# A prospective pilot study of the effect of acupuncture on insulin sensitivity in women with polycystic ovary syndrome and insulin resistance

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## ABSTRACT

**Objective:** To test the hypothesis that acupuncture improves insulin sensitivity in women with polycystic ovary syndrome (PCOS) and insulin resistance (IR).

**Design:** Prospective pilot study.

**Setting:** Guangzhou, China, 2014 to 2016.

**Participants:** Eighty women with PCOS aged 18 to 40 years with body mass index (BMI) above 18.5 $kg/m^2$ and with homeostatic model assessment for insulin resistance (HOMA-IR) index $\geqslant$2.14.

**Interventions:** Subjects received acupuncture with combined manual and low-frequency electrical stimulation of the needles three times per week for 6 months.

**Primary and secondary outcome measures:** The primary outcome was change in HOMA-IR after 6 months of acupuncture relative to baseline. Secondary outcomes included changes after 6 months of acupuncture and 3 months of follow-up (both relative to baseline) in oral glucose tolerance test (OGTT) parameters, glucose and insulin levels, anthropometric measurements and circulating metabolic and endocrine variables.

**Results:** HOMA-IR and fasting plasma glucose and insulin levels were significantly decreased after 6 months of acupuncture, and both HOMA-IR and fasting insulin remained significantly decreased at 3 months of follow-up. In a subgroup analysis of normal weight and overweight/obese women, HOMA-IR was reduced after 6 months of acupuncture in both subgroups, but there was no significant difference between the two groups.

**Conclusions:** Acupuncture treatment in Chinese women with PCOS and IR was associated with an encouraging improvement in insulin sensitivity. Further randomized controlled studies are required to confirm the efficacy of acupuncture for this indication.

**Trial registration:** ClinicalTrials.gov (NCT02026323) and Chinese Clinical Trial Registry (ChiCTR-OCH-13003921).

**Key words:** polycystic ovary syndrome, insulin resistance, acupuncture, insulin sensitivity

# INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine problems among women of reproductive age and is characterized by oligo-ovulation or anovulation, hyperandrogenism, hyperinsulinemia and/or polycystic ovarian morphology [1]. A survey showed that obesity, metabolic disorders and type 2 diabetes mellitus (DM) were considered to be the most important long-term concerns related to PCOS [2]. Moreover, longitudinal studies have indicated that worsening of insulin resistance (IR) over time in obese women with PCOS is associated with an increased risk of the early development of type 2 DM [3]. The prevalence of IR in PCOS can range from 44% to 70% [4, 5]. Normal-weight women with PCOS are also at increased risk of IR [6]. A recent meta-analysis showed that an intrinsic reduction of insulin sensitivity of 27% in women with PCOS is independent of body mass index (BMI) and that BMI has a greater impact on IR in PCOS patients than in controls [7].

The primary treatment of obese women with PCOS is lifestyle management, including weight reduction by diet and exercise, but patients do not always adhere to treatment [8]. Given the long-term implications of IR, treatment of women with PCOS using insulin-sensitizing agents such as biguanides and thiazolidinediones has been proposed [9], but the use of thiazolidinediones increases the risk of cardiovascular disease, bladder cancer and bone fractures, and is thus not recommended [10-12]. Metformin, a biguanide, is effective in the management of IR, but common gastrointestinal side effects such as diarrhea and nausea result in poor compliance [13]. Considering that pharmacological

treatments have significant side effects, there is a need to evaluate alternative therapies for women with PCOS and IR.

Acupuncture, as part of the system of traditional Chinese medicine, is gaining increasing popularity worldwide and has been shown to be safe in populations with different clinical conditions [14]. It can improve various metabolic disorders associated with IR, including hyperandrogenism, hyperglycemia, overweight and hyperlipidemia [15, 16]. It also has the potential to improve insulin sensitivity in rat models of IR [17-20]. Five weeks of acupuncture has been shown to decrease glycated hemoglobin (HbA1c) levels and to decrease circulating and adipose tissue concentrations of androgens in women with PCOS [21]; however, this was a feasibility study with a limited duration of treatment and no follow-up, and thus further studies are warranted [22]. The effect of acupuncture administered over a longer period of time in both normal weight and overweight/obese women with PCOS and IR, as well as any side effects, needs to be investigated. Therefore, we performed this prospective observational study to investigate the effects of a 6-month course of acupuncture on insulin sensitivity in Chinese women with PCOS and IR who were followed up for 3 months after the acupuncture treatment was completed.

# METHODS

## Study design

This prospective observational study was conducted at the First Affiliated Hospital of Guangzhou Medical University, China. Approval was granted from the hospital ethics committee (ref. 2013039). The study was registered at ClinicalTrials.gov (NCT02026323) and with the Chinese Clinical Trials Registry (ChiCTR-OCH-12003921) on 10 November 2013. Written informed consent was obtained from each woman before any study procedure was performed. The first woman was recruited on 18 February 2014 and the last follow-up was on 10 February 2016.

## Study participants

Chinese women with PCOS aged 18 to 40 years with a BMI above 18.5 kg/m$^2$ and with homeostatic model assessment for insulin resistance (HOMA-IR) index, calculated as $HOMA-IR = \frac{\text{fasting glucose (mmol/L)} \times \text{fasting insulin (mU/L)}}{22.5}$) value ≥ 2.14 [23] were recruited between February 2014 and May 2015 from the outpatient clinic. PCOS was diagnosed according to the Rotterdam criteria by the presence of two out of the following three criteria: oligo-anovulation (intermenstrual interval >35 days or <8 menstrual bleeds in the past year), hyperandrogenism (total serum testosterone concentration above 60 ng/dL [24] or modified Ferriman–Gallwey score ≥ 5 [25]), or polycystic ovaries (≥12 antral follicles measuring 2–9 mm in diameter or an ovarian volume >10 mL in either ovary on ultrasound [26]). They should not have had an immediate desire for pregnancy, and they had to agree to use barrier methods of contraception for one year.

Women were excluded if they had other endocrine disorders such as hyperprolactinemia, non-classic

congenital adrenal hyperplasia or androgen-secreting tumors. Furthermore, those with serum follicle-stimulating hormone (FSH) levels >15 mIU/mL, uncorrected thyroid disease, type 1 or type 2 DM, or suspected Cushing's syndrome were not recruited. Other exclusion criteria included receipt of acupuncture treatment within the past two months, the use of hormones or other medications – including Chinese herbal prescriptions – within the past three months, pregnancy (including miscarriages and induced abortions), delivery within the past six weeks, breastfeeding within the past six months, and bariatric surgery within the past 12 months [27].

Eligible women were categorized according to their BMI as normal weight (BMI 18.5–23 $kg/m^2$) or overweight/obese (BMI ≥23 $kg/m^2$) [28].

**Study procedures**

This study consisted of two phases. The first phase was acupuncture treatment for six months with three treatment sessions per week, and the second phase was a follow-up period of three months. The visit and measurement protocol has been described in detail previously [27].

**Intervention**

After screening and baseline measurements [27], acupuncture was started and lasted for 6 months. Acupuncture was given three times per week for a maximum of 72 sessions in total. The first treatment lasted 45 minutes and subsequent sessions lasted 30 minutes each. Disposable, sterilized, single-use stainless steel needles (0.20 mm × 30 mm and 0.20 mm × 40/50 mm; Hwoto, Suzhou Medical Appliance Factory, Suzhou, China) were inserted to a depth of 15–35 mm at segmental

acupuncture point locations in the abdominal and leg muscles. All needles were stimulated manually when inserted. Two sets of traditional acupuncture points [27], reported following the STRICTA recommendations, were used alternately for every other treatment session (supplemental table S1) [27], and the needles were stimulated manually or by an electrical stimulator (Export Abteilung, Schwa-Medico GmbH, Germany) at a frequency of 2 Hz for 30 min during each treatment session. The first set consisted of 14 needles at points located in the abdominal muscles (ST29 bilaterally, CV3 connected to CV12 (electrical stimulation)) and leg points (ST34 connected to ST33 bilaterally (electrical stimulation), and SP6 and ST36 bilaterally (manual stimulation)). Extra-segmental points were LI4 bilaterally, and these were stimulated manually four times during each 30-min treatment session. The second set consisted of 14 needles placed at abdominal points (ST27 bilaterally, CV6 connected to CV10, stimulated electrically) and leg points (SP10 connected to a needle inserted at a site not corresponding to any traditional acupuncture point located 6 *cun* proximal to the medial border of the patella (electrical stimulation), and SP6 and LR3 bilaterally (manual stimulation)). Extra-segmental points were PC6 bilaterally (manual stimulation). An electromagnetic spectrum therapy apparatus (TDP) was used on each of the subjects during the acupuncture treatment. The subjects received progestin if they did not menstruate for two months.

**Parameters measured**

The height, weight, waist circumference, hip circumference and hirsutism scores of all women were recorded, and blood samples were collected during the first 2–5 days of their menstrual cycle at 08:00-10:00 after fasting for 12 hours. The serum samples were batched and analyzed in the laboratory at the First Affiliated Hospital of Guangzhou Medical University for FSH, luteinizing hormone (LH),

estradiol (E2), total serum testosterone, prolactin, triglycerides, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), fasting plasma glucose (FPG) and fasting insulin. The intra-assay and inter-assay coefficients of variation were both less than 5%. FSH, LH, and total serum testosterone levels were measured on a Beckman-Coulter Unicel DXi800 automatic chemiluminescence analyzer (Beckman Coulter, Brea, USA). Triglycerides, total cholesterol, LDL, and HDL levels were measured with a Beckman-Coulter AU5800 automatic biochemical analyzer. Fasting insulin was measured on a Modular E170 automatic electrochemiluminescent analyzer (Roche Diagnostics, Mannheim, Germany) and fasting plasma glucose was analyzed using a Beckman Coulter LX20 automatic biochemical analyzer. All assays were performed by following the instructions of and with reagents and materials provided by the manufacturers.

**Insulin sensitivity**

An oral glucose tolerance test (OGTT) with 75 g glucose load was performed after an overnight fast before the start of acupuncture, after 6 months of acupuncture and again at 3 months of follow-up. Plasma glucose and serum insulin levels were measured at 0, 60 and 120 min [27]. HOMA-IR was calculated as described above; HOMA for beta cell function (HOMA-β) was calculated as $HOMA-\beta = \frac{20 \times \text{fasting insulin (mU/L)}}{\text{fasting plasma glucose (mmol/L)} - 3.5}$ [29]; the C-peptide index (CPI) was calculated as $CPI = \frac{\text{fasting C-peptide } \left(\frac{\text{nmol}}{\text{L}}\right) \times 100}{\text{fasting plasma glucose (mmol/L)}}$ [30]; and the free androgen index (FAI) was calculated as $FAI = \frac{\text{total testosterone (nmol/ L) x 100}}{\text{sex hormone binding globulin (nmol/ L)}}$ [31]. The area under the curve during the OGTT for glucose ($AUC_{glu}$) and insulin ($AUC_{ins}$) was calculated using the trapezoidal rule [32].

## Outcomes

The primary outcome was change in HOMA-IR after 6 months of acupuncture treatment.

Secondary outcomes included changes after 6 months of acupuncture and after 3 months of follow-up in the OGTT, glucose and insulin levels, anthropometric measurements and circulating metabolic and endocrine variables, as well as adverse events including local skin irritation, discomfort and vasovagal reactions during the acupuncture procedure.

### *Sample size calculation*

Our previous study on the treatment of obese women with PCOS using abdominal acupuncture showed that HOMA-IR was significantly reduced after treatment (2.5±1.7) compared with baseline measurements (3.9±1.4) [33]. HOMA-IR ≥2.14 was considered to be abnormal [23]. In the current study, we assumed that a moderate reduction in HOMA-IR of 20% would be clinically meaningful and that a minimum of 40 subjects would be required in both the normal weight and overweight/obese subgroups to achieve a power of 80% at a type I error rate of 5%. With an estimated 40% dropout rate, we planned to recruit 56 normal weight and 56 overweight/obese women with PCOS [27].

### *Data analysis*

The one-sample Kolmogorov–Smirnov test was used to test the normality of distribution of continuous variables. Continuous variables were reported as the mean ± standard deviation (SD) if normally distributed and as the median (interquartile range (IQR)) if not. Changes after 6 months of treatment and after follow-up at 3 months after the last treatment relative to baseline in all women and in women with BMI <23 kg/m$^2$ and ≥23 kg/m$^2$, respectively, were assessed by Friedman's test or Wilcoxon

signed rank test for continuous variables and by chi-square test for categorical variables where appropriate. Comparisons of the changes between normal weight and overweight obese women were assessed by Student's t-test or Mann–Whitney U-test for normally distributed data and skewed data, respectively. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 24.0 (SPSS Inc., Chicago, IL, USA), and a $p$ value $<0.05$ was considered statistically significant [27].

# RESULTS

### Baseline characteristics and treatment compliance

A total of 101 Chinese women were enrolled, underwent all baseline measurements and started the acupuncture treatment (figure 1). Twenty-one women did not complete the study because of living far away (n=4), heavy workload (n=5), becoming pregnant during the treatment or during the follow-up period (n=9), and moving away from the study area (n=3). Eighty-three women received 6 months of acupuncture, and 80 women completed 3 months of follow-up. The mean number of acupuncture treatments was 64.2 (SD 18.6). Data from the 80 women who completed 6 months of acupuncture and 3 months of follow-up were used for the analysis. The women had a mean age of 27.0 (SD 5.0) years with a mean baseline BMI of 23.9 (SD 6.5) kg/m$^2$. Forty-six (57.5%) of the 80 women had a baseline BMI $\geqslant$23 kg/m$^2$ and 34 (42.5%) had a baseline BMI <23 kg/m$^2$. Forty-four women (55%) fulfilled all three diagnostic criteria for PCOS, 34 (42.5%) presented with oligomenorrhea and polycystic ovarian morphology, two (2.5%) presented with oligomenorrhea and hyperandrogenism, and none (0%) presented with hyperandrogenism and polycystic ovarian morphology. The median HOMA-IR index was 3.02 (IQR 2.58, 4.14). Five women had received acupuncture more than 2 months before inclusion (two for irregular menstrual cycles and three for non-gynecological problems).

### Glucose metabolism and insulin resistance parameters

The changes in the indices of glucose and insulin homeostasis are detailed in table 1. Acupuncture for 6 months decreased HOMA-IR ($p$=0.002), FPG ($p$=0.009), fasting insulin ($p$=0.012), $AUC_{glu}$ ($p$=0.012), C-peptide ($p$<0.001), CPI ($p$=0.017) and HbA1c ($p$<0.001) compared with baseline. At 3 months of follow-up, HOMA-IR, fasting insulin, C-peptide, CPI and HbA1c remained significantly

decreased (all $p<0.001$).

**Endocrine profile**

The LH/FSH ratio was increased after 6 months of acupuncture treatment ($p<0.001$) with no change in serum testosterone level ($p=0.707$) and no significant change in the FAI ($p=0.064$) (table 1). These variables were not measured at follow-up.

**Lipid profile**

LDL decreased after 6 months of acupuncture ($p=0.004$), while total cholesterol, triglycerides and HDL did not change with acupuncture (all $p>0.05$) (table 1).

**Anthropometric measurements**

After 6 months of acupuncture, BMI and waist-to-hip ratio (WHR) decreased (both $p<0.001$) and both remained lower at 3 months of follow-up (both $p<0.001$) (table 1).

**Subgroup analysis in normal weight and overweight/obese women**

HOMA-IR decreased in both normal weight and overweight/obese subgroups after 6 months of acupuncture ($p=0.009$ and 0.048, respectively) and remained lower at the 3-month follow-up ($p<0.001$ and 0.007, respectively) (table 2). FPG was only reduced after 6 months of acupuncture in the overweight/obese subgroup ($p=0.025$). Fasting insulin was reduced after 6 months of acupuncture and at 3-month follow-up in the normal weight subgroup ($p=0.027$ and $p=0.004$, respectively). In the overweight/obese subgroup, a significant decrease in fasting insulin level was observed only at

3-month follow-up ($p$=0.005) (table 2). For HOMA-IR, FPG and fasting insulin, there were no significant changes after 6 months of acupuncture or at 3-month follow-up between the two subgroups (all $p$>0.05). There were also no significant changes after 6 months of acupuncture or at 3-month follow-up in $AUC_{ins}$, HbA1c, total cholesterol, HDL, C-peptide, CPI, LH/FSH or testosterone levels, BMI or WHR between the two groups (all $p$>0.05) (supplemental table S2).

**Side effects**

A few side effects were reported (n=40, representing 0.62% of the total number of acupuncture treatments), the most common of which were bruises (n=18, 45%) and muscular pain (n=3, 7.5%) related to the acupuncture. Urticaria (n=1, 2.5%), constipation (n=1, 2.5%), upper respiratory tract infection (n=13, 32.5%), gastrointestinal discomfort (n=2, 5.0%), vulvitis (n=1, 2.5%), and insomnia (n=1, 2.5%) were also reported.

# DISCUSSION

This prospective observational study found that 6 months of acupuncture was associated with an improvement in insulin sensitivity in women with PCOS and IR in both normal weight and overweight/obese women and that the effects appeared to last for at least 3 months after the last acupuncture treatment.

Acupuncture reduces FPG by promoting insulin production and improves insulin sensitivity in different rodent models [17-20], but only a few clinical studies have been performed. One recent clinical study found improved glucose homeostasis in overweight and obese women with PCOS after five weeks of acupuncture treatment as demonstrated by decreases in HbA1c, HOMA-IR and C-peptide, although the latter two were not statistically significantly [21]. The results of that trial were similar to what was observed when abdominal acupuncture treatment was given for 6 months to obese women with PCOS [33]. Another study assessed the impact of laser acupuncture on women with PCOS and showed that HOMA-IR was significantly decreased after 12 weeks of intervention with laser acupuncture when compared with the control group [34]. The strengths of the present study are the larger sample size and the longer follow-up time, although the lack of a contemporaneous control group (receiving sham or no treatment) means that a causal relationship between acupuncture and the observed outcomes cannot be proven.

The mechanism of action of acupuncture in the treatment of IR is still not known, but it is recognized that acupuncture activates sensory afferent fibers and modulates the autonomic nervous system to improve insulin sensitivity [19]. Stimulation of somatic tissues at the site of traditional acupuncture

points located in the abdominal and leg muscles corresponding to the innervation of the ovaries improves reproductive function by suppressing inflammation, attenuating sympathetic nerve activity and enhancing insulin signaling [22]. Insulin sensitivity and the aberrant adipose tissue gene expression associated with IR, obesity and inflammation can be improved and restored by acupuncture without any influence on adipose tissue mass and cellularity, which is in contrast to the effects of exercise [35]. Furthermore, electrical stimulation improves insulin sensitivity and modulates skeletal muscle gene and protein expression more than manual stimulation because of the activation of sensory afferents rather than because of muscle contraction [19]. The effect of acupuncture on glucose homeostasis is most likely mediated via modulation of the autonomic nervous system as recently suggested [20].

In the present study, we used a combination of manual and electroacupuncture (EA) based on previous studies and clinical trials treating women with PCOS [20, 21]. Both manual and electrical stimulation improved whole-body glucose uptake during a euglycemic hyperinsulinemic clamp test, although the mechanisms seem to be slightly different [19, 36]. Manual stimulation mainly works via activation of sensory nerve afferents, whereas EA also causes muscle contraction and therefore evokes non-insulin-stimulated glucose uptake via glucose transporter (GLUT)4 translocation [19, 36]. The latter effect can be completely abolished by administration of an adrenergic receptor blocker indicating that the effect of EA is mediated via regulation of the sympathetic nervous system [20].

In the present study, BMI, WHR, and LDL all decreased significantly after 6 months of acupuncture treatment. It is well established that a high WHR indicates abdominal and visceral fat accumulation.

Moreover, enlarged adipocytes and reduced serum adiponectin, together with a large waistline, have been shown to be key factors in the pathogenesis of IR in PCOS [37]. In addition, WHR is now considered to be a predictor for the risk of DM [38]. Thus, the observed reduction in WHR and BMI in the present study might further enhance the response to acupuncture [15]. In contrast, two previous studies did not demonstrate any significant improvement in BMI or lipid profile from acupuncture [15, 21], and the reason for this discrepancy might be the shorter treatment duration and smaller number of acupuncture sessions used in those studies.

The effects of acupuncture on IR in normal weight and overweight/obese women with PCOS seen in our study are similar to the effects of metformin and rosiglitazone in the study by Yilmaz et al. [39]. The subgroup analysis performed in this work showed no significant changes after 6 months of acupuncture or at 3-month follow-up between the two subgroups, which confirmed that IR with compensatory hyperinsulinemia is the major metabolic abnormality in PCOS regardless of BMI [40] and that acupuncture can improve insulin sensitivity in women with PCOS independently of the presence of obesity. PCOS represents a state of hyperinsulinemia and IR, which is primarily manifested through an increase in BMI [41], and both fasting and glucose-stimulated insulin are significantly decreased after bodyweight reduction of about 5%–10% [42]. In the present study, acupuncture in both overweight and normal weight women with PCOS appeared to enhance insulin sensitivity. In addition to acupuncture improving whole-body glucose uptake [20], the impact of acupuncture might also be through mechanisms related to weight reduction. Furthermore, hyperinsulinemia contributes to the unusual secretion of gonadotropin-releasing hormone (GnRH) [43], and animal studies have shown that acupuncture can standardize GnRH secretion and influence

peripheral GnRH levels [44].

We found a significant difference in HOMA-IR index following acupuncture, although the difference was less than 20%, which was the minimum anticipated difference for sample size calculation. Further studies should compare the efficacy of acupuncture and insulin-sensitizing agents for the treatment of IR with increased sample sizes.

In this study, only a few women reported bruising due to subcutaneous hemorrhage or local muscular soreness after acupuncture. Other adverse events, such as urticaria, constipation, upper respiratory tract infection, gastrointestinal discomfort, and vulvitis, were deemed unlikely to be related to acupuncture. Relevant studies [15, 45] also reported few cases of adverse events, including back spasm (which was subsequently determined to be unrelated to the treatment), hematomas, isolated redness, nausea, dizziness, and mild bleeding at the site of needle insertion, but no long-term adverse events occurred due to acupuncture. A few side effects of acupuncture were also reported by Stener-Victorin et al. [21], the most common being bruises and temporary pain.

In contrast to previous studies, we did not detect any changes in serum testosterone levels. The FAI showed a downwards trend, but it did not reach statistical significance. We found that the LH/FSH ratio was increased after 6 months of acupuncture treatment, and the reason for this might be the fact that post-treatment levels of LH and FSH were not analyzed in a standardized way relative to menstruation, therefore some women might have been tested before or during ovulation-induced increases in the LH/FSH ratio. By contrast, baseline LH and FSH levels were measured within the first 2–5 days of menses.

Women were instructed to use barrier methods of contraception during the study. However, nine women became pregnant during the study and had to be excluded from analysis.

The main limitation of this study is the fact that it is a prospective pilot study that lacked a control group for comparison. In addition, women received progestin if they did not have periods for 2 months, including 17 before recruitment and 23 during the 6 months of acupuncture, and thus the effect of acupuncture on menstrual pattern and ovulation frequency in these PCOS patients could not be assessed. Based on the results of this pilot study, we are currently performing a multicenter randomized controlled study to determine the effect of the combination of acupuncture and metformin on insulin sensitivity in women with PCOS and IR, currently registered at Clinicaltrial.gov (NCT02491333).

**Conclusion**

Acupuncture treatment in Chinese women with PCOS and IR was associated with an encouraging improvement in insulin sensitivity.

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## Ethics approval

This study was approved by the ethics committee of the First Affiliated Hospital of Guangzhou Medical University (ref. 2013039).

## Competing interest statement

The authors have no conflicts of interest to disclose.

## Author contributions

JL, WW, and ES-V contributed equally to this work. EHYN, HM, and ES-V conceived and designed the study. JL, EHYN, ES-V, and ML drafted and critically revised the manuscript. RHWL was responsible for statistical analysis. WW was the acupuncturist for this study and was responsible for data collection. HM, ML, YM, and HL were responsible for screening and recruiting subjects. YX was responsible for ultrasound scanning. HM, JL, and YX sought funding and YZ sought ethical approval. All authors contributed to the further editing of the manuscript and approved the final version of the manuscript accepted for publication.

## Patient consent

Written informed consent was provided by all subjects.

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**Figure Legends**

Fig 1.

Study flowchart

**Table 1. Changes after 6 months of acupuncture and 3 months of follow-up (both relative to baseline) in women with polycystic ovary syndrome and insulin resistance**

| Parameter | N | Baseline | 6 months of acupuncture | 3 months of follow-up |
|---|---|---|---|---|
| HOMA-IR index | 80 | 3.02 (2.58, 4.14) | 2.68 (2.15, 3.79) ** | 2.66 (2.01, 3.70) *** |
| FPG, mmol/L | 80 | 5.00 (4.70, 5.30) | 4.80 (4.60, 5.00) ** | 4.90 (4.70, 5.20) |
| Fasting insulin, mU/L | 80 | 14.32 (11.60, 18.51) | 12.54 (10.14, 17.21) * | 12.97 (9.66, 16.58) *** |
| HOMA-β, % | 80 | 192.90 (156.00, 279.30) | 204.80 (141.70, 315.80) | 194.10 (132.10, 268.70) |
| $AUC_{glu}$, mmol/L×min | 80 | 14.20 (12.40, 16.10) | 13.70 (11.60, 15.80) * | 14.30 (11.90, 16.20) |
| $AUC_{ins}$, mU/L×min | 80 | 181.20 (131.50, 254.60) | 184.20 (124.40, 265.10) | 171.80 (124.70, 273.50) |
| C-peptide, nmol/L | 80 | 0.94 (0.83, 1.16) | 0.89 (0.74, 1.12) *** | 0.86 (0.72,1.01) *** |
| CPI | 80 | 19.53 (16.44, 23.83) | 18.96 (16.04, 23.45) * | 17.96 (14.33, 21.59) *** |
| HbA1c, % | 73 | 5.4 (5.2, 5.7) | 5.3 (5.1, 5.5) ** | 5.2 (5.0, 5.3) *** |
| HbA1c, mmol/mol | 73 | 36 (33, 39) | 34 (32, 37) ** | 33 (31, 34) *** |

| | | | | |
|---|---|---|---|---|
| LH/FSH | 80 | 1.38 (0.84, 1.92) | 1.90 (1.38, 2.57) *** | |
| TT, ng/dL | 80 | 62.50 (53.25, 77.00) | 67.50 (50.00, 79.25) | |
| FAI | 80 | 2.35 (1.48, 3.17) | 1.93 (1.21, 2.89) | |
| CHOL, mmol/L | 79 | 5.16 (4.43, 5.71) | 5.05 (4.31, 5.52) | |
| TG, mmol/L | 79 | 1.35 (0.95, 1.81) | 1.20 (0.92, 1.78) | |
| HDL, mmol/L | 79 | 1.22 (1.10, 1.47) | 1.25 (1.08, 1.42) | |
| LDL, mmol/L | 78 | 3.33 (2.87, 3.83) | 3.08 (2.55, 3.51) ** | |
| BMI, $kg/m^2$ | 80 | 23.90 (21.80, 28.30) | 23.80 (21.10, 26.90) *** | 23.60 (21.20, 28.00) *** |
| WHR | 80 | 0.86 (0.82, 0.91) | 0.84 (0.79, 0.87) *** | 0.83 (0.78, 0.88) *** |

**Notes:**

Data are median ($25^{th}$, $75^{th}$ percentile). * $p$ <0.05 *vs.* baseline (Friedman's test); ** $p$ <0.01 *** $p$ <0.001 *vs.* baseline (Friedman's test or Wilcoxon signed rank test).

**Abbreviations:** HOMA-IR, homeostasis model of assessment for insulin resistance; FPG, fasting plasma glucose; HOMA-β, homeostatic model assessment for beta cell function; $AUC_{glu,}$ the area under the curve during the OGTT for glucose; $AUC_{ins}$, the area under the curve during the OGTT for insulin; CPI, C-peptide index; HbA1c, glycated hemoglobin; LH, luteinizing hormone; FSH, follicle-stimulating hormone; TT, total testosterone; FAI, free androgen index; CHOL, cholesterol; TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; BMI, body mass index; WHR, waist-to-hip ratio

**Table 2. Subgroup analysis for normal weight and overweight/obese women at baseline and after 6 months of acupuncture and 3 months of follow-up**

| Parameter | Normal weight women (N = 34) | | | Overweight/obese women (N = 46) | | |
|---|---|---|---|---|---|---|
| | Baseline | 6 months of acupuncture | 3 months of follow-up | Baseline | 6 months of acupuncture | 3 months of follow-up |
| HOMA-IR index | 2.68 (2.32, 3.05) | 2.34 (1.78, 2.76) ** | 2.22 (1.86, 2.77) *** | 3.65 (2.86, 5.55) | 3.47 (2.44, 4.75) * | 3.17 (2.44, 4.96) ** |
| FPG, mmol/L | 5.00 (4.86, 5.29) | 4.80 (4.60, 5.02) | 4.80 (4.69, 5.00) | 5.03 (4.68, 5.30) | 4.71 (4.50, 5.12) * | 4.96 (4.61, 5.32) |
| Fasting insulin, mU/L | 11.64 (10.57, 13.53) | 10.65 (8.50, 12.03) * | 10.32 (8.72, 13.20) ** | 17.05 (13.18, 23.87) | 16.04 (12.08, 20.68) | 14.89 (11.50, 20.28) ** |

**Notes:**

Data are median ($25^{th}$, $75^{th}$ percentile). * $p$ <0.05 ** $p$ <0.01 *** $p$ <0.001 *vs.* baseline (Friedman's test); †, $p$ <0.05 normal weight *vs.* overweight/obese women (Student's t-test or Mann–Whitney U-test).

**Abbreviations:** HOMA-IR, homeostasis model of assessment for insulin resistance; FPG, fasting plasma glucose.