ORIGINAL ARTICLE

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Body fat indices as effective predictors of insulin resistance in obese/non-obese polycystic ovary syndrome women in the Southwest of China

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Abstract

Purpose Insulin resistance (IR) is a common feature of polycystic ovary syndrome (PCOS). Body fat indices can be predictive markers of IR. This study is aimed to predict IR in Chinese women with PCOS of different body types based on body fat indices.

Methods A total of 723 women diagnosed with PCOS according to Rotterdam criteria were recruited in this study and were further divided into two groups based on their BMI. All participants underwent physical examinations and ultrasound; and blood was collected from them on the days 3–5 of the menstrual cycle. Their BMI, waist-to-hip ratio (WHR), waist-to-height ratio (WHtR), lipid accumulation product (LAP) index, visceral adiposity index (VAI), and the homeostasis model assessment index of insulin resistance (HOMA-IR) were calculated. The correlations between body fat indices and HOMA-IR and receiver operating characteristic (ROC) curves were evaluated.

Results In normal weight group (BMI < 24, $n = 333$), VAI (best cut-off value: 1.681, area under curve (AUC) = 0.754, $P < 0.01$) and LAP index (best cut-off value: 18.53, AUC = 0.734, $P < 0.001$) were the reliable indicators of IR based on HOMA-IR ≥ 2.77, while in overweight/obese group (BMI ≥ 24, $n = 390$), the BMI, WC, WHtR and LAP index had a significant correlation with HOMA-IR. The representative markers to assess IR were BMI (best cut-off value: 26.43, AUC = 0.644, $P = 0.001$) and WHtR (best cut-off value: 0.544, AUC = 0.604, $P = 0.021$).

Conclusions Body fat indices are predictive markers of IR in Chinese PCOS women, especially in those with normal weight.

Keywords Polycystic ovary syndrome · Insulin resistance · Body fat indexes · Body mass indexes

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine and metabolic abnormalities of premenopausal women characterised by hyperandrogenism and ovulatory dysfunction [1, 2]. Probably 4–10% of reproductive-aged women suffer from this gynaecological endocrinopathy. Insulin functions as a co-gonadotropin to modulate ovarian steroidogenesis, which is important for ovulation and body weight regulation and is also associated with dyslipidaemia and visceral adiposity accumulation [3, 4]. In PCOS women, insulin resistance (IR) and compensatory hyperinsulinemia contribute to the development of type 2 diabetes (T2DM) and cardiovascular disease (CVD) and also metabolic disturbances [1, 2]. Therefore, the early recognition of IR and related metabolic dysfunction is important to prevent cardiovascular involvement in these women.

Central body fat accumulation independent of obesity is one of the features in PCOS women with IR. The quantification of visceral obesity is usually determined by magnetic resonance imaging (MRI) or computed tomography (CT). However, these imaging techniques are not preferred

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because of high cost and radiation exposure. Alternatively, the anthropometric parameters such as body mass index (BMI), waist circumstance (WC), waist-to-height ratio (WHtR) and waist-to-hip ratio (WHR) can indicate visceral adiposity accumulation to some degree. These anthropometric parameters have correlations with IR, metabolic syndrome (MS) and cardio-metabolic risk [5–7]. However, body fat indices such as lipid accumulation product (LAP) index and visceral adiposity index (VAI), which combined anthropometric parameters with plasma lipid values, demonstrated high accuracy for visceral obesity discrimination [8]. Previous studies confirmed that LAP index and VAI can accurately predict IR, MS, T2DM and CVD in PCOS women [4, 7, 9–11]. LAP index and VAI are more effective in predicting IR and MS compared with traditional anthropometric parameters [4, 7].

There could be different metabolic profiles between normal-weight and overweight/obese women because of the different proportions of adipose tissue. No study has identified the predictive value of body fat indices for IR in obese and non-obese PCOS women. Besides, there are variations in metabolic profiles based on ethnic differences [12]. This study aims to predict IR in Chinese PCOS women based on body fat indices.

Materials and Methods

Study population

This is a cross-sectional study involving 723 PCOS women aged 19–40 years at the Reproductive Endocrinology Unit of West China Second University Hospital between January 2011 and October 2017. The diagnosis of PCOS was established according to the Rotterdam criteria [13]. The women suffered from thyroid dysfunction, hyperprolactinemia, congenital adrenal hyperplasia, androgen-secreting tumours and Cushing's syndrome were excluded from the study. None of the patients had received any steroid hormone or hypoglycaemic drugs within the past 3 months. This study was approved by the Ethics Committee of West China Second University Hospital, Sichuan University; the written informed consent was obtained from all the participants.

Study protocol

All participants underwent clinical examinations including height, body weight, waist circumference, hip circumference and blood pressure. Blood pressure was measured after 10-min seat rest. Body weight of the patient was evaluated after removing shoes and coats. Waist circumference was measured at the midpoint between the

lower rib margin and the top of the iliac crest at the end of exhalation. Hip circumference was measured at the level of the greater trochanter. The above indices had been measured and verified by two experienced investigators. Body mass index (BMI) was calculated as body weight (Kg) divided by square of body height (M). According to Cooperative Meta-analysis Group of China Obesity Task Force, overweight was defined as $24 \le BMI < 28$, and obesity as $BMI \ge 28$ [14]. Waist-to-hip ratio (WHR) was calculated as waist circumference divided by hip circumstance. Waist-to-height ratio (WHtR) was calculated as waist circumstance divided by body height. All the participants were divided into two groups based on their BMI (<24 normal weight; ≥24 overweight/obese).

After an overnight fasting, blood samples were drawn from the elbow veins on the days 3–5 of natural menstrual cycle or progestin-withdrawal bleeding when the patient had amenorrhoea. Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TGs) were determined by an enzymatic method (ADVI 2400, Siemens, Germany) with the inter- and intra-assay coefficients of variation (CV) of <7.5%. Fasting plasma glucose was measured by the hexokinase method (ADVI 2400, Siemens, Erlangen, Germany) with the inter- and intra-assay CV of <2.5%. Serum Oestradiol (E2), progesterone (P), testosterone (T), luteinising hormone (LH), follicle-stimulating hormone (FSH) and fasting insulin levels were measured by chemiluminescent immunoassay analysis (Advia Centaur, Siemens, Erlangen, Germany) with the inter- and intra-assay CV of <6.25%. Homeostasis model assessment of insulin resistance (HOMA-IR) index was calculated using the formula insulin (μIU/ml)×glucose (mmol/l)/22.5. Based on Yen's recommendation, IR was defined as HOMA-IR > 2.77 [15]. The LAP index and the VAI were calculated using the formula [WC (cm) – 58] × TG (mmol/l) and [WC (cm)/(36.58 + 1.89 × BMI)]×TG (mmol/l)/0.81 × 1.52/ HDL-C (mmol/l), separately [16, 17].

Statistical analysis

Continuous variables were expressed as medians and interquartile ranges or mean±SD as appropriate. The normality of distribution was assessed by the Kolmogorov–Smirnov test. Difference was compared by Mann–Whitney U test or Student's t-test. Spearman rank correlation analysis was used to assess the association of various body fat indices with HOMA-IR, considering their skewed distribution. Receiver operating characteristic (ROC) curves were generated for previously reported body fat indices using a HOMA > 2.77 as the reference value to define IR. The optimal values for sensitivity and specificity were identified to keep the Youden index at the maximum.

Table 1 Clinical, hormonal and metabolic features of normal weight PCOS women and overweight/obese PCOS women

	Normal weight ($n = 333$)	Overweight/obese ($n = 390$)
Age (years)	24 (21–27)	26 (23–29)[a]
BMI (kg/m²)	20.95 (19.47–22.50)	27.11 (25.39–29.33)[a]
WC (cm)	75.3 (70.2–79.9)	88.6 (83.2–93.6)[a]
WHR	0.83 (0.80–0.86)	0.88 (0.85–0.92)[a]
WHtR	0.47 (0.44–0.49)	0.56 (0.52–0.59)[a]
LH/FSH ratio	1.65 (0.88–2.20)	1.53 (1.01–1.98)
T (ng/ml)	0.56 (0.38–0.62)	0.5 (0.40–0.68)
FPG (mmol/l)	5.19 (4.95–5.43)	5.24 (5.00–5.50)[b]
Insulin (µUI/ml)	12.5 (9.89–15.65)	18.36 (14.89–25.02)[a]
HOMA-IR	2.90 (2.23–3.60)	4.29 (3.36–5.92)[a]
TC (mmol/l)	4.24 ± 0.71	4.56 ± 0.89[a]
TG (mmol/l)	1.15 (0.83–1.61)	1.24 (0.92–1.70)
HDL-C (mmol/l)	1.29 (1.11–1.55)	1.29 (1.10–1.53)
LDL-C (mmol/l)	2.64 (2.12–3.20)	2.69 ± 0.72
LAP index	18.09 (11.05–28.36)	36.61 (25.88–53.49)[a]
VAI	1.60 (1.05–2.48)	1.82 (1.23–2.28)[a]

Values are expressed as median (25–75 inter-quartile range) or mean ±SD

HOMA homeostasis model assessment, *TC* total cholesterol, *TG* triglycerides, *HDL-C* high density lipoprotein cholesterol, *LDL-C* low density lipoprotein cholesterol, *LH* luteinizing hormone, *FSH* follicle-stimulating hormone, *T* testosterone, *IR* insulin resistance, *LAP* lipid accumulation produce, *VAI* visceral adiposity index

[a]$P < 0.01$, [b]$P < 0.05$

All analyses were performed using the Statistical Package for Social Sciences (SPSS version 23.0, Chicago, IL, USA). Significance was accepted at a tow-tail $P < 0.05$.

Results

The clinical complaints of 723 patients were as follows: oligomenorrhea (602/723, 83.3%), abnormal uterine bleeding (55/723, 7.6%), hirsutism (293/723, 40.5%), acne (366/723, 50.6%) and infertility (311/595, 52.3%). Among 723 PCOS women, 333 were of normal weights and 390 overweight/obese. The clinical, hormonal and metabolic features of normal-weight and overweight/obese groups are shown in Table 1. The anthropometric parameters (WC, WHR and WHtR) in overweight/obese PCOS women were higher than those of normal-weight group, the metabolic profiles such as TC were worse and the profiles of TG, HDL-C, LDL-C, T and LH/FSH ratio had no significant difference between the two groups.

In normal-weight groups, there were 56.16% of PCOS patients with IR, their HOMA-IR was positively correlated with VAI ($r = 0.434$, $P < 0.001$) and LAP index ($r = 0.417$, $P < 0.001$); in overweight/obese PCOS women, there was more IR incidence (88.20%), their HOMA-IR was significantly related with LAP index ($r = 0.20$, $P < 0.001$), BMI ($r = 0.301$, $P < 0.001$), WC ($r = 0.283$, $P < 0.001$) and
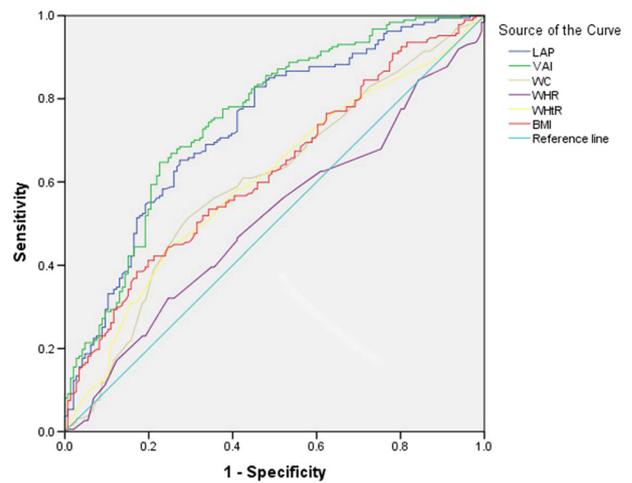

Fig. 1 ROC curves for body fat indexes with HOMA-IR in normal weight PCOS women. WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; LAP, lipid accumulation produce; VAI, visceral adiposity index

Fig. 2 ROC curves for body fat indexes with HOMA-IR in overweight/obese PCOS women. WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; LAP, lipid accumulation produce; VAI, visceral adiposity index
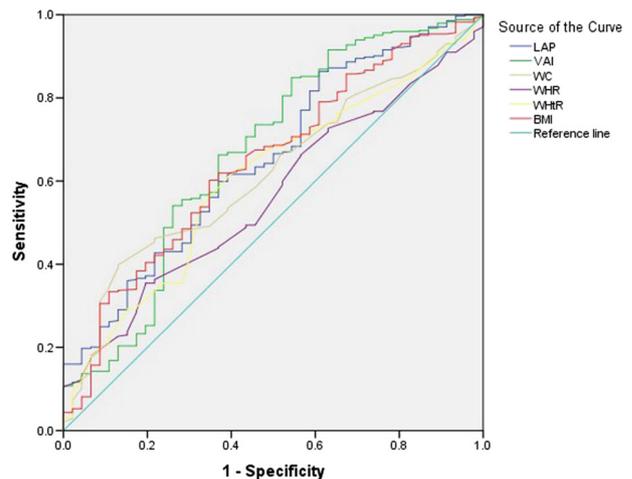
WHtR ($r = 0.264$, $P < 0.001$); however, there were almost no significant relationship with VAI ($r = 0.139$, $P = 0.06$).

ROC curve analysis showed that LAP index, VAI, BMI, WC and WHtR can predict IR in PCOS women. In normal-weight women, VAI (best cut-off value: 1.681, AUC = 0.754, $P < 0.001$) and LAP index (best cut-off value: 18.53, AUC = 0.734, $P < 0.001$) exhibited the greater diagnostic accuracy for IR. However, in overweight/obese women, BMI (best cut-off value: 26.43, AUC = 0.644, $P = 0.001$) and WHtR (best cut-off value: 0.544, AUC = 0.604, $P = 0.021$) (Figs. 1 and 2, Table 2) showed the greater diagnostic accuracy for IR.

Table 2 Efficacy of body fat indexes in predicting insulin resistance

Body fat Indexes	Cutoff values		SS (%)		SP (%)		PPV (%)		NPV (%)		AUC	
	NWP	OWP	NWP	OWP	NWP	OWP	NWP	OWP	NWP	OWP	AWP	OWP
BMI	22.1	26.43	41.2	60.2	80.1	65.2	67.4	63.4	57.7	62.1	0.624[a]	0.644[a]
WHR	0.859	0.908	32.1	35.5	75.3	80.4	56.5	64.4	52.6	55.5	0.512	0.653
WHtR	0.485	0.544	43.9	61.0	75.3	61.9	64.0	61.6	57.3	61.3	0.603[a]	0.604[b]
WC	76.25	90.25	51.3	39.8	70.5	87.0	63.5	75.4	59.1	59.1	0.601[a]	0.619[a]
LAP	1.681	1.07	65.2	86.3	72.6	31.9	70.4	55.9	67.6	67.0	0.734[a]	0.653[a]
VAI	18.53	22.92	64.7	84.9	77.4	45.7	74.1	61.0	68.7	75.2	0.754[a]	0.669[a]

PCOS polycystic ovary syndrome, *NWP* normal weight PCOS women, *OWP* overweight/obese PCOS women, *WC* waist circumference, *WHR* waist-to-hip ratio, *WHtR* waist-to-height ratio, *LAP* lipid accumulation produce, *VAI* visceral adiposity index, *SS* sensitivity, *SP* specificity, *PPV* positive predictive value, *NPV* negative predictive value, *AUC* area under curve

[a] $P < 0.01$, [b] $P < 0.05$

Discussion

As insulin levels have gonadotropin-augmenting effects, IR plays a central role in both the reproductive and metabolic disturbance observed in PCOS women. Insulin not only acts to augment ovarian and adrenal steroidogenesis but also promote pituitary LH release; therefore, IR has correlations with hyperandrogenism. As IR is implicated with the mechanism for pathogenesis and long-term complications of PCOS and also as an independent risk factor of CVD [3], it is of great importance to identify IR and provide insulin-sensitising therapy for patients with PCOS.

There were different optimal predictors of IR. The traditional parameters such as BMI, WC, WHR and WHtR were well correlated with IR, metabolic-risk and cardiovascular risk [5, 18–20]. In addition to these, anthropometric index, LAP index and VAI have been put forward recently [16, 17]. It is reported that LAP index and VAI have high accuracy in visceral obesity discrimination [8]. Several studies have demonstrated that these two indices can also predict IR, MS, T2DM and CVD in PCOS women [4, 7, 9, 10, 21]. Some studies have shown that LAP index and VAI present better efficacy for predicting IR than anthropometric parameters, as these combine anatomic and physiological alterations related to accumulation of fat [4, 7]. Obesity itself is a disease entity with the common manifestation of IR with PCOS; therefore, it is obvious that there are discrepant physiologic characteristics and metabolic profiles between normal-weight and overweight/obese PCOS women [22]. The Asian population are more prone to visceral fat accumulation and IR compared with western population [23, 24]. But most of the studies recruited overweight or obese women to investigate IR and adiposity indices, no stratified analysis in normal weight and overweight/obese groups [4, 5, 7, 11]. Our present study explores optimal cut-offs of body fat indexes to predict IR in Chinese population with PCOS based on different body

weights from normal-weight to overweight/obese. Our results showed 52.16% prevalence of IR in normal-weight PCOS women; their LAP index and VAI can well assess IR. Considering the ethnic difference, there may be an Asian (China) phenotype of PCOS as mentioned by Huang et al. [25]. For overweight/obese PCOS women, traditional body fat indices such as BMI and WHtR are more effective in predicting IR.

One limitation of the present study is that the subjects were recruited from the referral centre, where phenotypes of PCOS are possibly severe. And the BMI range for the definition of overweight/obese is for Chinese healthy adults, and it might be different for PCOS women.

Our study indicates that there are different IR predictors for different body types of Chinese PCOS women. The body fat indices LAP index and VAI can well predict IR in normal-weight PCOS women, but not in overweight/obese ones. The early recognition of PCOS women with normal body weight based on body fat indices is important to design therapy interventions to ameliorate IR.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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