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ARTICLE

Anthropometric indices to predict insulin resistance in women with polycystic ovary syndrome in China

BIOGRAPHY

Dr Wei Huang received her PhD in 1992 from West China Medical University, Chengdu Sichuan, China, and is currently full Professor of Obstetrics and Gynaecology at the university. Her research focus is mainly polycystic ovary syndrome, endometriosis, female infertility, female human decidual stem cells and miRNA.

Tingting Liu[1,2†], Qiuyi Wang[1,2,†], Wei Huang[1,2,*], Jing Tan[1,2], Dong Liu[1,2], Tianjiao Pei[1,2], Xueying Li[1,2], Guojun Zhou[1,2]

KEY MESSAGE

The waist-to-height ratio is the most accurate anthropometric indicator for predicting insulin resistance in Chinese women with polycystic ovary syndrome. We recommend waist-to-height ratio to predict insulin resistance in clinical practice.

ABSTRACT

Research question: Which anthropometric index (waist-to-height ratio, waist circumference, waist-to-hip ratio and body mass index) is the best in predicting insulin resistance among Chinese women with polycystic ovary syndrome?

Design: A total of 1124 patients with polycystic ovary syndrome at the Reproductive Endocrinology Division of West China Second University Hospital of Sichuan University were enrolled in this study. Identification of insulin resistance was based on homeostasis model assessment of insulin resistance scores 2.77 or over. Receiver operator characteristic analysis was carried out using the four anthropometric indices as the continuous variables and insulin resistance as the categorical variable to obtain the areas under the curve.

Result: The area under the curve for the waist-to-height ratio (0.748 ± 0.019) was greater than those for waist circumference (0.739 ± 0.019), body mass index (0.738 ± 0.017), and waist-to-hip ratio (0.659 ± 0.020) in the prediction of insulin resistance. The waist-to-height ratio also had the highest Youden indices compared with those of waist circumference, body mass index, and waist-to-hip ratio; the waist-to-height ratio cut-off was 0.49.

Conclusion: The waist-to-height ratio with a cut-off of 0.49 was the most accurate anthropometric indicator for predicting insulin resistance among Chinese women with polycystic ovary syndrome.

[1] Department of Obstetrics and Gynecology, West China Second University Hospital of Sichuan University, 20#, Section 3 Renminnanlu, Chengdu Sichuan 610041
[2] Key Laboratory of Birth Defects and Related Diseases of Women and Children of Ministry of Education, Chengdu Sichuan, China
†Contributed equally.

*Corresponding author. E-mail address: huang_wei@scu.edu.cn (W. Huang), https://doi.org/10.1016/j.rbmo.2018.10.001
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KEYWORDS

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Waist circumstance
Waist-height ratio

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, affecting 5.6% of Chinese women aged 19–45 years (Legro et al., 2013; Li et al., 2013). Its clinical manifestations include chronic anovulation and cutaneous signs of androgen excess, including hirsutism and acne. Polycystic ovary syndrome is also considered to be a metabolic disorder (Azziz et al., 2011). Among cases of PCOS, 50–70% are accompanied by insulin resistance (The Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group, 2004).

Insulin resistance, an independent risk factor for cardiovascular disease, can further develop into a number of metabolic disorders, such as diabetes mellitus, dyslipidaemia, metabolic syndrome (MetS) and sleep apnoea. As one of the common metabolic dysfunctions, the diagnosis of insulin resistance should be considered in the long-term management of women with PCOS. A number of methods are used to identify insulin resistance, including the homeostatic model assessment (HOMA) method, fasting insulin level, quantitative insulin sensitivity check index and the hyperinsulinaemic normal blood glucose clamp, which is considered to be the gold-standard quantification method (DeFronzo et al., 1979). The hyperinsulinaemic normal blood glucose clamp, however, is expensive, invasive and time-consuming, failing to offer convenience in clinical practice and large-scale research (Keskin et al., 2005). The homeostasis model assessment of insulin resistance (HOMA-IR) is a convenient, trusted and cost-effective method, which has been demonstrated to be closely correlated to the hyperinsulinaemic normal blood glucose clamp in the assessment of insulin sensitivity (Bonora et al., 2000). The HOMA is also reportedly more predictive of insulin resistance than fasting insulin level in women with PCOS (Majid et al., 2017). Furthermore, HOMA has been widely used in clinical practice.

Metabolic abnormalities are more severe in obese women than in non-obese women with PCOS (El-Mazny et al., 2010; Lim et al., 2012; Sam et al., 2015). Abdominal obesity is particularly associated with insulin resistance because of the accumulation of visceral adiposity. Overweight and obesity, especially abdominal obesity, are common in women with PCOS, and central body fat accumulation is a common feature in these patients (Carmina et al., 2007; Chun-Sen et al., 2011).

Currently, the use of tools for the clinical diagnosis of abdominal obesity-related health risks has emphasized their importance. The anthropometric methods are simple, non-invasive and cheap. Waist circumference, waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) are common anthropometric indices to assess abdominal obesity in individuals and groups as they can reflect body fat distribution and upper body adiposity (Li and McDermott, 2010; Dong et al., 2016).

In a study of metabolic disorders, WHtR was shown to better predict metabolic disorders (including hypertension, hyperlipidaemia, hyperglycaemia and hyperuricaemia) and cardiovascular disease risk factors than waist circumference and WHR (Hsieh and Muto, 2005; Li and McDermott, 2010; Matos et al, 2011; Dong et al., 2016). In women with PCOS, waist circumference is the best predictor of insulin resistance compared with WHR and BMI (Ramezani Tehrani et al., 2014). Costa et al. (2012) reported that waist circumference and WHtR are better than WHR in predicting MetS in Brazilian women with PCOS (Costa et al., 2012). Studies on the value of WHtR as a predictor of insulin resistance in Chinese women with PCOS, however, are lacking. We, therefore, conducted this cross-sectional study to analyse the accuracy of waist circumference, WHR, BMI, and WHtR in predicting insulin resistance and to find the optimal cut-off points for Chinese patients with PCOS.

MATERIALS AND METHODS

Study population

A total of 1124 patients were enrolled in our study. Patients with PCOS were recruited between December 2011 and December 2016 at the Reproductive Endocrinology Division of West China Second University Hospital of Sichuan University, Chengdu Sichuan, China. The diagnosis of PCOS was based on the Rotterdam criteria (The Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group, 2004).

The exclusion criteria for this study were abnormal renal or hepatic function and use of medications, such as hormonal contraceptives or anti-androgenic drugs treatment, within the previous 3 months. Women who suffered from genetic disorders, such as Turner's syndrome, primary hypopituitarism, primary premature ovarian failure and primary insulin resistance, were excluded from the study. Pregnant women and women aged under 18 years were also excluded from the study.

The Ethics Committee of Sichuan University approved this study (number 2010016, dated 13 October 2010), and informed consent was obtained from all participants. Data on age of menarche, duration of menstrual periods, menstrual cycle, a fertility desire and infertile history were recorded. Oligomenorrhoea was defined as a menstrual cycle lasting longer than 35 days. Polymenorrhoea was defined as a menstrual cycle lasting less than 24 days. Amenorrhoea was defined as an absence of menses for more than 6 months or menstruation that stopped for more than three cycles according to their original menstrual cycle. Irregular cycles were defined as an abnormal variation in the length of menstrual cycles, typically cycle length variations of up to 8 days between the shortest and longest cycle lengths. Infertility was defined as the failure to achieve pregnancy in a couple who engaged in regular and non-contraceptive intercourse for at least 1 year. The hirsutism scores were assessed using the modified Ferriman–Gallwey scoring method as an Ferriman–Gallwey score of 6 or over (Ferriman, Gallwey, 1961). Acne was scored based on the Global Acne Grading System (Doshi et al., 1997).

Measurements

All participants had their body weight, height, waist circumference and hip circumference measured in bare feet and while wearing light clothing. Electronic portable scales were used to measure body weight (measured to the nearest 0.1 kg). Portable stadiometers were used to measure height (measured to the nearest 1 cm), with the participants' feet placed together with heels, buttocks and shoulder blades against the stick and head positioned on the horizontal plane. Waist and hip circumferences were measured using an inextensible anthropometric tape, with the participants standing erect with their arms at their sides and feet positioned close together. Waist circumference (measured to the nearest 1 cm) was measured midway between the lowest border of the rib cage and the upper border of the iliac crest, at the end of normal expiration. Two observers independently and separately measured the waist circumference and confirmed their measurements with each other. They also assisted each other in keeping the measuring tape at the same level when measuring participants with high BMI and large waist circumference. Hip circumference (measured to the nearest 1 cm) was measured at the widest part of the hip at the level of the greater trochanter. The WHtR was calculated as the waist circumference (cm) divided by height (cm). The WHR was calculated as waist circumference (cm) divided by the hip circumference (cm). Body mass index was calculated as the body weight (kg) divided by the square of the body height (m^2).

Biochemical measurements

Blood samples were drawn from elbow veins after a 12-h overnight fast on the third day of a spontaneous cycle or progestin-induced bleeding in the case of amenorrhoea. The serum oestradiol, progesterone, testosterone, LH, FSH, prolactin (PRL) and fasting insulin levels were determined by chemiluminescent immunoassay analysis (Advia Centaur, Siemens, Erlangen, Germany). The intra-and inter-assay variability was less than 6.25%. Fasting plasma glucose levels were measured by the hexokinase method (ADVI 2400, Siemens, Erlangen, Germany). The intra-and inter-assay variability was less than 2.5%. The total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglyceride levels were measured by an enzymatic method (ADVI 2400, Siemens, Germany), for which the intra-and inter-assay variability was less than 7.5%. The HOMA-IR was calculated using the following formula: fasting plasma glucose (mmol/l) × fasting insulin (IU/ml)/22.5 (*Matthews et al., 1985; Bonora et al., 1998*). *Bonora et al. (1998)* proposed the value of 2.77 as the threshold for insulin resistance based on the lower limit of the top quantile of HOMA-IR distribution. HOMA-IR 2.77 or greater was chosen to identify insulin resistance (*Yen et al., 2001*). In a recent study, the cut-off point of 2.77 was used to evaluate insulin resistance (*Berezin et al., 2016*). Therefore, we defined 2.77 or over as our cut-off point for insulin resistance in our study.

Statistical analysis

STATA 14.0 (Stata Corp, College Station, USA) was used to analyse the data. Continuous variables were expressed as means ± SD or as medians (interquartile range 25–75) when the variable was not normally distributed, using Shapiro–Wilk tests. Comparisons of continuous variables were evaluated by two independent sample t-tests or Wilcoxon signed-rank tests when the data were not normally distributed. Spearman correlation analysis was used to analyse the relationships among WHtR, waist circumference, WHR, BMI and insulin resistance. Receiver operator characteristic (ROC) analysis was conducted using WHtR, waist circumference, WHR and BMI as continuous variables and insulin resistance as the categorical variable to obtain the area under the curve (AUC). The maximum value of the Youden's index (sensitivity + specificity – 1) corresponded to the optimal cut-off point of each index. For all analyses, $P < 0.05$ was considered statistically significant.

RESULTS

The mean age of the women with PCOS was 25.6 ± 4.1 (18–40) years. The mean age of menarche was 12.8 ± 1.3 (9–18) years. Most participants (1028/1124 [91.5%,]) presented with abnormal menstrual cycles, including oligomenorrhoea (n = 865), polymenorrhoea (n = 19), irregular menstrual cycles (n = 46), and amenorrhoea (n = 98). The remaining 96 patients (8.5%) had normal menstrual cycles. Infertile women accounted for 42.2% (474/1124) of the participants, with an infertility duration of 2 (1, 3) years. Among the 1124 women with PCOS, 162 (14.4%) were diagnosed as hirsutism and 493 (43.86%) with acne (mild: n = 488; moderate: n = 4; severe: n = 1). The mean body weight and mean height of all participants was 62.3 ± 10.7 (36.9–119.2) kg and 158.7 ± 4.9 (140.0–178.0) cm, respectively; the mean BMI was 24.73 ± 4.02 (15.62–47.75) kg/m^2. The mean waist circumference and hip circumference were 82.5 ± 9.42 (60–122) cm and 95.6 ± 7.16 (77–134) cm, respectively; the mean WHR was 0.86 ± 0.51 (0.67–1.10) and the mean WHtR was 0.52 ± 0.06 (0.38–0.77).

Among the study participants, 933 (83.0%) were diagnosed with insulin resistance based on HOMA-IR 2.77 or over; therefore, the patient cohort was further divided into insulin resistance and non-insulin resistance groups. Their clinical characteristics are presented in TABLE 1. Menstrual disorder was a common symptom in the two groups, and the insulin resistance group was significantly more likely to suffer from oligomenorrhoea ($P < 0.001$). The insulin resistance group ($P < 0.001$) contained significantly more infertile women. The incidence of hyperandrogenism, modified Ferriman–Gallwey and Global Acne Grading System scores did not differ significantly between the insulin resistance and non-insulin resistance groups. The BMI, waist circumference, WHtR and WHR anthropometric indices were significantly higher in the insulin resistance group than those in the non-insulin resistance group ($P < 0.05$).

Endocrine and metabolic parameters are presented in TABLE 2. The endocrine factor did not differ significantly between the insulin resistance and non-insulin resistance groups. Metabolic parameters, however, such as fasting insulin level, HOMA-IR, total cholesterol, low-density lipoprotein and high-density lipoprotein levels were significantly higher in the insulin resistance group than those in the non-insulin resistance group ($P < 0.001$).

The Spearman correlation coefficients between WHtR, waist circumference, BMI, WHR and insulin resistance were 0.48, 0.49, 0.46, and 0.37, respectively ($P < 0.001$). The ROC curves of WHtR, waist circumference, WHR and BMI regarding the ability to identify insulin resistance are presented in FIGURE 1. The areas under the ROC curves of various anthropometric indicators and 95% confidence intervals are presented in TABLE 3. The optimal cut-offs and the sensitivities, specificities and Youden indices of the four anthropometric indicators are presented in TABLE 4. The WHtR had the highest AUC value and Youden indices compared with waist circumference, WHR and BMI; the cut-off point of WHtR was 0.49.

DISCUSSION

This large cross-sectional study compared the diagnostic value of anthropometric indices in predicting insulin resistance in patients with PCOS in China. The prevalence of insulin resistance was 83% in our study, higher than that in a previous study (Li *et al.*, 2014) based on data randomly collected from several provinces in China. Our participants were outpatients with symptoms, including

TABLE 1 CLINICAL AND ANTHROPOMETRIC CHARACTERISTICS ACCORDING TO INSULIN RESISTANCE STATUS

	Non-insulin resistant (n = 191)	Insulin resistant (n = 933)
Menstrual cycle		
Oligomenorrhoea[a]	120	745
Polymenorrhoea	6	13
Amenorrhoea	12	86
Irregular menstrual cycles	14	32
Normal menstrual cycle	39	57
Infertility		
Number[a]	60	414
Infertile duration, years	2 (1,3)	2 (1,3)
Hyperandrogenism		
Hirsutism	38	124
m-FG score	7 (6,8)	7 (6,9)
Acne	103	390
GAGS	2 (1,4)	3 (1,5)
Anthropometric index		
Height, cm	159.2 ± 4.58	158.6 ± 4.95
Weight kg[a]	55.0 ± 8.27	63.9 ± 10.51
BMI, kg/m^2[b]	21.69 ± 3.20	25.35 ± 3.89
Waist circumference, cm[b]	76.2 ± 7.67	83.8 ± 9.23
WHtR	0.48 ± 0.05	0.53 ± 0.06
WHR[b]	0.84 ± 0.05	0.87 ± 0.06

BMI, body mass index; GAGS, Global Acne Grading System; m-FG, modified Ferriman–Gallwey scoring; WHtR, waist to height ratio; WHR, waist to hip ratio.

Data are expressed as means ± SD or median (25th–75th percentile).

[a] P <0.001.

[b] P < 0.05.

TABLE 2 ENDOCRINE AND METABOLIC PARAMETERS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME WITH OR WITHOUT INSULIN RESISTANCE

	Non-insulin resistant (n = 191)	Insulin resistant (n = 933)
FPG, mmol/l	5.10 (4.83, 5.38)	5.30 (5.03, 5.60)
FINS, IU/ml[a]	9.70 (8.30, 10.80)	17.30 (14.48, 23.07)
HOMA-IR[a]	2.20 (1.89, 2.47)	4.06 (3.30, 5.58)
Oestradiol, pg/ml	50.6 ± 12.05	45.6 ± 11.96
Progesterone, ng/ml	0.53 ± 0.06	0.48 +0.05
Testosterone, ng/ml	0.61 ± 0.21	0.59 ± 0.23
LH, mU/ml	11.06 ± 5.55	11.87 ± 5.36
FSH, mU/ml	6.61 ± 1.88	6.49 ± 1.43
LH/FSH ratio	1.54 ± 0.88	2.01 ± 1.26
PRL, ng/ml	13.2 ± 6.13	11.71 ± 5.00
Total cholesterol, mmol/l[a]	4.31 ± 0.55	4.45 ± 0.81
Triglyceride, mmol/l	1.01 ± 0.48	1.55 ± 1.29
LDL, mmol/l[a]	2.51 ± 0.57	2.77 ± 0.79
HDL, mmol/l[a]	1.54 ± 0.40	1.28 ± 0.29

FINS, fasting insulin; FPG, fasting plasma glucose; HDL, high-density lipoprotein;

HOMA-IR, homeostasis model assessment of insulin resistance; LDL-C, low-density lipoprotein; PRL, prolactin.

Data are expressed as means ± SD or median (25th–75th percentile) depending on the data distribution.

[a] P < 0.001.

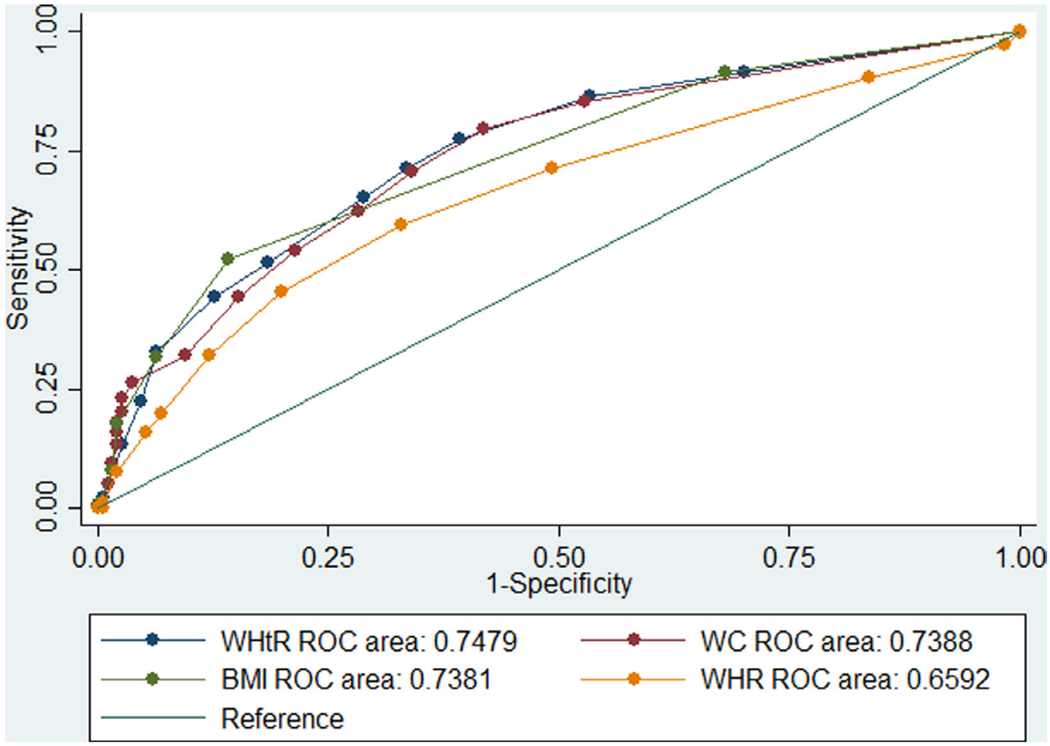

FIGURE 1 Receiver operating characteristic (ROC) curves of WHtR, WC, WHR, and BMI for the predictive performance of insulin resistance in women with polycystic ovary syndrome. BMI, body mass index; WC, waist circumference; WHR, waist to hip ratio; WHtR, waist to height ratio.

TABLE 3 AREA (95% CI) UNDER THE RECEIVER OPERATOR CHARACTERISTIC CURVES OF EACH ANTHROPOMETRICS INDEX FOR THE PRESENCE OF INSULIN RESISTANCE

Variables	AUC	SE	95% CI
WHtR	0.748	0.019	0.711 to 0.785
Waist circumference	0.739	0.019	0.702 to 0.777
BMI	0.738	0.017	0.705 to 0.772
WHR	0.659	0.020	0.620 to 0.698

AUC, area under the curve; BMI, body mass index; CI, confidence interval; SE, standard error; WHR, waist to hip ratio; WHtR, waist to height ratio.

TABLE 4 OPTIMAL CUT-OFF POINTS FOR EACH ANTHROPOMETRICS INDEX AND THEIR SENSITIVITIES, SPECIFICITIES, AND YOUDEN'S INDICES FOR INSULIN RESISTANCE

Variables	Cut-off point	Sensitivity (%)	Specificity (%)	Youden indices
WHtR	0.49	77.60	60.73	38.33
Waist circumference	77.0	79.42	58.12	37.54
BMI	25.0	52.09	85.86	37.95
WHR	0.86	59.49	67.02	26.51

BMI, body mass index; WHR, waist to hip ratio; WHtR, waist to height ratio.

menstrual disorder and infertility. Our findings are concordant with those of Ovalle et al. (2002) who reported that 68% of Japanese women with PCOS also had insulin resistance. All anthropometric indices (WHtR, waist circumference, WHR and BMI) in our study were significantly positively correlated with insulin resistance. The AUC features of the four anthropometric parameters were greater than 0.5, which indicates that these parameters were valuable for predicting insulin resistance in PCOS.

The AUC of WHtR was greater than those of waist circumference, BMI, and WHR. Our findings are consistent with other studies showing the advantage of waist circumference over BMI and WHR in the assessment of insulin resistance in patients with PCOS (Costa et al., 2012; Ramezani Tehrani et al., 2014). Waist circumference is considered a direct estimate of abdominal obesity. Schneider et al. (2011) found that short women had higher levels of risk factors and a 30% higher prevalence of MetS than tall women if grouped by waist circumference but not by WHtR. In the present study, BMI had a high specificity (85.86%) but low sensitivity (52.09%). In addition, BMI has been demonstrated to reflect overall obesity rather than abdominal obesity. The numerator and denominator of WHR changed synchronously, indicating that when the waist circumference gets larger, hip circumference also increases (data not shown). The WHtR had a relatively better sensitivity (77.60%) than BMI and WHR, and a relatively better specificity (60.73%) than waste circumference. The WHtR included both waist circumference and height. Studies have confirmed that the WHtR can identify metabolic risk factors better than other obesity indices, including BMI, waist circumference and WHR in Chinese populations (*Guan et al., 2016; Zeng et al*., 2014; *Zhou et al., 2014*).

In the present study, the optimal WHtR cut-off to predict insulin resistance in PCOS was 0.49, close to the 0.5 cut-off recommended by other studies using WHtR to predict abdominal obesity and cardiovascular disease (*Browning et al., 2010; Bacopoulou et al., 2015*); however, *Guan et al. (2016)* proposed 0.52 as the optimal WHtR cut-off to indicate metabolic risk factors. One possible explanation for this difference may be differences in the study population, age, or both, of the participants. Our study had several limitations, however. First, this study was a cross-sectional survey and a further cohort study is needed; second, the study population was recruited from a single centre in China; therefore, multiple-centre studies are also required.

In conclusion, our results revealed that the WHtR is the most accurate anthropometric indicator for the prediction of insulin resistance in women with PCOS. We recommend a WHtR cut-off of 0.49 for the assessment of insulin resistance in Chinese women with PCOS.

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