Impact of Central Obesity on Women with Polycystic Ovary Syndrome Undergoing In Vitro Fertilization

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Abstract
Central obesity (CO) is a defining characteristic of polycystic ovary syndrome (PCOS) and PCOS-induced disorders are likely to be exacerbated in the presence of CO. This study aims to evaluate the impact of CO on infertile women with PCOS undergoing in vitro fertilization (IVF). It is a retrospective and case–control study. One hundred eighty-eight infertile PCOS women undergoing IVF were divided into CO group (n = 70, waist circumference [WC] ≥ 80 cm) and noncentral obesity (NCO) group (n = 118, WC < 80 cm). Baseline characteristics, parameters of ovarian stimulation and laboratory, and pregnancy outcomes were compared between two groups. After controlling for body mass index (BMI), WC positively correlated with fasting insulin (r = 0.210, p = 0.007), homeostatic model assessment for insulin resistance (r = 0.249, p = 0.006) and free androgen index (r = 0.249, p = 0.006). Compared with NCO group, CO group had significantly increased endocrine and metabolic disorders and needed significantly higher dose of gonadotropins, longer duration of ovarian stimulation (p < 0.05), but had significantly lower peak serum estradiol level (p < 0.01) and less oocytes retrieved (p = 0.032). CO group had significantly lower live birth and implantation rates (53.8% vs. 86.8%, p = 0.001; and 24.3% vs. 36.3%, p = 0.019, respectively) and higher early spontaneous miscarriage rate (38.5% vs. 7.5%, p = 0.002). For the multivariate analysis, by adjusting for age, BMI, insulin resistance, and hyperandrogenism (HA), CO was significantly independent risk factor for early miscarriage (adjusted relative ratio = 16.87, 95% confidence interval = 2.15–132.70, p = 0.007). CO is associated with insulin resistance, hyperinsulinemia, and HA independent of BMI and is associated with poor pregnancy outcome in infertile women with PCOS undergoing IVF.

Keywords: central obesity; in vitro fertilization; polycystic ovary syndrome; pregnancy outcome

Introduction
Polycystic ovary syndrome (PCOS) is the most common and complicated endocrine disorder in women of reproductive age, with multiple endocrine and metabolic disorders. Subfertile women with PCOS will usually benefit from conventional treatments, such as lifestyle changes, laparoscopic ovarian drilling, or ovulation induction. However, when undergoing in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI), PCOS women may suffer from high rates of cycle cancellations, spontaneous miscarriage, and decreased rate of fertilization.2–4 PCOS women represent a cohort of people with a higher prevalence of overweight and obesity compared...
with healthy women, although there is a wide variability in the estimates of obesity in PCOS women across different countries and ethnicities. The prevalence ranges from 66% to 80% in PCOS women from the Western populations and about 23% in Chinese PCOS women.

It is found that overweight and obesity are closely related to the severity of endocrine disorders, such as insulin resistance, impaired glucose tolerance, and other metabolic abnormalities in PCOS women. Furthermore, it is also important to emphasize that visceral, rather than subcutaneous, fat, also named central obesity (CO), is a defining characteristic of PCOS. CO can induce local and systemic oxidative stress in PCOS patients, which suggest that PCOS-induced disorders are likely to be exacerbated in the presence of CO.

The present study aims to evaluate whether CO is associated with ovarian stimulation and pregnancy outcome in Chinese infertile PCOS women undergoing IVF/ICSI.

Materials and Methods

Study population

This was a retrospective study. From January 2009 to December 2010, PCOS women who accepted their first fresh IVF/ICSI cycles at the IVF center of Sun Yat-sen Memorial Hospital, Sun Yat-sen University were included. This study was approved by the local Medical Ethics Committee.

The PCOS patients were diagnosed according to the 2003 Rotterdam diagnostic criteria. Patients were excluded if they had uterine malformation, untreated intrauterine lesions, and previous ovarian surgery. Women with waist circumference (WC) more than 80 cm were defined as CO based on the 2005 International Diabetes Foundation consensus (http://idf.org/home). Patients were divided into CO group and noncentral obesity (NCO) group.

The phenotypes in PCOS women were divided according to previous studies. Following these studies, PCOS features were defined hyperandrogenism (HA), oligoanovulatory ovarian dysfunction (OAD), and polycystic ovarian morphology (PCOM). Then four different PCOS phenotypes were identified: phenotype A or complete phenotype (HA, OAD, and PCOM), phenotype B or non-PCOM phenotype (HA and OAD without PCOM), phenotype C or ovulatory PCOS phenotype (HA and PCOM with ovulatory cycles), phenotype D or normoandrogenic PCOS (OAD and PCOM without HA).

Clinical and biochemical measurements

Data on characteristic features, ultrasonographic, and laboratory variables were collected. The height, weight, WC, and hip circumference of a patient were measured according to World Health Organization recommendation. Transvaginal ultrasonography was performed on day 3–5 of menstrual cycle or after a progestin-induced withdrawal bleeding to exclude any pelvic pathology and to determine the antral follicle count (AFC).

Serum hormone levels (follicle-stimulating hormone [FSH], luteinizing hormone [LH], estradiol [E₂], total testosterone [TT], androstenedione, free testosterone [FT], dehydroepiandrosterone sulfate [DHEA-S], estrone, sex hormone-binding globulin [SHBG], and 17α-hydroxyprogesterone) on day 3–5 of menstrual cycle or after a progestin-induced withdrawal bleeding and other serum biochemical evaluations (cholesterol, triglycerides [TG], high-density lipoprotein-cholesterol [HDL-C], low-density lipoprotein [LDL-C] levels, plasma glucose, and insulin) were measured.

Impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and type 2 diabetes mellitus (DM2) were diagnosed according to American Diabetes Association 2007 Standards. The homeostatic model assessment for insulin resistance (HOMA-IR) and free androgen index (FAI) were calculated as following: (fasting plasma insulin [mIU/L] × fasting plasma glucose [mmol/l])/22.5, and (100 × TT [nmol/L])/SHBG [nmol/L], respectively. Insulin resistance was defined as HOMA-IR > 2.14 according to our previous study.

IVF/ICSI and embryo transfer procedures

All PCOS patients were pretreated according to the consensus on PCOS patients’ treatment. When patients were defined as insulin resistant, IFG, or IGT, metformin was administrated for 1–3 month. Standard controlled ovarian stimulation protocol was performed as follows. All patients were treated with oral contraceptive pills (Yasmin, Scherring, Germany) from cycle days 3 or days 3 after a progestin-induced withdrawal bleeding.

Then long-acting triptorelin acetate (Diphereline, Ipsen, France) was given at the 17th–19th day with a single dose of 1.25 mg subcutaneously. Fourteen days after triptorelin acetate was given, when the endometrium with the thickness of ≤5 mm and suppressed ovaries (no antral follicles ≥10 mm) were detected by ultrasound scan and serum estradiol levels ≤50 pg/mL and LH levels ≤5 IU/L were confirmed, ovarian stimulation was started. Around
112.5–225 IU/day recombinant FSH (Gonal-F; Merck Serono, Germany) was administered according to the patient’s age, AFC, and basal FSH level. If necessary, the dosage of recombinant FSH was adjusted or 75–150 IU/day recombinant LH (Luveris; Merck Serono, Germany) was added according to ovarian response.

Urinary human chorionic gonadotropin (hCG; Lizhu, China) was given for triggering when at least two follicles had reached a diameter of ≥18 mm or three follicles had reached a diameter of ≥17 mm. Around 4000–10,000 IU of hCG was administrated depending on follicular numbers, peak E_{2} level, and body mass index (BMI). Transvaginal oocyte retrieval was scheduled 36–37 h after the hCG injection.

Then, standard laboratory procedures for conventional IVF/ICSI were followed. Evaluation of the quality of embryos was performed on day 3 according to “embryo grading.” Embryos of modified Hu’s grades 1 or 2 were considered of high quality (7–9 cell; blastomeres of equal size; 0–20% cytoplasmic fragments). When available, two embryos were transferred in young women (<35 years) and three embryos were transferred in older women (≥35 years). Embryo transfers (ET) were performed under ultrasound guidance with a full bladder using a Wallace catheter (Wallace Ltd, Colchester, England). Luteal phase support was sustained with natural progesterone in oil 60 mg intramuscular injection daily from the day of oocyte retrieval.

Pregnancy outcomes
Biochemical pregnancy was defined as elevated serum β-hCG (≥25 IU/L) 14 days after ET. Clinical pregnancy was defined as the presence of gestational sac(s) by ultrasonography 4–5 weeks after ET.

Statistical analysis
Statistical analysis of the data was performed using SPSS version 21.0 (SPSS, Inc., Chicago, IL). Continuous variables were compared using Student’s t-test or analysis of variance for parametric data and Mann–Whitney test or Kruskal–Wallis test for nonparametric data. Categorical data were compared using Chi-squared test. Pearson partial correlation was used for correlation analysis between two continuous variables after adjusting some confounding factor.

We estimated the crude relative ratio (RR) and 95% confidence interval (CI) for the relation between early miscarriage and other confounders, such as age, BMI, CO, fasting glucose insulin, and FAI. For the multivar-iate analysis, we adjusted these confounders. The RR was calculated using a median unbiased estimator for binary data in an unconditional logistic regression model. All tests were considered statistically significant at p < 0.05.

### Table 1. Baseline Characteristics in Polycystic Ovary Syndrome Women With or Without Central Obesity

| Central obesity (n = 70) | Noncentral obesity (n = 118) |
|-------------------------|-----------------------------|
| No. of cycles           | 70                          | 118                         |
| Age (years)             | 30.2 ± 3.5                  | 29.5 ± 3.5                  |
| Duration of infertility (years) | 5.38 ± 3.28 | 4.76 ± 3.15 |
| Primary infertility (n, %) | 42 (60.0)         | 72 (61.0)                  |
| Cause of infertility (n) |                             |                             |
| PCOS                    | 20                          | 28                          |
| PCOS and tubal factor   | 38                          | 64                          |
| PCOS and male factor    | 10                          | 20                          |
| PCOS and endometriosis  | 2                           | 6                           |
| Times of cycle          | 1.21 ± 0.41                 | 1.16 ± 0.37                 |
| PCOS phenotypes         |                             |                             |
| HA, OAD, and PCOM       | 39 (55.7)                   | 53 (44.9)                   |
| HA and OAD without PCOM | 13 (18.6)                   | 17 (14.4)                   |
| HA and PCOM with ovulatory cycles | 4 (5.7) | 16 (13.6) |
| OAD and PCOM without HA | 14 (20.0)                   | 32 (27.1)                   |
| BMI (kg/m²)             | 24.9 ± 2.2*                 | 20.4 ± 2.4*                 |
| Waist circumference (cm) | 86.1 ± 6.2*                | 71.0 ± 4.4*                 |
| Hip circumference (cm)  | 97.5 ± 6.4*                 | 89.3 ± 4.2*                 |
| Waist–hip ratio         | 0.88 ± 0.06*                | 0.80 ± 0.05*                |
| Basal FSH (IU/L)        | 7.21 ± 2.82                 | 7.32 ± 2.30                 |
| Basal LH (IU/L)         | 7.90 ± 5.13                 | 8.09 ± 5.32                 |
| Basal TT (nmol/L)       | 2.03 ± 0.72                 | 2.14 ± 0.87                 |
| FT (pg/mL)              | 3.92 ± 2.37                 | 3.11 ± 2.35                 |
| FAI                     | 5.73 ± 4.73*                | 3.17 ± 2.47*                |
| DHEA-S (ng/mL)          | 2221.4 ± 983.5              | 2200.4 ± 1077.1             |
| SHBG (nmol/L)           | 57.8 ± 44.8*                | 103.4 ± 85.1*               |
| Serum fasting glucose (mmol/L) | 65.35 ± 0.78** | 50.8 ± 0.44**          |
| Serum fasting insulin (mU/L) | 11.63 ± 7.17*            | 6.34 ± 3.63*                |
| HOMA-IR                 | 2.87 ± 2.44*                | 1.44 ± 0.84*                |
| Insulin resistance (n, %) | 45 (64.3)**                 | 20 (16.9)                   |
| 2-h glucose (mmol/L)    | 8.38 ± 3.03*                | 6.54 ± 2.14*                |
| 2-h insulin (mU/mL)     | 111.98 ± 68.36*             | 64.26 ± 47.65*              |
| IFG (n, %)              | 17 (24.3)**                 | 14 (11.9)**                 |
| IGT (n, %)              | 17 (24.3)**                 | 13 (11.0)**                 |
| Type II DM (n, %)       | 8 (11.4)                    | 4 (0.3)                     |
| CHOL (mmol/L)           | 5.11 ± 0.55                 | 4.83 ± 0.90                 |
| TG (mmol/L)             | 2.70 ± 2.30*                | 1.25 ± 0.65*                |
| HDL-C (mmol/L)          | 1.37 ± 1.35**               | 1.52 ± 0.27**               |
| LDL-C (mmol/L)          | 3.10 ± 0.68                 | 2.80 ± 0.85                 |
| Volume of left ovary (mL) | 7.68 ± 5.92                | 7.23 ± 3.17                 |
| Volume of right ovary (mL) | 7.46 ± 6.13                | 7.82 ± 4.34                 |
| AFC                     | 25.8 ± 9.1                  | 25.8 ± 8.5                  |

Values are expressed as mean ± SD or numbers (percentages).
*Significant differences between two groups, p < 0.01.
**Significant differences between two groups, p < 0.05.

PCOS, polycystic ovary syndrome; PCOM, polycystic ovarian morphology; HA, hyperandrogenism; OAD, oligoanovulatory ovarian dysfunction; BMI, body mass index; FSH, follicle-stimulating hormone; LH, luteinizing hormone; TT, total testosterone; FT, free testosterone; FAI, free androgen index; DHEA-S, dehydroepiandrosterone sulfate; SHBG, sex hormone-binding globulin; HOMA-IR, homeostatic model assessment for insulin resistance; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; DM, diabetes mellitus; CHOL, cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; AFC, antral follicle count; SD, standard deviation.
Results

Baseline characteristics
A total of 188 women with PCOS met the eligibility criteria. There were 70 and 118 women within the CO and NCO groups, respectively.

The baseline characteristics of the subjects are shown in Table 1. When comparing CO with NCO group, BMI, WC, hip circumference, waist–hip ratio, FAI, fasting glucose, fasting insulin (FIN), HOMA-IR, 2-h glucose and insulin in oral glucose tolerance test, serum TG, and the occurrence rates of IR, IFG, IGT were significantly higher, whereas serum SHBG and HDL-C was significantly lower (p < 0.05). There was no significant difference in age, duration of infertility, baseline serum hormones (FSH, LH, TT, FT, DHEA-S), Serum TC, LDL-C, bilateral volumes of ovaries, AFC, and rates of primary infertility and DM2 between the two groups (p > 0.05). In addition, the PCOS phenotypes were not significant between the two groups (p > 0.05).

After controlling for BMI, WC positively correlated with FIN (r = 0.210, p = 0.007), HOMA-IR (r = 0.249, p = 0.006), and FAI (r = 0.249, p = 0.006).

Parameters during IVF/ICSI
The detailed parameters during IVF/ICSI treatment are shown in Table 2. One cycle was cancelled in CO group, whereas three in NCO group due to poor ovarian response. Compared with NCO group, CO group needed significantly higher dose of gonadotropin, longer duration of ovarian stimulation, higher dose of hCG for trigger (p < 0.05), but had significantly lower peak serum estradiol level, less mature follicles on trigger day, and less oocytes retrieved (p < 0.05). There were no significant differences in endometrial thickness, cleavage rate, number of frozen embryos, percentage of embryos available, number of high-quality embryos, and rates of completed cycles, ICSI cycles, and fertilization rate between the two groups.

Pregnancy outcomes
CO group had significantly lower rates of implantation and live birth (24.3% vs. 36.3%, p = 0.019; and 53.8% vs. 86.8%, p = 0.001, respectively) and higher rate of early spontaneous miscarriage (38.5% vs. 7.5%, p = 0.002), compared with the NCO group (Table 3). Two groups showed similar rates of moderate ovarian hyper-stimulation syndrome (OHSS), biochemical, clinical, multiple and ectopic pregnancy, and number of transferred embryos.

Multivariate analysis for early miscarriage showed that when compared with NCO, the crude RR for CO was 7.50 (95% CI = 2.06–27.25, p = 0.002) and remained statistically significant (adjusted RR = 16.87, 95% CI = 2.15–132.70, p = 0.007) after adjusting for age, BMI, insulin resistance, and HA (Table 4). In addition, the RR for age

Table 2. Parameters During In Vitro Fertilization in Polycystic Ovary Syndrome Women With or Without Central Obesity

| Parameter                                      | Central obesity (n = 70) | Noncentral obesity (n = 118) |
|------------------------------------------------|-------------------------|------------------------------|
| Cycle cancellation for poor response (n, %)    | 1 (1.4)                 | 3 (2.5)                      |
| Total dose of gonadotropin (IU)                | 2014.8±825.8*           | 1491.2±558.9*                |
| Duration of gonadotropin stimulation (days)    | 12.5±4.0*               | 10.7±3.0*                    |
| Peak E2 (pg/mL)                                | 2320.4±1303.6*          | 3256.3±1456.0*               |
| Endometrial thickness (mm)                     | 11.7±3.0                | 11.5±2.8                     |
| Dose of hCG (IU)                               | 6869.6±1971.6**         | 6134.8±1652.1**              |
| No. of mature follicles                        | 9.6±4.6**               | 11.5±5.2**                   |
| No. of completed cycles (n, %)                 | 69 (98.6)               | 115 (97.5)                   |
| No. of ICSI cycles (n, %)                      | 12 (17.1)               | 23 (19.5)                    |
| No. of oocytes retrieved                       | 11.6±5.7**              | 13.8±7.3**                   |
| Fertilization rate (%)                         | 0.64±0.24               | 0.61±0.21                    |
| Cleavage rate (%)                              | 0.96±0.16               | 0.97±0.14                    |
| No. of frozen embryos                          | 4.72±4.50               | 5.98±5.35                    |
| Percentage of embryos available                | 0.74±0.23               | 0.73±0.22                    |
| No. of high quality embryos                    | 3.67±3.14               | 4.03±3.96                    |

Values are expressed as mean±SD or numbers (percentages).
*Significant differences between two groups, p < 0.01.
**Significant differences between two groups, p < 0.05.
E2, estradiol; hCG, human chorionic gonadotropin; ICSI, intracytoplasmic sperm injection.

Table 3. Pregnancy Outcomes in Polycystic Ovary Syndrome Women With or Without Central Obesity

| Outcome                                      | Central obesity (n = 70) | Noncentral obesity (n = 118) |
|----------------------------------------------|-------------------------|------------------------------|
| Moderate OHSS (n, %)                          | 4 (5.8)                 | 10 (8.7)                     |
| Embryo transfer cancellation                  | 5 (7.2)                 | 17 (13.8)                    |
| Embryo transfer cycles (n, %)                 | 64 (91.4)               | 96 (81.4)                    |
| No. of embryos transferred                   | 2.14±0.53               | 2.13±0.42                    |
| Biochemical pregnancy (n, %)                  | 28 (43.8)               | 56 (58.3)                    |
| Clinical pregnancy (%)                        | 26/64 (40.6)            | 53/96 (55.2)                 |
| Implantation (%)                              | 34/140 (24.3)*          | 74/204 (36.3)*               |
| Multiple pregnancies (%)                      | 8/26 (30.8)             | 22/53 (41.5)                 |
| Early miscarriage (%)                         | 10/26 (38.5)**          | 4/53 (7.5)**                 |
| Ectopic pregnancy (%)                         | 0/26 (0)                | 1/53 (1.9)                   |
| Live birth (%)                                | 14/26 (53.8)**          | 46/53 (86.8)**               |

Values are expressed as mean±SD or numbers (percentages).
*Significant differences between two groups, p < 0.05.
**Significant differences between two groups, p < 0.01.
Biochemical pregnancy rate: biochemical pregnancy cycles/embryo transfer cycles; clinical pregnancy rate: clinical pregnancy cycles/embryo transfer cycles; implantation rate: no. of implantation gestational sac/no. of total embryos transferred; multiple pregnancy rates: multiple pregnancy cycles/clinical pregnancy cycles; early miscarriage rate: early miscarriage cycles/clinical pregnancy cycles; ectopic pregnancy rate: ectopic pregnancy cycles/clinical pregnancy cycles; live birth rate: live birth cycles/clinical pregnancy cycles.
OHSS, ovarian hyper-stimulation syndrome.
Previous studies had shown the PCOS phenotypes played an important role in the variability of pregnancy complication\(^{16}\) and oocyte competence.\(^{17}\) Therefore, in this study, patients were subclassified according to the four phenotypes, and there were no significant differences between the two groups.

Obese PCOS patients needed more dose of gonadotropins, had less mature follicles on hCG day, and less oocytes retrieved after COS.\(^{29–31}\) Altered pharmacokinetics of gonadotropin and high intrafollicular leptin concentration may be related to gonadotropin resistance in obese PCOS women.\(^{30}\) Patients with gonadotropin resistance might have increased the rate of cycle cancellations due to poor ovary responses in common population. However, the condition of increased cycle cancellations did not appear in our CO group. It may be because more AFC was found in PCOS patients, which can recruit more follicles after adjusting the dose of gonadotropin during ovarian stimulation. CO patients accepted higher dose of gonadotropin, which may increase follicle recruitment and oocytes retrieved.

The present study indicated that PCOS women in CO group had decreased clinical pregnancy rate, significantly higher early spontaneous miscarriage rate, and lower live birth rate compared with the NCO group. Insulin resistance may be responsible for this condition.\(^{32,33}\) Moreover, in CO group, the number of high-quality embryos, and rate of biochemical pregnancy were lower than NCO group, although it was not significant. In multivariate analysis we could see that CO was a significantly independent risk factor for early miscarriage. It remained significant after adjusting for insulin resistance, which indicated that PCOS infertile women with CO in China were at a greater risk in early spontaneous miscarriage.

Possible mechanism of poor pregnancy outcome in PCOS women with CO is that metabolic disturbance such as insulin resistance result in abnormalities during folliculogenesis, follicular growth, oocyte meiotic maturation processes, and uterine receptivity, through circulating endocrine and local paracrine/autocrine mechanisms.\(^{34–36}\) With regard to incidence of moderate OHSS and freeze-all cycles due to the risk of OHSS, the NCO group showed higher rates. It can be explained that lean PCOS patients are a high-risk group of OHSS in itself.\(^{37}\)

The special strength of this study was that CO could be a better indicator to identify the comprehensive endocrine and metabolic disorders and poor pregnancy outcome

### Discussion

PCOS is the most common and complicated endocrine dysfunction in women of childbearing age. A majority of PCOS patients are obese or have a normal BMI, but are metabolically obese with WC more than 80 cm. Pregnancy achievement and maintenance is adversely affected by obesity, overweight, or elevated BMI. Huang et al. reported that obese PCOS patients obtained lower clinical pregnancy and live birth rates.\(^{25}\) However, WC may be a good indicator to identify insulin resistance and metabolic syndrome, especially among population of BMI ≤30 (kg/m²).\(^{26,27}\) WCs seem to help identify those at increased health risk within the normal weight, overweight, and class I obese BMI categories.\(^{26}\)

This study was to evaluate the effects of CO on the outcomes of IVF/ICSI in women with PCOS. Among these patients in this study, 98.9% women had BMI ≤30 kg/m²; CO was associated with endocrinal and metabolic disorders in women with PCOS and was significantly associated with insulin resistance, hyperinsulinemia, and HA independent of BMI. This suggested that WC could be a better marker than BMI for Chinese women, which is in accordance with a study conducted by Stepto et al.\(^{28}\) Therefore, WC could be a good and simple indicator for distinguishing patients with different metabolic status in PCOS women, to CO and NCO groups.

### Table 4. Crude and Adjusted Relative Ratios for Early Miscarriage

|                      | Crude RR (95% CI) | p    | Adjusted RR* (95% CI) | p    |
|----------------------|-------------------|------|-----------------------|------|
| **Age (years)**      |                   |      |                       |      |
| >35 vs. ≤35          | 25.20 (2.55–249.00) | 0.006 | 43.39 (2.15–692.53)   | 0.008 |
| **BMI (kg/m²)**      |                   |      |                       |      |
| <18.5 vs. ≥24        | 0.67 (0.06–7.23)   | 0.739 | 2.96 (0.05–174.47)    | 0.602 |
| 18.5–23.9 vs. >24    | 0.42 (0.12–1.45)   | 0.172 | 1.57 (0.22–11.32)     | 0.653 |
| **Central obesity**  |                   |      |                       |      |
| Yes vs. No           | 7.50 (2.06–27.25)  | 0.002 | 16.87 (2.15–132.70)   | 0.007 |
| **Insulin resistance**|                   |      |                       |      |
| Yes vs. No           | 1.95 (0.60–6.34)   | 0.267 | 1.02 (0.21–4.95)      | 0.983 |
| **Hyperandrogenism** |                   |      |                       |      |
| Yes vs. No           | 1.67 (0.42–6.64)   | 0.469 | 1.35 (0.24–7.59)      | 0.732 |

*Adjusted for age, BMI, central obesity, insulin resistance and hyperandrogenism.

RR, relative ratio; CI, confidence interval.
undergoing IVF treatment among Chinese women with PCOS, who have much higher proportion of normal weight, overweight, and class I obese BMI categories than western population.

The main limitation of this study is the relatively small sample size and retrospective nature. Further studies in larger populations are needed to come up with more supporting data. Furthermore, because of differences in ethnicity, effects of the CO on PCOS women could account for some conflicting results. However, to our knowledge, this study is the first to identify the association of CO and pregnancy outcome in PCOS women undergoing IVF/ICSI.

In summary, PCOS patients with CO have severe insulin resistance and metabolic disorders independent of BMI. When undergoing IVF, they need more dose of gonadotrophin and longer duration of ovarian stimulation, but have lower number of retrieved oocytes. PCOS patients with CO have higher early miscarriage rate, reduced implantation, and live birth rates after IVF/ICSI.

Details of Ethics Approval

This study was approved by the Ethics Committee of Sun Yat-sen Memorial Hospital, Sun Yat-sen University (No. 201408).

Author Disclosure Statement

No competing financial interests exist.

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Abbreviations Used
AFC = antral follicle count
BMI = body mass index
CHOL = cholesterol
CI = confidence interval
CO = central obesity

DHEA-S = dehydroepiandrosterone sulfate
DM = diabetes mellitus
DM2 = type 2 diabetes mellitus
E2 = estradiol
ET = embryo transfers
FAI = free androgen index
FIN = fasting insulin
FSH = follicle-stimulating hormone
FT = free testosterone
HA = hyperandrogenism
hCG = human chorionic gonadotropin
HDL-C = high-density lipoprotein-cholesterol
HOMA-IR = homeostatic model assessment for insulin resistance
IFG = impaired fasting glucose
IGT = impaired glucose tolerance
IVF = in vitro fertilization
LDL-C = low-density lipoprotein
LH = luteinizing hormone
NCO = noncentral obesity
OAD = oligoanovulatory ovarian dysfunction
PCOM = polycystic ovarian morphology
PCOS = polycystic ovarian syndrome
RR = relative ratio
SD = standard deviation
SHBG = sex hormone-binding globulin
TG = triglycerides
TT = total testosterone
WC = waist circumference

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