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Original Article

The association of Pro12Ala polymorphism in the peroxisome proliferator-activated receptor-gamma2 gene with the metabolic characteristics in Chinese women with polycystic ovary syndrome

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Abstract: Background: The Pro12Ala polymorphism in the peroxisome Proliferator-activated receptor-gamma2 PPARγ2) gene that account for metabolic dysfunction in women with polycystic ovary syndrome (PCOS) remain elusive. Aim: To explore the association between PPARγ2 gene pro12ala polymorphism and the metabolic characteristics in Chinese women with PCOS. Methods: PPARγ2 gene Pro12Ala polymorphism was assayed by PCR/RFLP methods in 120 Chinese women with PCOS and 118 normal subjects. All subjects were examined by anthropometry, lipid profile, sex hormone, oral glucose tolerance tests and insulin tolerance tests. Results: In PCOS patients, women with the non-Pro/Pro genotypes of the PPARγ2 gene Pro12Ala polymorphism showed statistically significantly higher fasting triglycerides (TG) levels and WHR value than those with the Pro/Pro genotype (*P*=.006 for both). There was no significant difference with PPARγ2 Pro12Ala polymorphism distributions between Chinese Han women with PCOS and controls. Conclusion: PPARγ2 gene Pro12Ala polymorphism was not supposed to be susceptible genes in PCOS. However, in PCOS patients, the PPAR-gamma Pro12Ala polymorphism may modulate the concentrations of serum fasting TG levels and fat-deposition in abdomen, respectively.

Keywords: Polycystic ovary syndrome, peroxisome proliferator-activated receptor-gamma2, polymorphism, central obesity, hypertriglyceridemia

Introduction

Polycystic ovary syndrome (PCOS) is known to affect 6-10% of reproductive-aged women [1]. It is viewed as a heterogeneous androgen excess disorder with varying degrees of hormonal and metabolic abnormalities [2]. The interactions of multiple genetic and environmental factors are involved in the occurrence and development of PCOS and its complications. However, the exact pattern of inheritance is yet to be fully explained.

Hyperinsulinemia and insulin resistance (IR) has been considered to be the most important etiological aspect of reproductive and metabolic abnormalities in PCOS. Women with PCOS demonstrate a form of IR intrinsic to the syndrome [3]. In addition, only a substantial proportion of women with PCOS are susceptible to gaining weight and showing phenotype with metabolic abnormalities. Therefore, an important consideration is whether the role of genes such as peroxisome proliferator-activated receptor-gamma (PPARγ), a candidate gene involved in insulin action and secretion, energy metabolism and adiposeness [4], are also implicated in the pathogenesis of PCOS.

PPARγ is a nuclear receptor which controls transcription of genes involved in free fatty acid uptake and lipogenesis, and plays an important role in regulation of insulin sensitivity and adipose tissue metabolism [5], a strong candidate gene predisposing to obesity via increased adiposity. PPARγ2, which is most abundantly

expressed in adipose tissue, mediated an important function of PPARγ. A functional polymorphism in exon 2 of PPARγ2, the Pro12Ala (rs1801282) [6], has been suggested Ala allele lowered the risk of type 2 diabetes with a protective effect via an effect on the adipocyte [7-9]. In addition, this genotype has been associated with decreased receptor activity, lower body mass index (BMI) and improved insulin sensitivity in type 2 diabetes [6]. These findings suggested that PPARr2 Pro12Ala polymorphism may play a protective role in metabolic dysfunction. However, in contrast with the findings of Deeb's study [6], Tok and coworkers [10] reported that PPARγ2 Ala homozygotes had higher BMI and nearly 3 times higher fasting insulin levels compared with Pro homozygote in PCOS. Moreover, recently studies showed conflicting results on the association of Pro12Ala polymorphism with glucose and lipid metabolism and insulin sensitivity in PCOS [10-14]. Thus, the issue on whether Pro12Ala posed as a primary defect in women with PCOS was also unsettled.

In the present study, we investigated the association of the Pro12Ala polymorphism of the PPARγ2 gene with PCOS and the possible effect of this polymorphism on the metabolic characteristics of PCOS in Chinese Han women.

Materials and methods

A total of 238 subjects were included in this study. They were recruited from the Outpatient Department of Endocrinology and Gynecology of Shanghai Renji Hospital between 2006. Of these patients, 120 women were with PCOS and 118 women were control subjects. The diagnosis of PCOS was according to the 1990 National Institutes of Health criteria [15]. Pregnancy was excluded by a urinary pregnancy test. All women had normal thyroid function and prolactin levels, and late-onset nonclassic congenital hyperplasia was excluded by a basal 17-ahydroxyprogesterone value of <300 ng/dl [16]. Women receiving glucocorticoids, antiandrogens, or oral contraceptives within the previous 30 days, or ovulation induction agents, antiobesity medications, or insulin-sensitizing agents within the previous 60 days were excluded. All women were evaluated by transvaginal ultrasonography to define ovarian morphology [17]. Control subjects were healthy volunteers or endocrinology outpatients without any endocrine related diseases except for simple overweight/obesity and screened by medical history, physical examination, laboratory evaluation, and transvaginal ultrasound. Normal weight women were defined as those with a BMI <25 kg/m^2, and obesity was defined as those with a BMI of ≥25 kg/m^2 according to the 2000 WHO-WPR criteria [18]. All study evaluations and procedures were conducted in accordance with the guidelines of Helsinki Declaration on human experimentation. The study was approved by the ethics committee of Shanghai Renji Hospital, and all subjects provided written informed consent.

Anthropometric measurements

General characteristics and history of diseases were obtained by a standardized questionnaire. All subjects received physical examination by a special investigator, including height, weight, waist circumference (WC), hip circumference (HC) and blood pressure. The height and weight of each subject wearing light clothing was measured to the nearest 0.1 cm and 0.1 kg respectively using a digital scale and stadiometer. Body mass index (BMI) was calculated as body weight (kg) divided by height (m) squared. WC was determined by measuring the circumference at the narrowest point between the lower border of the rib cage and the iliac crest. HC was determined by measuring the circumference at the level of the symphysis pubis and the greatest gluteal protuberance. The waist-to-hip ratio (WHR) was then calculated by dividing the WC by the HC.

Laboratory analysis

All laboratory evaluations were performed at 08:00 h after an overnight fast during the early follicular phase (days 2-5) of a spontaneous menstrual cycle, except in subjects with amenorrhoea >3 months who were examined randomly. Competitive electrochemiluminescence immunoassays on the Elecsys Autoanalyzer 2010 (Roche Diagnostics, Indianapolis, IN) were used to quantify serum total testosterone, oestradiol (E2), luteinizing hormone (LH), follicle stimulating hormone (FSH). Plasma glucose was determined using the glucose oxidase methodology. All measurements were performed with Roche reagents (D 2400 and E 170 Modular Analytics modules with Roche/Hitachi analyzers; Roche Diagnostics). Total

Table 1. Demographical and clinical characteristics between women with PCOS and controls

Variable	PCOS	Controls	*P*-value	*P**-value
N	120	118	N/A	
Age (ys)	23.96±6.62	31.82±1.06	<.001	NS
BMI (kg/m^2)	26.52±5.19	24.79±5.74	.016	.036▲
WHR	0.86±0.07	0.84±0.08	.083	.001▲▲
Waist circumference (cm)	83.40±13.11	78.91±14.82	.014	.033▲
Hip circumference (cm)	96.90±9.78	93.51±11.21	.013	.02▲
SBP (mmHg)	120.69±12.8	119.42±11.97	.493	.202
DBP (mmHg)	78.24±10.13	76.89±9.03	.415	.043▲
Oestradiol (pmol/L)	181.49±141.25	251.49±241.29	.015	.009▲▲
Total testosterone (nmol/L)	2.62±1.31	2.23±1.21	.002	.034▲
LH/FSH	1.31±0.83	0.73±0.59	<.001	<.001▲▲
Total cholesterol (mmol/L)	4.50±1.00	4.30±1.51	.248	.025▲
Triglycerides (mmol/L)	1.33±0.78	1.04±.70	.006	<.001▲▲
HDL cholesterol (mmol/L)	1.44±0.40	1.56±0.56	.070	.122
LDL cholesterol (mmol/L)	2.75±0.90	2.53±0.68	.041	.005▲▲
FINS (mU/L)	16.61±9.98	10.73±8.05	<.001	<.001▲▲
2h INS (mU/L)	95.15±64.95	65.03±54.11	.001	.012▲
FPG (mmol/L)	5.04±0.71	5.10±1.09	.962	.517
2hPG (mmol/L)	6.82±2.12	6.83±2.29	.975	.637
HOMA-IR	3.84±2.87	2.39±1.79	<.001	<.001▲▲

Data are means±SD. BMI - body mass index, WHR - waist-to-hip ratio, SBP - Systolic blood pressure, DBP - Diastolic blood pressure, LH/FSH - luteinizing hormone to follicle stimulating hormone ratio, FINS - fasting insulin, 2h INS - 2h postprandial insulin, FPG - fasting plasma glucose, HOMA-IR - homeostasis model assessment-insulin resistance index. ▲*P*<.05 ▲▲*P*<.01 (*P* value for t-test) *P** adjusted by age (*P** value for analysis of covariance).

cholesterol (TC), high density lipoprotein cholesterol (HDL-C) and triglycerides were determined by enzymatic methods (Olympus 600, Clinical Chemistry Analyser, Olympus Diagnostica GmbH, Ireland). Low density lipoprotein cholesterol (LDL-C) was calculated by the Friedewald equation. Insulin levels were measured by RIA. The intra-assay CV of insulin and of steroid hormone assays were 5.5 and <10% respectively.

Oral glucose tolerance test

All the subjects underwent a standard OGTT with 75 g of glucose. After 08:00 h overnight fasting, blood samples were drawn for the determination of glucose and insulin before the glucose load, and they were then drawn again at 30, 60, 120, and 180 min. Insulin resistance was estimated by homeostasis model assessment (HOMA-IR = fasting plasma insulin (mU/L)*fasting plasma glucose (mmol/L)/22.5) [19].

Genotype analysis

Genomic DNA was isolated from peripheral blood leukocytes of women with PCOS and the controls. To determine single nucleotide polymorphisms (SNPs), we conducted polymerase chain reaction (PCR). The Pro12Ala polymorphism of the PPARγ gene was genotyped by amplification of genomic DNA using the following primers [5], F5'-GCCAATTCAAGCCCAGTC-3' and R5'-GATATGTTTGCAGACAGTGTATCAGTGAAGGAATCGCTTTCCG-3'. The polymorphism was typed with enzyme BstU-I and the digestion products were resolved after electrophoresis in 2.5% agarose gel and stained with ethidium bromide and detected by the UV light. In order to confirm our results, all positive samples were sent to Shanghai Sangon Biotech Co., Ltd to detect the DNA sequence (Applied ABI Prism 3730 Genetic Analyzers/Sequencers, BigDye terminator v3.1 Reagents).

Statistical analysis

All statistical analyses were performed using SPSS version 17.0 (Statistical Package for the Social Sciences, USA). Distributions of continuous variables were tested for normality by use of the Kolmogorov–Smirnov test. Part of results not normally distributed, based on the normal quartile plot, was log-transformed for all statistical analyses and reported back-transformed in their original units. Continuous data were

Table 2. Distribution of PPARγ2 Genotypes and Allele frequency in Subjects with or without PCOS

Group	n	genotype			Allele	
		P/P	P/A	A/A	P	A
PCOS	120	0.925 (111)	0.075 (9)	0	0.962 (231)	0.038 (9)
Controls	118	0.856 (101)	0.144 (17)	0	0.928 (219)	0.072 (17)
		X^2=2.917 *P*=.09			X^2=2.748 *P*=.10	

P value for chi-square test.

reported as means±SD and t-test was conducted to determine the difference between groups. Analysis of covariance was used to adjust the difference of age between groups. Genotype and allele frequencies were compared among the study groups using the chi-square test. Hardy-Weinberg equilibrium was also estimated by the chi-square test. *P*-values <.05 were considered significant.

Results

Demographical and clinical characteristics between in women with PCOS and normal controls

The clinical characteristics and biochemical variables for the women with and without PCOS are summarized in **Table 1**. The analysis of covariance was used to adjust for the difference of age between groups. As expected, there were significant differences in BMI, WHR, diastolic blood pressure (DBP), total testosterone, LH/FSH, TC, TG, LDL-C, fasting insulin, 2h postprandial insulin (2h INS) and HOMA-IR in PCOS group compared with control group (*P*<.05 for all) after adjusted by age. However, the levels of oestradiol in PCOS group was lower significantly than controls (*P*=.009). Significant differences in HDL-C, fasting glucose and 2h postprandial glucose values between PCOS and control women were not observed (*P*>.05 for all).

Distribution of allelic and genotypic frequencies (Pro12Ala) between PCOS and controls

The characteristics of the study population were presented in **Table 2**. The Pro12Ala polymorphism of the PPARγ2 gene was in Hardy-Weinberg equilibrium in both patients and controls (chi-square, *P*>.05). The frequency of the Ala allele was 5.44% in our study population. The Pro/Ala genotype frequency was 14.4% and 7.5% for controls and cases, representatively. And Ala allele frequency was 7.2% and 3.8% for controls and Observations, respectively. However, there was no significant difference in Pro/Ala genotype frequency or Ala allele frequency between groups (*P*>.05 for both).

Demographical and clinical characteristics between Pro/Pro genotype and Pro/Ala genotype in PCOS and controls

The demographical and clinical characteristics of Pro/Pro genotype and Pro/Ala genotype were shown in the **Tables 3** and **4**. As shown in **Table 3**, there was no significant difference in all biochemical detection outcomes between these two genotypes in control group (*P*>.05 for all). While as shown in **Table 4**, compared with Pro/Pro genotype, Pro/Ala genotype carriers have higher WHR (*P*<.01) and higher fasting TG (*P*<.01) in the PCOS group. In addition, they seemed to have larger WC without significant difference (*P*=.075). Furthermore, in order to investigate the impact of Pro/Ala genotype and Ala allele frequency on TG, we divided the PCOS group into two subgroups according the cutoff point of normal TG (1.7 mmol/L) [20]: TG normal group (PCOS-NTG) and hypertriglyceridemia group (PCOS-HTG). We found that the Ala allele frequency in PCOS-HTG groups was 19.4% and the Pro/Ala genotype frequency was 9.7%. Both of them were significantly higher than the PCOS-NTG group (2% and 3%, respectively; genotype frequency *P*=.009, allele frequency *P*=.01). In addition, there was no significant difference between these two genotypes in glucose and insulin levels, HOMA-IR and hormone profile in PCOS group(*P*>.05 for all).

Discussion

The main finding of this study is the demonstration that a significant increase in fasting TG levels and an increased WHR in Ala allele carriers in a distinct phenotypic group of Chinese PCOS women characterized by biochemical hyperandrogenemia. This metabolic dysfunction in lipid profile and abdominal obesity is perhaps regarded as an important indicator for cardiovascular disease (CVD) in these genotype women with PCOS in china. In addition, we did not find this genotype has been associated with decreased glucose levels and attenuated

Table 3. Demographical and clinical characteristics between Pro/Pro and Pro/Ala genotype in control group

Variable	Pro/Pro	Pro/Ala	*P*-value
N	101	17	N/A
Age (ys)	32.05±9.81	30.56±11.58	.564
BMI (kg/m^2)	24.51±5.62	26.45±6.24	.189
Waist circumstance (cm)	78.23±14.29	82.69±17.43	.241
Hip circumstance (cm)	93.21±11.15	95.17±11.68	.498
WHR	0.84±0.07	0.86±0.09	.174
SBP (mmHg)	118.32±11.93	124.29±11.22	.063
DBP (mmHg)	75.80±8.93	79.82±6.98	.086
Oestradiol (pmol/L)	260.73±251.13	187.00±159.00	.309
Total testosterone (nmol/L)	2.30±1.26	1.83±.88	.210
LH/FSH	0.74±0.62	0.67±0.39	.735
Total cholesterol (mmol/L)	4.44±1.49	3.59±1.60	.066
Triglycerides (mmol/L)	1.01±0.60	1.28±1.16	.196
HDL cholesterol (mmol/L)	1.57±0.60	1.50±0.33	.684
LDL cholesterol (mmol/L)	2.51±0.71	2.57±0.51	.794
FINS (mU/L)	10.59±8.20	11.32±7.39	.729
2h INS (mU/L)	63.67±54.37	72.67±54.16	.584
FPG (mmol/L)	4.99±1.10	5.33±0.81	.221
2hPG (mmol/L)	6.70±2.23	7.45±2.57	.268
HOMA-IR	2.30±1.78	2.95±1.81	.181

Data are means±SD. BMI - body mass index, WHR - waist-to-hip ratio, SBP - Systolic blood pressure, DBP - Diastolic blood pressure, LH/FSH - luteinizing hormone to follicle stimulating hormone ratio, FINS - fasting insulin, 2h INS - 2h postprandial insulin, FPG - fasting plasma glucose, HOMA-IR - homeostasis model assessment-insulin resistance index. *P* value for t-test.

Table 4. Demographical and clinical characteristics between Pro/Pro and Pro/Ala genotype in PCOS group

Variable	Pro/Pro	Pro/Ala	*P*-value
N	111	9	N/A
Age (ys)	23.86±6.61	25.22±7.08	.554
BMI (kg/m^2)	26.32±5.34	28.06±4.38	.343
Waist circumstance (cm)	82.79±13.01	90.89±12.75	.075
Hip circumstance (cm)	96.78±1.04	98.39±5.62	.638
WHR	0.85±0.07	0.92±0.09	.006▲▲
SBP (mmHg)	119.63±10.50	131.38±25.41	.234
DBP (mmHg)	77.83±9.20	82.38±17.28	.228
Oestradiol (pmol/L)	174.98±133.03	254.6±210.82	.110
Total testosterone (nmol/L)	2.64±1.31	2.38±0.90	.583
LH/FSH	1.24±0.79	1.72±1.24	.721
Total cholesterol (mmol/L)	4.47±1.00	4.92±0.97	.187
Triglycerides (mmol/L)	1.27±0.74	2.00±0.97	.006▲▲
HDL cholesterol (mmol/L)	1.45±0.39	1.31±0.50	.308
LDL cholesterol (mmol/L)	2.64±0.83	2.77±0.71	.249
FINS (mU/L)	16.88±10.25	13.15±4.89	.282
2h INS (mU/L)	93.11±65.82	119.91±49.65	.236
FPG (mmol/L)	5.07±.66	4.64±0.68	.067
2hPG (mmol/L)	6.80±2.15	7.00±1.84	.830
HOMA-IR	3.93±2.95	2.71±1.07	.222

Data are means±SD. BMI - body mass index, WHR - waist-to-hip ratio, SBP - Systolic blood pressure, DBP - Diastolic blood pressure, LH/FSH - luteinizing hormone to follicle stimulating hormone ratio, FINS - fasting insulin, 2h INS - 2h postprandial insulin, FPG - fasting plasma glucose, HOMA-IR - homeostasis model assessment-insulin resistance index. ▲▲*P*<.01 (*P* value for t-test).

IR estimated by HOMA-IR in Chinese women with PCOS. Lastly, our data did not show significant difference with PPARγ2 Pro12Ala polymorphism distributions between Chinese Han women with PCOS and controls.

Findings from previous studies regarding a link between Pro12Ala polymorphism and lipid metabolism in patients with different degree of metabolic dysfunction were wide spread [6-8] and have showed conflicting results [21-23]. Hamada's [21] group reported a significantly higher serum TG levels in general Japanese subjects with the X/Ala genotype (Pro/Ala + Ala/Ala), but there's no difference in serum TC, LDL-C and HDL-C levels between Pro/Pro and X/Ala two genotypes. Cardona F et al [22] have reported that the Pro12Ala PPARγ2 sequence variant together with a non-E3/E3 APOE genotype is associated with a high risk for postprandial hypertriglyceridemia in patients with metabolic syndrome, indicating a close association between these genes and the regulation of lipoproteinase clearance. But it should be noted that postprandial hypertriglyceridemia is affected obviously by eating and dietary habits. Hence, it was limited in assessing the impact on overall lipid metabolism. Findings from Swarbrick's study [23] showed that obese carriers of the Pro12Ala polymorphism have a greater risk of developing combined hyperlipidemia, possibly due to impaired activation of PPARγ target genes. Main explanations for the alleged disparity in these findings can be hypothesized that differences

in study subject demographics (specifically ethnicity, different composition of the diet) and clinical characteristics.

Data concerning a link between Pro12Ala polymorphism and lipid metabolism in women with PCOS are limited. In present study, we found a positive association between Ala allele frequency and fasting TG level, implying Pro12Ala polymorphism may play a role in lipid metabolism in PCOS women. In conflict with our results, findings from several study in European [11, 13, 14] showed that no significant differences in lipid levels were observed between and within genotype groups in PCOS and control women. It implied Pro12Ala polymorphism of the PPARγ gene may did not contribute to the lipid metabolism in PCOS women. The discrepancies with the results of these studies may be explained by the differences in genetic and ethnic background under investigation. However, in Chae's study [24], lean PCOS patients which base on Rotterdam criteria in Korea with the non-Pro/Pro genotype of the PPARγ Pro12Ala polymorphism have higher HDL-c levels than those with the Pro/Pro genotype, which implied a protective effect of this genetic mutant on HDL concentration. Several explanations for the apparent disparity in these findings can be hypothesized, including differences in study subject demographics (different PCOS criteria) and clinical characteristics (i.e. higher prevalence of obesity in our study).

PPARγ plays an important role in adipose tissue metabolism and Pro12Ala polymorphism has been reported to be associated with abdominal obesity in patients with metabolic dysfunction. In our study, we found an increasing of WHR implied a higher prevalence of abdominal obesity and fat accumulation in ala allele carriers. Until now, fewer studies observed an increase in WHR in PCOS cohort while data were shown in obese people. In Kim's study [23], which is similar to our result, PA/AA was found to be associated with significantly higher subcutaneous and visceral fat among overweight Korean female subjects with BMI of greater than 25. However, among lean subjects with BMI of less than 25, no significant differences associated with PPAR gamma 2 genotype were found. Their results suggested that the fat-accumulating effects of the PA/AA genotype were evident only among overweight subjects, but not among lean subjects. Moreover, Sramkova and coworkers reported a higher WHR in Czech obese women with the 12Ala allele [25]. The disparate effects of the Ala allele on body fat accumulation in lean and overweight subjects suggested the impact of PPARγ2 genotype might be modified by the higher mRNA expression level in obese patients, the increased expression level of PPARγ2 mRNA could enlarge the impact caused by Pro12Ala substitution [23].

In our study, the most important findings were that the Pro12Ala polymorphism in the PPARγ2 gene was positively associated with an increasing fasting TG and WHR among Chinese women with PCOS. This implied Pro12Ala polymorphism in the PPARγ2 gene has a potential effect on lipid profile and accumulation of abdominal adipose. Since simultaneous greater waist girth and HTG is proved to be a signal for high risk of cardiovascular disease [26], whether Pro12ala polymorphism have impact on CVD risk in PCOS women required long-term longitudinal studies to confirm.

The exactly mechanism about these potential effect is not clear yet. Some investigators showed that impact of PPARγ2 Ala12 on regulation of lipoprotein lipase (LPL) gene transcription was decreased by 20-30%, and the influence of Ala12 on LPL is greater than that of the frequent polymorphisms in the LPL gene itself [6]. Since LPL, a key enzyme of plasma lipoprotein metabolism plays a major role of hydrolyzing TG into circulating chylomicron (CM) and very low density lipoprotein (VLDL), releasing fatty acid, CM remnant and LDL [27]. The ability of TG hydrolysis is reduced along with the down-regulation of LPL gene, finally circulating TG concentration increases. It is noteworthy that the mutation of Pro12Ala locates at N ligand-independent activation function domains, which plays an important role in PPARγ gene regulation. Deeb and coworkers [6] reported that the PPARγ2 Ala allele showed decreased binding affinity to the cognate promoter element and reduced ability to trans-activate responsive promoters. Here, Pro12Ala variation reduced the transcription activity of PPAR-responsive element and decreased UCP2 gene transcription, which made an inadequate expression of UCP2 gene and reduced energy expenditure in Ala allele carriers. Interestingly, obesity and nutritional factors only influence the expression of PPARγ2 in human adipocytes. Furthermore, previous studies [23, 28] showed

that abdominal adipose was increased in Ala 12 carriers with diabetes or obesity. Their findings indicated that the primary influence target of Pro12Ala was located at adipose tissue, especially abdominal adipose. Consequently, we hypothesized that Pro12Ala polymorphism in the PPARγ2 gene may play a central role in the accumulation of abdominal adipose in women with PCOS. However, given the cross-sectional design of our study, causality cannot be established. The precise mechanisms of this genotype in the accumulation of abdominal adipose in women with PCOS must be further investigated.

In present study, we found genotype and allele frequencies of Pro12Ala polymorphism of the PPARγ were no different comparing PCOS women and controls. Our results are in agreement with the most studies [10, 12, 15, 16, 29]. In addition, our data did not show any association between Pro12Ala polymorphism and IR estimated by HOMA-IR, which also was consistent with other studies [15, 16]. However, our results are in contrast with other studies [11, 12] in Caucasian women with PCOS showed that Ala allele carriers with PCOS were more insulin-sensitive with lower HOMA-IR. They also mentioned that this polymorphism does not appear to contribute to the variation in insulin resistance among this population with relative low frequency of the Ala allele. Hence, studies of a larger group of PCOS women will be necessary to assess the effects of the Pro12 Ala polymorphism on insulin resistance.

There were several limitations of this study should be considered. Although our sample was relatively small, we based the diagnosis of PCOS on the 1990 NIH criteria, and thus represent a less heterogeneous group of women; we also made rigorous experimental design to reduce bias. We only chose WHR as the assessment for body fat distribution without confirming the results by CT or MRI. However, WHR is considered as a good predictor for abdominal obesity [30] and it is also available conveniently for large sample.

In conclusion, our study showed a close association between PPARγ2 gene Pro12Ala polymorphism and lipid metabolism and accumulation of abdominal adipose in PCOS women. This genotype posed at least partially metabolic dysfunction in Chinese women with PCOS. Confirming the relationship between Pro12Ala polymorphism and metabolism in PCOS women may provide evidence for individualized treatment in PCOS patients.

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Disclosure of conflict of interest

The authors have no financial or conflicts of interest to disclose.

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