricemia were 33.0 cm (Youden index = 0.49), 23.81 kg/m2 (Youden index = 0.51), 90.0 cm (Youden index = 0.39) and 0.86 cm (Youden index = 0.47), respectively. The specificity (SP) and positive predictive value (PPV) of NC were 75.22% and 53.69%, which were comparatively higher than those of BMI (SP: 67.32%; PPV: 49.83%), HC (SP: 46.93%; PPV: 40.24%) and WHR (SP: 66.01%; PPV: 47.98%).

Discussion

This cross-sectional descriptive analysis among women with PCOS revealed that NC was strongly associated with MetS. Additionally, NC was significantly associated with risk factors of MetS and independently contributed to predicting the likelihood of MetS in women with PCOS. To the best of our knowledge, this is the first study to demonstrate such a correlation between neck circumference and MetS in women with PCOS.

Metabolic syndrome, a constellation of adverse health conditions associated with obesity, abnormal glycolipid metabolism and elevated blood pressure, raises the risk of type 2 diabete, cardiovascular morbidity and all cause mortality(22). With higher prevalence of obesity, insulin resistance and dyslipidemia, women with PCOS are more susceptible to metabolic syndrome (MetS) compared with non-PCOS(2). Studies have shown that the prevalence of MetS in women with PCOS was approximately 27.2%, almost two-fold higher than age-matched women in general population(6, 23). In this study, the results are in line with the previous findings and showed that 28.0% of PCOS women were diagnosed with MetS. Therefore, it is of great importance to find a simple and reliable screening method for early recognition and timely precautions in those high-risk populations during symptomless periods.

Many simple anthropometric indices, including waist circumference, body mass index, hip circumference, and waist-to-hip ratio are widely applied in the clinical practice as markers to reflect obesity or central obesity and predict cardiovascular risks. Neck circumference, reflecting the ectopic fat deposition in the upper body, has been applied in determining the degree of obesity and obesity-related metabolic disorders including cardiovascular diseases and insulin resistance(24, 25). NC measurement is reported to be more associated with MetS and cardiovascular risk factors than other anthropometric parameters and can be regarded as an independent predictor for MetS(26). Although many studies have reported that NC is related to the risk of hypertension, hyperglycemia, obesity, central obesity and dyslipidemia, they did not adjust for relavent variables and failed to explore the independent correlation between NC and each metabolic risk factors(27, 28).

In the current study, the prevalence of MetS and metabolic risk factors increased significantly from the lowest quartile to the highest quartile of NC. Even after adjusting for confounding factors, NC is still independently correlated with MetS and metabolic risk factors including hypertension, obesity and central obesity, which indicates that ectopic fat deposition might play a critical part in the development of MetS in women with PCOS. A large cohort study showed that NC was still associated with hypertension after

the adjustment for BMI(29), which is consistent with our findings. Moreover, the comparison of AUCs between NC and other anthropometric measurements indicates that NC possesses the predictive values for MetS. Since WC has been included in the diagnostic criteria of MetS, we did not compare the predictive ability between NC and WC due to inevitable bias. Interestingly, we identified that the optimal NC cutoff value is 33 cm in PCOS women for the prediction of MetS, the value of which is comparatively smaller than in normal female population (11, 12, 30), suggesting that earlier precautions need to be taken in PCOS women compared with the normal one.

Several potential mechanisms contribute to the high prevalence of MetS in PCOS women with larger NC. Firstly, it has been reported that the obstructive sleep apnea is 5 to 30 times more likely to be presented in women with PCOS, and the prevalence of metabolic syndrome is 6 to 9 times higher in individuals with OSA than in general population(31). Hypoxemia, one of the most typical characteristics of OSA, increases the release of adipokines from adipose tissue, contributing to a collection of metabolic abnormalities, including declined glucose tolerance and insulin sensitivity. Sencondly, recent compelling evidence indicates that NC is independently associated with hyperuricemia in women with PCOS, and elevated serum uric acid level has been well-acknowledged as a risk factor of metabolic risk factors(32). Thirdly, it has been demonstrated that NC is a reliable indicator for insulin resistance in women with PCOS(33). Insulin resistance, although has not been included in the diagnostic criteria of metabolic syndrome, is a central factor in the pathogenesis of both MetS and PCOS(34). In addition, increasing evidence has shown that the variation of NC directly reflects the subcutaneous adipose deposition, from which more than 60% of free fatty acids (FFAs) are released (35). Excessive FFAs have emerged as a major cause of insulin resistance in insulin target organs, which consequently precipitate the development of MetS(36).

To the best of our knowledge, this study is the first to assess the correlation of NC with MetS and metabolic risk factors in women with PCOS. The strengths of our study lie in the complete and validated metabolic data, as well as the standardized measurement of NC, which make our findings easily applicable to clinical practice. Most infertile women with PCOS tend to neglect the importance of long-term management of PCOS after conception by assisted reproductive technology. However, several limitaions should be taken into consideration. Firstly, the single-center retrospective design in this study limits its ability interpreting the causality of associations. Secondly, the selection bias could not be excluded since all the participants were infertile women with PCOS seeking ART treatment in our reproductive center, and we failed to assess the association of NC and MetS in women with PCOS conceived naturally. Thus, prospectively designed studies on a larger scale should be conducted to strengthen our findings.

Conclusions

In summary, we found that NC was positively and independently correlated with the prevalence of MetS and metabolic risk factors including hypertension, obesity and central obesity in women with PCOS. Therefore, NC could be recommended as a simple, stable and highly reproducable measuring method in

the routine clinical assessment and long-term management of women with PCOS to screen those at high risk of MetS.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University (2021N07). Written informed consent for the whole procedure was obtained from all participating patients.

Consent for publication

All the authors approved the publication.

Availability of data and material

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Competing interests

The authors declare that they have no competing interests.

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Authors' Contributions

CL and LM drafted and finished the manuscript equally. CL and LD participated in the collection of data and literature. CL, LM and LD participated in the statistical analysis. ZC and HY designed and revised the manuscript.

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Tables

Table 1. Baseline characteristics according to quartiles of neck circumference in PCOS

	Quartiles of NC				
Variables	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*P* for trend
	200	189	150	94	
Age (year)	28.61±3.68	30.27±3.80	29.52±3.77	30.25±3.47	0.23
Current smoker (n, %)	2 (1.0%)	4 (2.1%)	2 (1.3%)	1 (1.1%)	0.99
History of DM (n, %)	0 (0.0%)	1 (0.5%)	3 (2.0%)	6 (6.4%)	<0.001
BMI (kg/m^2)	20.64±2.29	23.33±2.41	25.84±3.01	27.72±2.91	<0.001
NC (cm)	29.98±0.99	32.47±0.50	34.53±0.50	37.20±1.48	<0.001
WC (cm)	71.39±6.21	78.79±6.81	85.87±7.29	91.51±7.80	<0.001
HC (cm)	87.63±5.12	92.79±5.10	98.79±5.63	101.71±7.13	<0.001
WHR	0.81±0.06	0.85±0.06	0.87±0.06	0.90±0.05	<0.001
SBP (mmHg)	107.12±10.57	112.26±11.21	116.57±12.70	122.20±12.60	<0.001
DBP (mmHg)	71.46±7.62	75.21±8.36	77.23±9.52	80.99±10.00	<0.001
Basal LH (IU/L)	7.20 (5.19-10.76)	6.56 (4.46-9.63)	6.59 (4.40-10.89)	6.41 (3.88-9.65)	0.07
Basal FSH (IU/L)	7.15±2.88	6.95±1.74	6.55±1.74	6.70±1.50	0.07
LH/FSH ratio	1.09 (0.76-1.60)	0.98 (0.68-1.38)	1.04 (0.72-1.53)	1.03 (0.59-1.40)	0.14
Basal E2 (pmol/L)	174.00 (114.00-241.00)	177.00 (121.00-225.50)	172.00(117.00-209.00)	159.30 (130.00-192.00)	0.35
Basal T (nmol/L)	1.84 (1.39-2.45)	2.02 (1.61-2.53)	2.08 (1.59-2.62)	2.11 (1.60-2.67)	0.03
AMH (ng/mL)	7.91 (6.16-11.61)	8.34 (6.54-11.33)	8.60 (5.94-10.74)	7.80 (5.57-11.02)	0.38
FBG (mmol/L)	5.10±0.39	5.20±0.49	5.43±1.00	5.64±1.99	<0.001
FINS (mIU/L)	8.32 (5.78-11.08)	11.21 (7.72-14.18)	14.50 (10.19-22.61)	16.30 (12.51-22.86)	<0.001
HOMA-IR	1.80 (1.31-2.55)	2.59 (1.77-3.43)	3.36 (2.44-5.70)	3.90 (2.85-6.10)	<0.001
HOMA-β	100.18 (75.09-143.99)	129.22 (94.46-182.33)	172.08 (114.41-235.46)	198.64 (137.26-264.84)	0.01
TC (mmol/L)	4.88±0.85	5.05±1.00	4.96±0.99	5.07±0.93	0.21

TG (mmol/L)	1.04 (0.74-1.38)	1.33 (0.90-1.97)	1.47 (1.00-2.09)	1.72 (1.26-2.31)	<0.001
HDL (mmol/L)	1.49±0.33	1.35±0.30	1.22±0.27	1.14±0.20	<0.001
LDL (mmol/L)	2.70 (2.23-3.08)	2.83 (2.40-3.40)	2.89 (2.46-3.52)	2.95 (2.48-3.50)	0.003

Note: DM = diabetes mellitus; BMI = body mass index; NC = neck circumference; WC = waist circumference; HC = hip circumference; WHR = waist to hip ratio; SBP = systolic blood pressure; DBP = diastolic blood pressure; LH = luteinizing hormone; FSH = follicle stimulating hormone; E2 = estradiol; T = testosterone; AMH = anti-mullerian hormone; FBG = fasting plasma glucose; FINS = fasting insulin; HOMA-IR = homeostasis model assessment of insulin resistance; HOMA-β = homeostasis model assessment of β cell function; TC = total cholesterol; TG = triglycerides; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

Table 2. Prevalence ratios for MetS based on the quartiles of NC in PCOS

	Quartiles of NC				
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*P* for trend
MetS					
Model 1	1.00 (Reference)	4.47 (2.15-9.30)	17.08 (8.38-34.81)	33.53 (15.64-71.87)	<0.001
Model 2	1.00 (Reference)	3.14 (1.47-6.70)	11.29 (5.41-23.57)	15.99 (7.20-35.53)	<0.001
Model 3	1.00 (Reference)	2.23 (0.68-7.35)	8.23 (2.35-28.81)	9.94 (2.41-40.99)	<0.001

Note: Model 1 was unadjusted. Model 2 was adjusted for age, SBP, and DBP. Model 3 was further adjusted for BMI, HC, LH/FSH ratio (log-transformmed), TG (log-transformmed), HDL and HOMA-IR (log-transformmed). NC = neck circumference; SBP = systolic pressure; DBP = diastolic pressure; BMI = body mass index; HC = hip circumference; TG = triglycerides; HDL = high-density lipoprotein; HOMA-IR = homeostasis model assessment of insulin resistance; CI = confidence interval; OR = odds ratio.

Table 3. Odds ratios for metabolic risk factors based on quartiles of NC in PCOS

	Quartiles of NC				
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*P* for trend
Hypertension					
Odds ratio (95%)[a]	1.00 (Reference)	1.84 (0.58-5.84)	3.63 (1.06-12.43)	6.34 (1.70-23.61)	0.03
Obesity					
Odds ratio (95%)[b]	1.00 (Reference)	3.84 (1.39-10.64)	12.52 (4.55-34.43)	54.74 (17.30-173.23)	<0.001
Central obesity					
Odds ratio (95%)[c]	1.00 (Reference)	3.88 (2.22-6.79)	11.98 (6.25-22.98)	15.48 (5.62-42.65)	0.004
Hyperglycemia					
Odds ratio (95%)[d]	1.00 (Reference)	1.00 (0.54-1.86)	1.51 (0.75-3.04)	1.14 (0.50-2.60)	0.34
Dyslipidaemia					
Odds ratio (95%)[e]	1.00 (Reference)	1.99 (1.20-3.29)	1.96 (1.07-3.60)	2.92 (1.43-5.94)	0.17

Note: [a], Data were adjusted for obesity, central obesity, hyperglycemia and dyslipidaemia; [b], Data were adjusted for hypertension, central obesity, hyperglycemia and dyslipidaemia; [c], Data were adjusted for hypertension, obesity, hyperglycemia and dyslipidaemia; [d], Data were adjusted for hypertension, obesity, central obesity and dyslipidaemia; [e], Data were adjusted for hypertension, obesity, central obesity and hyperglycemia.

Table 4. AUC, Cutoff points, sensitivities, specificities, positive and negative predictive values of anthropometric measures for MetS

Variables	AUC	Cut-off points	Youden Index	SE (95% CI)	SP (95% CI)	PPV (%)	NPV (%)
NC (cm)	0.813	33.00	0.49	74.01 (66.90 – 80.30)	75.22 (71.00 - 79.10)	53.69	88.18
BMI (kg/m^2)	0.808	23.81	0.51	83.62 (77.30 - 88.70)	67.32 (62.80 - 71.60)	49.83	91.37
HC (cm)	0.740	90.00	0.39	92.09 (87.10 – 95.60)	46.93 (42.30 - 51.60)	40.24	93.86
WHR	0.789	0.86	0.47	80.79 (72.40 - 86.30)	66.01 (61.50 - 70.30)	47.98	89.85

NC = neck circumference; BMI = body mass index; HC = hip circumference; WHR = waist to hip ratio; AUC = area under the curve; 95% CI = 95% confidence interval; SE = sensitivity; SP = specificity; PPV = positive predictive value; NPV = negative predictive value

Figures

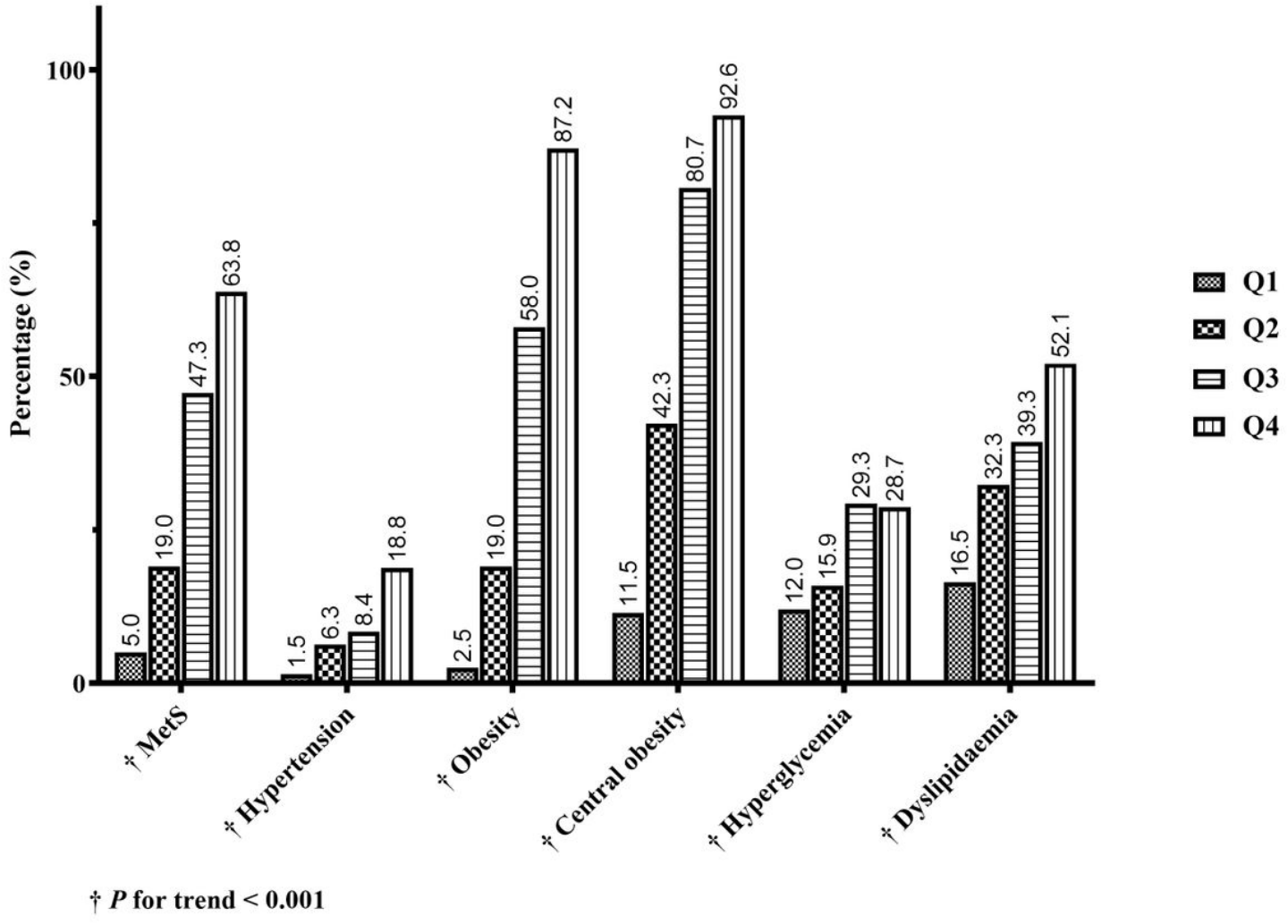

Figure 1

Percentage of MetS and metabolic risk factors across the quartiles of NC in PCOS

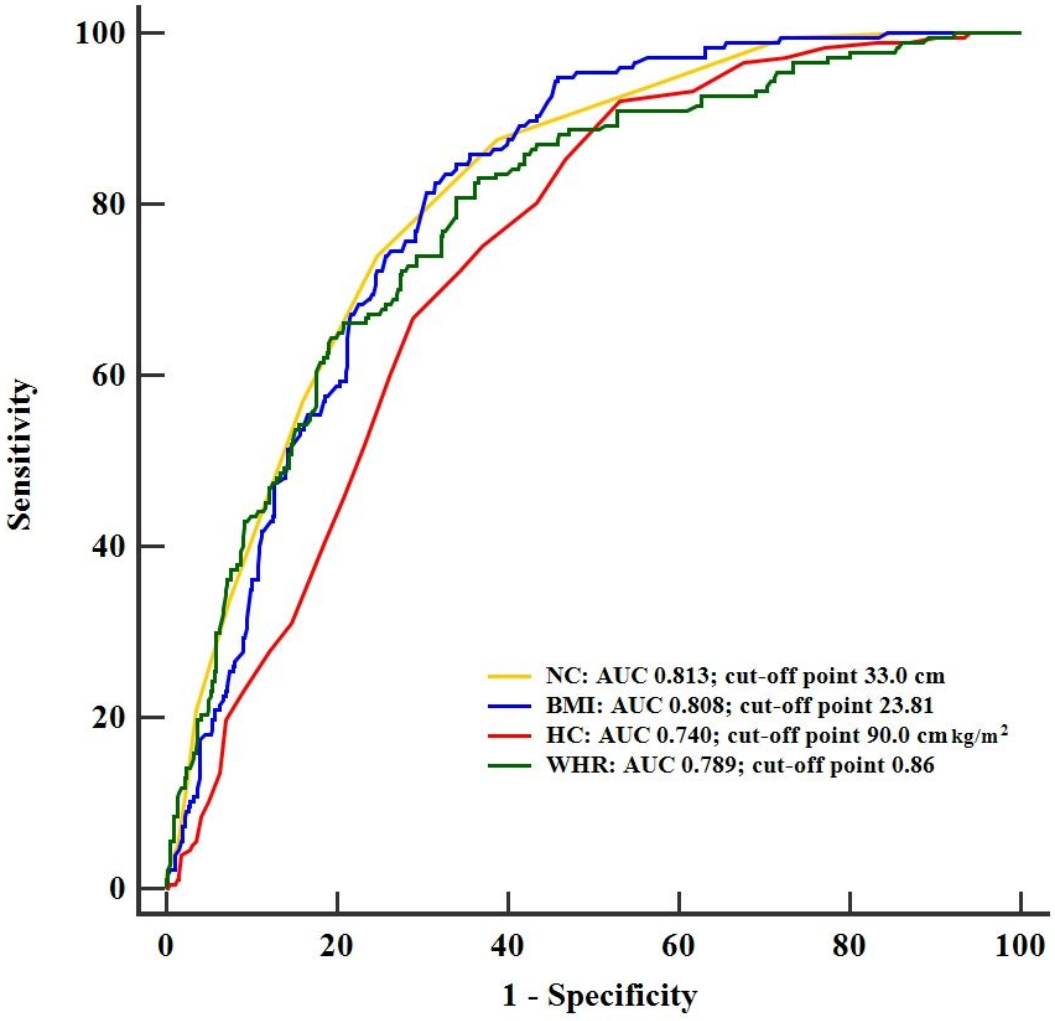

Figure 2

Receiver operating characteristic curves for the detection of MetS using NC, BMI, HC and WHR
Abbreviations: NC = neck circumference; BMI = body mass index; HC = hip circumference; WHR = waist to hip ratio

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplimentaryTable1.docx