Research
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# 基于就医人群的中国多囊卵巢综合征女性的临床表型和治疗结局——身体质量指数与地理分布的影响

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A R T I C L E   I N F O

摘要

遗传因素、生活方式和环境因素与多囊卵巢综合征（PCOS）的发生相关。身体质量指数（BMI）的增加会加剧生殖及代谢障碍，降低PCOS女性的生育能力。本文对在中国大陆21个研究中心开展的一项大样本、多中心、随机对照试验进行二次分析。共有1000名PCOS女性参加本试验。其中，998名PCOS女性被纳入分析。BMI增加与月经失调加剧、高睾酮水平、高代谢综合征患病率以及生活质量降低相关。BMI正常组、超重组和肥胖组的女性人均排卵率分别为83.0%、78.2%和63.6%（$P < 0.001$），活产率分别为23.6%、18.1%和15.3%（$P = 0.030$）。与中国南方的PCOS患者相比，北方的PCOS患者生殖结局较差，血糖和血脂代谢不良，运动量少，以及总排卵率更低（81.2% vs 74.8%，绝对差：6.4%，95%置信区间：1.2%~11.5%）。结果显示，中国南北方的汉族PCOS女性具有典型的表型特征。与生活在中国南方的女性相比，在同样的干预措施下，中国北方的女性BMI更高，糖脂代谢障碍更严重，临床结局更差。表型特征及排卵的差异可以通过BMI差异加以解释。

## 1. 引言

多囊卵巢综合征（PCOS）是女性最常见的内分泌紊乱疾病之一，育龄女性的PCOS患病率为5%~10%。PCOS主要有高雄激素血症、排卵障碍和超声检查卵巢呈多囊样三大特征[1]。虽然PCOS的病因尚不清楚，但大多数专家认为它是一种多因素疾病。促性腺激素紊乱、胰岛素抵抗、高胰岛素血症、脂肪组织功能障碍和高雄激素血症可能在PCOS病理生理机制中起着重要作用[2]。基因/种族差异、情绪障碍、生活方式和环境因素也与PCOS的病因密切相关[3]。PCOS的表型多样性可能受种族、地域，甚至风俗习惯的影响[4]。与欧洲和北美洲的PCOS女性相比，亚洲的PCOS女性通常身材矮小，BMI较低，高雄激素血症表型较轻，但月经失调更严重[5]。

虽然中国有56个不同的民族，但汉族人口占中国人口的92% [6]，因此，中国女性在基因、种族或民族特征方面几乎没有差异。中国的领土位于北纬18°~54°之

间。这一辽阔的地理区域通常沿秦岭—淮河线（大致沿着秦岭和淮河延伸）分为北方和南方。中国北方和南方的气候有明显差异，因此对地理分布的研究可能有助于了解生活方式和环境因素对PCOS流行病学和表型的影响。

近年来，由于久坐不动的生活方式越来越普遍，饮食也发生了变化，肥胖已成为世界性的流行病[7]，并且肥胖在PCOS女性中尤为常见。越来越多的证据表明，肥胖会对女性的生育能力和产科结局产生不良影响，包括流产、母婴并发症的风险增加[8,9]。最近一项随机试验表明，强化饮食和生活方式干预导致体重明显减轻，但对计划进行体外受精（IVF）的肥胖女性的活产率没有实质影响[9]。

本文总结了1000名PCOS受试者的基线特征，并介绍了BMI和地域对表型特征及克罗米芬和针刺干预的临床结局的影响。

# 2. 材料与方法

## 2.1. 背景

针刺和克罗米芬治疗多囊卵巢综合征不孕症患者（PCOSAct）是一项针对中国PCOS女性不孕症的大样本、多中心、随机对照试验，于2012年7月至2015年10月开展。这是迄今为止基于医院就诊患者进行的规模最大的PCOS临床试验。在该试验中，PCOS女性来自全国各地的21家研究中心（27家医院），大致可代表中国的PCOS女性。本试验的详细方案和初始研究已发表[10,11]。临床试验编号为NCT01573858。

## 2.2. 研究人群

研究样本为1000名根据修订的Rotterdam标准[12]诊断为PCOS的女性。这一诊断标准与中华医学会的中国PCOS标准[13]一致：月经稀发或闭经，并伴有临床或生化的高雄激素血症。其他必要的纳入标准包括：年龄在20~40岁之间；至少一侧输卵管通畅、子宫腔正常；精液分析中丈夫精子浓度 ≥ $1.5 \times 10^7$ mL$^{-1}$，总运动率 ≥ 40%，或者总运动精子数 ≥ 1000万；夫妻同意在研究期间有定期的性生活（每周2~3次）。

## 2.3. 干预

入组女性随机分为四组：第一组接受克罗米芬和有效针刺；第二组接受安慰剂和有效针刺；第三组接受克罗米芬和安慰针刺；第四组接受安慰剂和安慰针刺。每个周期从月经第3天至第7天服用克罗米芬或安慰剂，初始剂量为50 mg（1片），然后根据治疗效果将剂量增加至150 mg（3片）。如果患者反应不佳，下一个周期的剂量增加一片。参加者每周接受两次有效针刺或安慰针刺，每次治疗持续30 min。有效针刺组针刺于穴位上，而安慰针刺组针刺于非穴位。治疗周期为4个月。在妊娠试验阳性后停止所有治疗。如果患者没有受孕，在排卵周期月经第三天或在无排卵周期最后一次针刺治疗后一周内重复所有测量。一旦患者受孕，停止治疗，并在一周内结束研究访视。

## 2.4. 变量

临床结局为排卵、受孕、妊娠、活产和流产。所有孕妇（包括活产）的结局在分娩或妊娠结束后进行随访[14]。收集所有受试者基线状态的生物特征、既往史、超声检查结果、生活方式和问卷调查等数据。我们还获取了大多数男性伴侣的年龄、吸烟史和饮酒史。生物特征数据包括身高、体重、腰围、臀围、血压、脉搏、呼吸频率、痤疮、多毛和黑棘皮情况。所有患者的既往病史包括一般病史、妊娠史、不孕治疗史、家族史。助理研究员均由国际专家进行培训和测试后，在当地研究中心对患者进行体检并获取病史信息。

基线时还测量生殖和代谢激素水平。在月经期第三天采血，所有血样冷冻保存于当地研究中心，然后每三个月用干冰运送至黑龙江中医药大学中心实验室。实验室已通过ISO 15189认证。生殖激素包括孕酮（P）、黄体生成素（LH）、卵泡刺激素（FSH）、雌二醇（E2）、睾酮（T）和性激素结合球蛋白（SHBG）。代谢指标包括胰岛素、血糖、高密度脂蛋白（HDL）、低密度脂蛋白（LDL）、胆固醇、甘油三酯（TG）、载脂蛋白A（APOA）、载脂蛋白B（APOB）。游离雄激素指数（FAI）由总T和SHBG的可测值进行计算，公式如下：FAI = 总睾酮（nmol·L$^{-1}$）/[SHBG（nmol·L$^{-1}$）] × 100。胰岛素抵抗指数（HOMA-IR）通过以下计算得到：HOMA-IR = 血糖水平（mmol·L$^{-1}$）×胰岛素水平（mU·L$^{-1}$）/22.5。代谢综合征的诊断依据为腰围、甘油三酯、高密度脂蛋白、血压和空腹血糖[12]，并且符合以下五项标准中的任意三项，便可确诊：①腰围大于88 cm；②甘油三酯高于150 mg·dL$^{-1}$；③HDL低于50 mg·dL$^{-1}$；④收缩压

高于130 mmHg（1 mmHg≈133.322 Pa）或舒张压高于85 mmHg；⑤空腹血糖水平在110~126 mg·dL$^{-1}$之间。本文将中国女性的体重正常定义为BMI<24，超重定义为24≤BMI<28，肥胖定义为BMI≥28 [15]。所有BMI的单位为kg·m$^{-2}$。

## 2.5. 数据分析

本研究中的所有数据输入均在当地各研究中心完成。在耶鲁大学科学统计数据协调委员会的监督下，哈尔滨项目办公室进行了数据管理、数据审计和数据分析。在不同治疗方式、不同BMI水平以及中国南北方地域之间进行了数据比较。各组分类变量用频率和百分比表示。各组连续变量用均值和标准差表示。使用Student $t$检验或Kruskal–Wallis $H$检验确定连续变量的统计学意义，使用卡方检验或Fisher精确检验确定分类变量的统计学意义。$P < 0.05$时，认为差异有统计学意义。所有分析使用SAS 9.4版进行。

## 2.6. 伦理

该方案已获得所有研究中心当地伦理委员会的批准。所有女性在参加本试验前均签署了知情同意书。

## 3. 结果

1000名受试者的基线数据和临床特征见表1。患者的平均年龄为28岁，平均BMI为24.2。多毛症和痤疮的发生率分别为26.6%和32.4%。18.5%的女性有黑棘皮症，22.2%的女性月经失调严重（闭经），91.7%的女性有卵巢多囊样改变（PCOM）。男性伴侣的平均年龄为30岁，平均精子浓度为9.74 × 10$^7$ mL$^{-1}$。

既往史显示7.2%的女性曾患有脂肪肝。家族史最常见的疾病是糖尿病（19.6%）。50.2%的女性有一次妊娠史，其中仅5.7%活产。不孕时间平均为24.0个月。既往接受过治疗的女性相对较少（29.4%接受过克罗米芬，12.4%接受过针刺）。在所有女性中，13.8%每天锻炼，17.9%每周锻炼，20.7%每月锻炼1~3次，47.7%不进行任何锻炼。治疗组的详细血清情况见初始研究[11]。

随着BMI增加，月经失调和黑棘皮症愈加严重；血压、游离睾酮、FAI、胰岛素、血糖、HOMA-IR、LDL、胆固醇、TG、APOB和脂蛋白水平均升高；HDL、APOA、E2、SHBG、LH和LH/FSH水平均降低；代谢综合征的发生率增加（表2）。

就不同BMI组之间的临床结局而言，治疗效果与

表1 各治疗组的基线特征

| Biometrics | Clomiphene and acupuncture N = 250 | Clomiphene and control acupuncture N = 250 | Placebo and acupuncture N = 250 | Placebo and control acupuncture N = 250 |
| --- | --- | --- | --- | --- |
| Age (years) | 28.2 ± 3.4 (250) | 27.8 ± 3.4 (249) | 27.8 ± 3.2 (250) | 28.0 ± 3.3 (249) |
| Height (cm) | 161.3 ± 4.9 (250) | 161.0 ± 5.2 (249) | 161.1 ± 5.1 (250) | 161.4 ± 5.2 (249) |
| Weight (kg) | 62.2 ± 11.9 (250) | 63.5 ± 11.9 (249) | 62.9 ± 12.8 (250) | 64.1 ± 13.0 (249) |
| BMI (kg·m$^{-2}$) | 23.8 ± 4.2 (250) | 24.4 ± 3.9 (249) | 24.2 ± 4.4 (250) | 24.6 ± 4.5 (249) |
| < 24 | 137/250 (54.8%) | 129/249 (51.8%) | 140/250 (56.0%) | 123/249 (49.4%) |
| 24–28 | 74/250 (29.6%) | 71/249 (28.5%) | 67/250 (26.8%) | 81/249 (32.5%) |
| ≥ 28 | 39/250 (15.6%) | 49/249 (19.7%) | 43/250 (17.2%) | 45/249 (18.1%) |
| Hip circumference (cm) | 97.9 ± 8.5 (250) | 98.3 ± 9.0 (249) | 98.6 ± 8.5 (250) | 99.0 ± 8.5 (249) |
| Waist circumference (cm) | 84.6 ± 11.6 (250) | 85.8 ±10.9 (249) | 85.6 ± 11.6 (250) | 85.7 ± 11.8 (249) |
| WHR | 0.9 ± 0.1 (250) | 0.9 ± 0.1 (249) | 0.9 ± 0.1 (250) | 0.9 ± 0.1 (249) |
| ≥ 0.8 | 208/250 (83.2%) | 218/249 (87.6%) | 212/250 (84.8%) | 204/249 (81.9%) |
| Menstrual period (d) | | | | |
| 35–90 | 196/250 (78.4%) | 194/249 (77.9%) | 198/250 (79.2%) | 186/249 (74.7%) |
| ≥ 90 | 54/250 (21.6%) | 55/249 (22.1%) | 51/250 (20.4%) | 62/249 (24.9%) |
| PCOM | 222/242 (91.7%) | 214/240 (89.2%) | 219/237 (92.4%) | 227/243 (93.4%) |
| Hirsutism score | 3.0 ± 2.6 (250) | 2.9 ± 2.6 (249) | 3.3 ± 3.1 (250) | 2.9 ± 2.9 (249) |
| ≥ 5 | 68/250 (27.2%) | 65/249 (26.1%) | 72/250 (28.8%) | 60/249 (24.1%) |
| Acne | 70/250 (28.0%) | 85/249 (34.1%) | 81/250 (32.4%) | 87/249 (34.9%) |
| Acne score | 0.3 ± 0.6 (250) | 0.5 ± 0.8 (249) | 0.4 ± 0.7 (250) | 0.5 ± 0.9 (249) |

| Biometrics | Clomiphene and acupuncture N = 250 | Clomiphene and control acupuncture N = 250 | Placebo and acupuncture N = 250 | Placebo and control acupuncture N = 250 |
|---|---|---|---|---|
| Acanthosis nigricans score | 1.2 ± 0.4 (250) | 1.2 ± 0.5 (249) | 1.2 ± 0.5 (250) | 1.2 ±0.5 (249) |
| > 0 | 40/250 (16.0%) | 51/249 (20.5%) | 50/250 (20.0%) | 44/249 (17.7%) |
| SBP (mmHg) | 111.7 ± 9.8 (250) | 112.8 ± 9.4(249) | 112.3 ± 8.9 (250) | 112.4 ± 9.6 (249) |
| DBP (mmHg) | 74.8 ± 8.1 (250) | 74.9 ± 7.8 (249) | 74.8 ± 7.7 (250) | 74.9 ± 8.1 (249) |
| Partner age (years) | 30.1 ± 4.3 (250) | 29.6 ± 4.3 (248) | 29.5 ± 3.7 (249) | 30.0 ± 4.3 (249) |
| Sperm concentration ($\times 10^6$ mL$^{-1}$) | 104.6 ± 112.0 (249) | 92.1 ± 94.7 (247) | 100.0 ± 126.5 (248) | 92.9 ± 89.7 (248) |
| Participants in northern sites | 124/250 (49.6%) | 123/250 (49.2%) | 124/250 (49.6%) | 125/250 (50.0%) |
| Participants in southern sites | 126/250 (50.4%) | 127/250 (50.8%) | 126/250 (50.4%) | 125/250 (50.0%) |
| General disease history | | | | |
| Fatty liver | 20/250 (8.0%) | 16/249 (6.4%) | 17/250 (6.8%) | 19/249 (7.6%) |
| Thyroid diseases | 7/250 (2.8%) | 3/249 (1.2%) | 3/250 (1.2%) | 2/249 (0.8%) |
| Diabetes | 1/250 (0.4%) | 0/249 (0) | 0/250 (0) | 2/249 (0.8%) |
| Hypertension | 1/250 (0.4%) | 1/249 (0.4%) | 0/250 (0) | 0/249 (0) |
| Family history | | | | |
| Hypertension | 96/250 (38.4%) | 109/249 (43.8%) | 104/250 (41.6%) | 93/249 (37.3%) |
| Diabetes | 49/250 (19.6%) | 53/249 (21.3%) | 40/250 (16.0%) | 54/249 (21.7%) |
| Oligomenorrhea or amenorrhea | 36/250 (14.4%) | 43/249 (17.3%) | 33/250 (13.2%) | 36/249 (14.5%) |
| Alopecia premature | 25/250 (10.0%) | 28/249 (11.2%) | 21/250 (8.4%) | 27/249 (10.8%) |
| Genital system neoplasms | 12/250 (4.8%) | 16/249 (6.4%) | 13/250 (5.2%) | 19/249 (7.6%) |
| Pregnancy complications | 1/250 (0.4%) | 2/249 (0.8%) | 3/250 (1.2%) | 3/249 (1.2%) |
| Reproductive history | | | | |
| Prior pregnancy | 144/250 (57.6%) | 122/250 (48.8%) | 114/250 (45.6%) | 122/250 (48.8%) |
| Prior delivery | 17/250 (6.8%) | 11/250 (4.4%) | 17/250 (6.8%) | 12/250 (4.8%) |
| Prior spontaneous abortion | 38/250 (15.2%) | 29/250 (11.6%) | 31/250 (12.4%) | 35/250 (14.0%) |
| Prior early-induced abortion | 78/250 (31.2%) | 74/250 (29.6%) | 59/250 (23.6%) | 62/250 (24.8%) |
| Prior late-induced abortion | 4/250 (1.6%) | 4/250 (1.6%) | 4/250 (1.6%) | 6/250 (2.4%) |
| Prior premature labor | 2/250 (0.8%) | 1/250 (0.4%) | 2/250 (0.8%) | 1/250 (0.4%) |
| Prior full-term birth | 13/250 (5.2%) | 7/250 (2.8%) | 10/250 (4.0%) | 9/250 (3.6%) |
| Prior ectopic pregnancy | 5/250 (2.0%) | 3/250 (1.2%) | 4/250 (1.6%) | 6/250 (2.4%) |
| Length of time subject had been attempting conception (months) | 24.5 ± 17.5 (238) | 23.4 ± 18.7 (234) | 23.8 ± 17.9 (240) | 24.2 ± 17.2 (236) |
| Treatment history | | | | |
| Diagnosis of infertility | 243/250 (97.2%) | 244/249 (98.0%) | 239/250 (95.6%) | 240/249 (96.4%) |
| Secondary to ovulation disorders (PCOS) | 236/236 (100.0%) | 241/241 (100.0%) | 236/237 (99.6%) | 228/228 (100.0%) |
| Ovulation disorders (PCOS) | 236/236 (100.0%) | 241/241 (100.0%) | 236/237 (99.6%) | 228/228 (100.0%) |
| Previous medication for infertility | 138/250 (55.2%) | 141/249 (56.6%) | 139/250 (55.6%) | 142/249 (57.0%) |
| Previous exposure to CC | 65/236 (27.5%) | 73/239 (30.5%) | 74/240 (30.8%) | 68/238 (28.6%) |
| Previous exposure to acupuncture treatment | 23/243 (9.5%) | 32/239 (13.4%) | 35/246 (14.2%) | 31/245 (12.7%) |
| Lifestyle-exercise | | | | |
| Every day | 41/250 (16.4%) | 31/249 (12.4%) | 31/248 (12.5%) | 34/249 (13.7%) |
| Every week | 40/250 (16.0%) | 50/249 (20.1%) | 46/248 (18.5%) | 42/249 (16.9%) |
| 1–3 times a month | 63/250 (25.2%) | 46/249 (18.5%) | 56/248 (22.6%) | 41/249 (16.5%) |
| Never | 106/250 (42.4%) | 122/249 (49.0%) | 115/248 (46.4%) | 132/249 (53.0%) |

The values in parentheses are total numbers or percentages.

WHR: waist-to-hip ratio; PCOM: polycystic ovary morphology; SBP: systolic blood pressure; DBP: diastolic blood pressure; CC: clomiphene citrate.

表2 不同BMI分类的主要特征

| Characteristics | Group A BMI < 24 | Group B 24 ≤ BMI < 28 | Group C BMI ≥ 28 | P value[a] | A vs B | A vs C | B vs C |
|---|---|---|---|---|---|---|---|
| Age (years) | 27.7 ± 3.2 (529) | 28.1 ± 3.6 (293) | 28.2 ± 3.3 (176) | 0.099 | 0.109 | 0.063 | 0.692 |
| Partner age (years) | 29.6 ± 4.0 (528) | 30.2 ± 4.6 (293) | 29.7 ± 3.9 (175) | 0.337 | 0.147 | 0.571 | 0.498 |
| Biometric | | | | | | | |
|   Height (cm) | 160.8 ± 5.0 (529) | 161.2 ± 5.1 (293) | 162.7 ± 5.1 (176) | < 0.001 | 0.339 | < 0.001 | < 0.001 |
|   Weight (kg) | 54.4 ± 6.1 (529) | 67.3 ± 5.3 (293) | 82.5 ± 9.3 (176) | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
|   BMI (kg·m$^{-2}$) | 21.0 ± 1.9 (529) | 25.9 ± 1.1 (293) | 31.1 ± 2.7 (176) | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
|   Hip circumference (cm) | 93.2 ± 6.0 (529) | 101.1 ± 5.2 (293) | 109.9 ± 6.6 (176) | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
|   Waist circumference (cm) | 78.3 ± 7.6 (529) | 89.0 ± 7.0 (293) | 100.9 ± 9.0 (176) | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| WHR | 0.8 ± 0.1 (529) | 0.9 ± 0.1 (293) | 0.9 ± 0.1 (176) | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
|   ≥ 0.8 | 396/529 (74.9%) | 274/293 (93.5%) | 172/176 (97.7%) | < 0.001 | < 0.001 | < 0.001 | 0.047 |
| Menstrual period (d) | | | | | | | |
|   35–90 | 442/529 (83.6%) | 216/293 (73.7%) | 116/176 (65.9%) | < 0.001 | < 0.001 | < 0.001 | 0.076 |
|   ≥ 90 | 85/529 (16.1%) | 77/293 (26.4%) | 60/176 (34.1%) | | | | |
| Hirsutism score | 3.0 ± 2.8 (529) | 3.0 ± 2.7 (293) | 3.2 ± 2.9 (176) | 0.891 | 0.969 | 0.664 | 0.652 |
|   ≥ 5 | 140/529 (26.5%) | 77/293 (26.3%) | 48/176 (27.3%) | 0.971 | 1.000 | 0.844 | 0.830 |
| Acne | 357/529 (67.5%) | 195/293 (66.6%) | 123/176 (69.9%) | 0.755 | 0.816 | 0.577 | 0.476 |
| Acne score | 0.4 ± 0.7 (529) | 0.4 ± 0.8 (293) | 0.4 ± 0.8 (176) | 0.862 | 0.818 | 0.686 | 0.587 |
| Acanthosis nigricans score | 1.1 ± 0.4 (529) | 1.2 ± 0.5(293) | 1.5 ± 0.7(176) | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| SBP (mmHg) | 110.2 ± 9.8 (529) | 113.3 ± 8.0 (293) | 116.8 ± 8.5 (176) | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| DBP (mmHg) | 73.4 ± 7.9 (529) | 75.9 ± 7.7 (293) | 77.5 ± 7.2 (176) | < 0.001 | < 0.001 | < 0.001 | 0.042 |
| Pulse pressure (mmHg) | 36.9 ± 7.6 (529) | 37.4 ± 7.1 (293) | 39.3 ± 7.9 (176) | < 0.001 | 0.360 | < 0.001 | 0.003 |
| MAP | 85.7 ± 7.8 (529) | 88.4 ± 7.1 (293) | 90.6 ± 6.7 (176) | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| Imaging-PCOM | 464/506 (91.7%) | 260/284 (91.5%) | 157/171 (91.8%) | 1.000 | 1.000 | 1.000 | 1.000 |
| General history | | | | | | | |
|   Fatty liver | 7/529 (1.3%) | 32/293 (10.9%) | 33/176 (18.8%) | < 0.001 | < 0.001 | < 0.001 | 0.019 |
|   Thyroid diseases | 7/529 (1.3%) | 6/293 (2.0%) | 2/176 (1.1%) | 0.728 | 0.560 | 1.000 | 0.716 |
|   Diabetes | 0/529 (0) | 1/293 (0.3%) | 2/176 (1.1%) | 0.058 | 0.356 | 0.062 | 0.559 |
|   Hypertension | 1/529 (0.2%) | 1/293 (0.3%) | 0/176 (0) | 1.000 | 1.000 | 1.000 | 1.000 |
| Treatment history | | | | | | | |
|   Using contraception | 143/529 (27.0%) | 91/291 (31.3%) | 44/176 (25.0%) | 0.281 | 0.225 | 0.623 | 0.171 |
|   Previous exposure to CC | 152/503 (30.2%) | 88/286 (30.8%) | 40/164 (24.4%) | 0.304 | 0.873 | 0.165 | 0.159 |
|   Previous exposure to acupuncture treatment | 49/512 (9.6%) | 43/290 (14.8%) | 29/171 (17.0%) | 0.013 | 0.028 | 0.012 | 0.596 |
|   Treatment for regulating the menstrual cycle | 21/52 (40.4%) | 15/43 (34.9%) | 4/30 (13.3%) | 0.030 | 0.673 | 0.013 | 0.057 |
|   Treatment for infertility | 22/47 (46.8%) | 13/42 (31.0%) | 3/28 (10.7%) | 0.004 | 0.136 | 0.002 | 0.080 |
|   Treatment for PCOS | 14/37 (37.8%) | 8/32 (25.0%) | 2/22 (9.1%) | 0.045 | 0.306 | 0.018 | 0.173 |
|   Medication to adjust menstrual cycle | 351/529 (66.4%) | 200/293 (68.3%) | 125/176 (71.0%) | 0.510 | 0.589 | 0.266 | 0.605 |
| Lifestyle-exercise | | | | | | | |
|   Every day | 60/528 (11.4%) | 46/293 (15.7%) | 31/175 (17.7%) | 0.755 | 0.602 | 0.694 | 0.485 |
|   Every week | 105/528 (19.9%) | 52/293 (17.8%) | 21/175 (12.0%) | | | | |
|   1–3 times a month | 116/528 (22.0%) | 57/293 (19.5%) | 33/175 (18.9%) | | | | |
|   Never | 247/528 (46.8%) | 138/293 (47.1%) | 90/175 (51.4%) | | | | |
| Laboratory | | | | | | | |
|   Total T (nmol·L$^{-1}$) | 1.6 ± 0.6 (514) | 1.7 ± 0.7 (280) | 1.7 ± 0.6 (164) | 0.336 | 0.304 | 0.184 | 0.729 |
|   ≥ 1.67 | 226/514 (44.0%) | 131/280 (46.8%) | 84/164 (51.2%) | 0.255 | 0.456 | 0.106 | 0.378 |
|   Free T (pg·mL$^{-1}$) | 2.2 ± 0.8 (514) | 2.4 ± 0.9 (279) | 2.5 ± 0.8 (161) | < 0.001 | 0.001 | < 0.001 | 0.081 |

| Characteristics | Group A<br>BMI < 24 | Group B<br>24 ≤ BMI < 28 | Group C<br>BMI ≥ 28 | P value[a] | A vs B | A vs C | B vs C |
|---|---|---|---|---|---|---|---|
| SHBG (nmol·L⁻¹) | 52.0 ± 30.8 (508) | 33.7 ± 27.6 (281) | 28.6 ± 23.4 (164) | < 0.001 | < 0.001 | < 0.001 | 0.005 |
| FAI | 4.4 ± 3.5 (507) | 7.1 ± 4.6 (278) | 8.2 ± 5.1 (163) | < 0.001 | < 0.001 | < 0.001 | 0.021 |
| E2 (pmol·L⁻¹) | 289.9 ± 323.3 (513) | 267.3 ± 380.5 (280) | 211.3 ± 107.8 (164) | < 0.001 | 0.001 | 0.001 | 0.900 |
| P (ng·mL⁻¹) | 2.9 ± 6.4 (513) | 2.2 ± 2.7 (279) | 2.1 ± 3.2 (162) | 0.069 | 0.094 | 0.045 | 0.558 |
| LH (mIU·mL⁻¹) | 12.0 ± 6.5 (513) | 9.3 ± 4.9 (279) | 7.9 ± 4.1 (164) | < 0.001 | < 0.001 | < 0.001 | 0.009 |
| FSH (mIU·mL⁻¹) | 6.2 ± 1.7 (513) | 6.0 ± 1.7 (279) | 6.0 ± 1.5 (164) | 0.018 | 0.016 | 0.031 | 0.974 |
| LH/FSH | 2.0 ± 1.1 (513) | 1.6 ± 1.3 (278) | 1.3 ± 0.7 (164) | < 0.001 | < 0.001 | < 0.001 | 0.011 |
| Glucose (mmol·L⁻¹) | 4.9 ± 0.8 (514) | 5.0 ± 1.0 (279) | 5.5 ± 1.2 (164) | < 0.001 | 0.004 | < 0.001 | < 0.001 |
| Insulin (pmol·L⁻¹) | 68.7 ± 67.7 (513) | 115.3 ± 96.4 (280) | 149.5 ± 98.1 (163) | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| HOMA-IR | 2.2 ± 2.6 (509) | 3.8 ± 4.2 (277) | 5.2 ± 3.8 (162) | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| Cholesterol (mmol·L⁻¹) | 4.6 ± 1.0 (512) | 4.8 ± 1.1 (279) | 5.1 ± 1.1 (165) | < 0.001 | 0.026 | < 0.001 | 0.001 |
| TG (mmol·L⁻¹) | 1.3 ± 0.8 (512) | 1.8 ± 0.9 (280) | 2.0 ± 1.0 (165) | < 0.001 | < 0.001 | < 0.001 | 0.003 |
| HDL (mmol·L⁻¹) | 1.4 ± 0.4 (514) | 1.2 ± 0.4 (279) | 1.2 ± 0.3 (164) | < 0.001 | < 0.001 | < 0.001 | 0.756 |
| LDL (mmol·L⁻¹) | 2.8 ± 0.8 (511) | 3.0 ± 0.9 (280) | 3.3 ± 0.9 (165) | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| APOA (g·L⁻¹) | 1.6 ± 0.3 (512) | 1.5 ± 0.3 (280) | 1.5 ± 0.3 (165) | < 0.001 | < 0.001 | < 0.001 | 0.269 |
| APOB (g·L⁻¹) | 0.8 ± 0.2 (511) | 1.0 ± 0.3 (280) | 1.1 ± 0.3 (165) | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| Lipoprotein (mg·L⁻¹) | 130.3 ± 105.6 (510) | 121.4 ± 77.7 (279) | 140.4 ± 113.3 (165) | 0.385 | 0.575 | 0.171 | 0.409 |
| Metabolic syndrome | 20/529 (3.8%) | 85/293 (29.0%) | 91/176 (51.7%) | < 0.001 | < 0.001 | < 0.001 | < 0.001 |

The values in parentheses are total numbers or percentages.

MAP: mean arterial pressure.

SI conversion factors: To convert LH and FSH to IU·L⁻¹, multiply by 1.0; P to nmol·L⁻¹, multiply by 3.18; E2 to pmol·L⁻¹, multiply by 3.671; total T to nmol·L⁻¹, multiply by 0.0347; SHBG to nmol·L⁻¹, multiply by 8.896; free T to nmol·L⁻¹, multiply by 0.0000347; glucose to mmol·L⁻¹, multiply by 0.0555; insulin to pmol·L⁻¹, multiply by 6.945; triglycerides to mmol·L⁻¹, multiply by 0.0113; and total cholesterol, HDL-C, and LDL-C to mmol·L⁻¹, multiply by 0.0259.

[a] The Kruskal–Wallis test was used to compare the differences between the three groups.

BMI呈负相关（表3）。在正常组、超重组和肥胖组中人均排卵率分别为83.0%、78.2%和63.6%（$P < 0.001$）；每个治疗周期的排卵率为52.6%、47.9%和36.6%（$P < 0.001$）；受孕率为34.6%、32.4%和23.9%（$P = 0.028$）；妊娠率为25.1%、19.1%和16.5%（$P = 0.023$）；活产率为23.6%、18.1%和15.3%（$P = 0.030$）。三个BMI组的流产率类似（$P > 0.05$）。

中国北方的PCOS女性比中国南方的PCOS女性有更高的BMI和腰臀比（WHR）（25.4 vs 23.0, 0.88 vs 0.86）以及更严重的痤疮（表4）。此外，中国北方PCOS女性的代谢较差，其中血糖、HOMA-IR、APOA和TG水平较高，HDL水平较低。中国北方的大多数女性有脂肪肝病史，以及高血压、生殖系统肿瘤和妊娠并发症的家族史。中国南方PCOS女性经常锻炼。相比中国北方PCOS女性，中国南方PCOS女性先前接受过克罗米芬和针刺的治疗更多。与中国南方PCOS女性相比，中国北方PCOS女性人均排卵率较低（81.2% vs. 74.8%，绝对差6.4% [95%置信区间（CI）1.2%~11.5%]），危险比为0.9

（95% CI 0.9~1.0，$P = 0.015$）（表5），而中国北方PCOS女性与中国南方PCOS女性的活产率、受孕率、怀孕率和流产率类似。

## 4. 讨论

该临床试验在中国21个研究中心开展，代表了中国整体PCOS女性群体。这是有史以来针对中国PCOS患者的最大随机队列研究。在纳入研究的女性中，529名BMI正常（BMI＜24），293名超重（BMI在24~28之间），176名肥胖（BMI＞28）。中国女性几乎没有基因、种族或民族差异，但是中国南北方之间存在明显的气候差异，从而导致不同的生活环境和生活方式。参与本试验的中国北方女性和南方女性数量相当（496 vs 504名）。

### 4.1. BMI 增加加重 PCOS 表型

与三年前对644名中国PCOS女性开展的一项研究相比[16]，两项研究的受试者年龄、BMI、WHR、总睾

表3 不同BMI分类的临床结局

| Outcomes [a] | Group A BMI < 24 | Group B 24 ≤ BMI < 28 | Group C BMI ≥ 28 | Total | P value[b] | A vs B Abs. diff. (95% CI) | A vs B P value | B vs C Abs. diff. (95% CI) | B vs C P value | A vs C Abs. diff. (95% CI) | A vs C P value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Ovulations/total no. of women | 439/529 (83.0%) | 229/293 (78.2%) | 112/176 (63.6%) | 780/998 (78.2%) | <0.001 | 4.8 (−0.9 to 10.5) | 0.09 | 14.5 (6.0 to 23.1) | <0.001 | 19.4 (11.6 to 27.1) | <0.001 |
| Ovulations/total no. of treatment cycles | 940/1787 (52.6%) | 462/964 (47.9%) | 227/620 (36.6%) | 1629/3371 (48.3%) | <0.001 | 4.7 (0.8 to 8.6) | 0.02 | 11.3 (6.4 to 16.2) | <0.001 | 16.0 (11.5 to 20.4) | <0.001 |
| Conceptions/total no. of women | 183/529 (34.6%) | 95/293 (32.4%) | 42/176 (23.9%) | 320/998 (32.1%) | 0.028 | 2.2 (−4.5 to 8.9) | 0.53 | 8.6 (0.3 to 16.8) | 0.050 | 10.7 (3.2 to 18.2) | 0.010 |
| Pregnancies/total no. of women | 133/529 (25.1%) | 56/293 (19.1%) | 29/176 (16.5%) | 218/998 (21.8%) | 0.023 | 6.0 (0.2 to 11.9) | 0.05 | 2.6 (−4.5 to 9.7) | 0.470 | 8.7 (2.1 to 15.3) | 0.020 |
| Live births/total no. of women | 125/529 (23.6%) | 53/293 (18.1%) | 27/176 (15.3%) | 205/998 (20.5%) | 0.030 | 5.5 (−0.2 to 11.2) | 0.06 | 2.7 (−4.2 to 9.7) | 0.440 | 8.3 (1.9 to 14.7) | 0.020 |
| Pregnancy loss/total no. of women who conceived | 56/181 (30.9%) | 41/94 (43.6%) | 13/40 (32.5%) | 110/315 (34.9%) | 0.110 | −12.7 (−24.8 to −0.6) | 0.04 | 11.1 (−6.5 to 28.8) | 0.230 | −1.6 (−17.6 to 14.4) | 0.850 |
| Pregnancy loss in the first trimester/ total no. of women who conceived | 51/181 (28.2%) | 38/94 (40.4%) | 12/40 (30.0%) | 101/315 (32.1%) | 0.120 | −12.2 (−24.1 to −0.4) | 0.04 | 10.4 (−6.9 to 27.7) | 0.250 | −1.8 (−17.5 to 13.8) | 0.820 |
| Pregnancy loss in the second or third trimester/total no. of women who conceived | 5/181 (2.8%) | 3/94 (3.2%) | 1/40 (2.5%) | 9/315 (2.9%) | 1.000 | −0.4 (−4.7 to 3.9) | 1.00 | 0.7 (−5.3 to 6.7) | 1.000 | 0.3 (−5.1 to 5.7) | 1.000 |
| Biochemical factor/total no. of women who conceived | 42/181 (23.2%) | 29/94 (30.9%) | 9/40 (22.5%) | 80/315 (25.4%) | 0.370 | −7.6 (−18.8 to 3.5) | 0.17 | 8.4 (−7.6 to 24.3) | 0.330 | 0.7 (−13.6 to 15.0) | 0.920 |

Abs. diff.: absolute difference; CI: confidence interval.

[a] Live birth was defined as the delivery of a live-born infant ≥ 20 weeks' gestation. Conception was defined as any positive serum level of human chorionic gonadotropin. Pregnancy was defined as an intrauterine pregnancy with fetal heart motion as determined by ultrasonography. Ovulation was defined as a serum progesterone level according to the standard of the local site laboratory (minimum value of luteal phase). Biochemical factor was defined as a positive urine or serum human chorionic gonadotropin test, but no fetus or gestational sac was visible on ultrasound.

[b] The chi-square test was used to compare the difference between three groups.

酮水平，以及血糖和血脂水平都相似。我们还对PCOSAct和以前在中国开展的另一项基于社区的流行病学研究进行了比较，结果发现，PCOSAct受试者表现出更严重的表型，包括更高的BMI、HOMA-IR、多毛症评分及更高的PCOM发生率。这一发现表明医院环境中的PCOS女性比社区环境中的PCOS女性表现出更严重的表型。与PCOSAct受试者相比，中国台湾的另一项PCOS队列研究中PCOS患者有相似的特征，包括相似的BMI、WHR、多毛症评分、生殖激素和代谢激素水平[17]。韩国的一项队列研究[18]也显示了相似的BMI以及高雄激素血症和PCOM患病率。这些研究结果表明，东亚女性与中国汉族女性表型相似，因而这些人群的PCOS特征一致。

在美国针对PCOS不孕女性开展了两项大型多中心试验[多囊卵巢综合征妊娠（PPCOS）I、II]，参加者包括不同民族和种族的受试者[19,20]，与之相比，中国患者的BMI、睾酮和多毛症评分明显较低，血脂代谢状况较好。中国女性的平均BMI明显低于美国女性；然而，17名参与PPCOS I试验的亚洲人与参与PCOSAct的中国人有相似的表型。同样，PCOSAct中女性的基线特征与PPCOS II中BMI<30的女性的基线特征类似[21]。这一发现表明，在世界各地不同人群中，BMI对PCOS表型的表达起着至关重要的作用。

表4 按地理分布的主要特征

| Characteristics | Northern China N = 496 | Southern China N = 504 | P value[a] | Absolute difference (95% CI) |
|---|---|---|---|---|
| Age (years) | 28.1 ± 3.2 (495) | 27.7 ± 3.4 (503) | 0.090 | 0.4 (−0.1 to 0.8) |
| Height (cm) | 162.7 ± 5.0 (495) | 159.8 ± 4.8 (503) | < 0.001 | 2.9 (2.3 to 3.5) |
| Weight (kg) | 67.5 ± 12.6 (495) | 58.9 ± 10.6 (503) | < 0.001 | 8.6 (7.1 to 10.0) |
| BMI (kg·m$^{-2}$) | 25.4 ± 4.4 (495) | 23.0 ± 3.8 (503) | < 0.001 | 2.4 (1.9 to 2.9) |
| < 24 | 199/495 (40.2%) | 330/503 (65.6%) | | |
| 24–28 | 171/495 (34.5%) | 122/503 (24.3%) | < 0.001 | |
| ≥ 28 | 125/495 (25.3%) | 51/503 (10.1%) | | |
| Hip circumference (cm) | 100.8 ± 8.7 (495) | 96.2 ± 8.0 (503) | < 0.001 | 4.6 (3.6 to 5.6) |
| Waist circumference (cm) | 88.3 ± 11.6 (495) | 82.6 ± 10.6 (503) | < 0.001 | 5.7 (4.3 to 7.1) |
| WHR | 0.88 ± 0.07 (495) | 0.86 ± 0.07 (503) | < 0.001 | |
| ≥ 0.8 | 435/495 (87.9%) | 497/503 (80.9%) | 0.002 | 7.0 (2.5 to 11.4) |
| Menstrual period (d) | | | | |
| 35–90 | 117/495 (23.6%) | 105/503 (20.9%) | 0.660 | |
| ≥ 90 | 377/495 (76.2%) | 397/503 (78.9%) | | |
| Hirsutism score | 2.8 ± 2.6 (495) | 3.3 ± 3.0 (503) | 0.003 | −0.5 (−0.9 to −0.2) |
| ≥ 5 | 114/495 (23.0%) | 151/503 (30.0%) | 0.012 | −7.0 (−12.4 to −1.5) |
| Acne | 318/495 (64.2%) | 357/503 (71.0%) | 0.023 | 6.7 (0.9 to 12.5) |
| Acne score | 0.5 ± 0.8 (495) | 0.4 ± 0.7 (503) | 0.023 | 0.1 (0 to 0.2) |
| Acanthosis nigricans | 115/495 (23.2%) | 70/503 (13.9%) | < 0.001 | |
| Acanthosis nigricans score | 1.26 ± 0.52 (495) | 1.16 ± 0.43 (503) | < 0.001 | 0.1 (0 to 0.2) |
| SBP (mmHg) | 113.5 ± 9.0 (495) | 111.1 ± 9.7 (503) | < 0.001 | 2.4 (1.2 to 3.5) |
| DBP (mmHg) | 75.7 ± 8.4 (495) | 74.1 ± 7.3 (503) | 0.001 | 1.6 (0.6 to 2.6) |
| MAP (mmHg) | 88.3 ± 7.8 (495) | 86.4 ± 7.4 (503) | < 0.001 | 1.9 (0.9 to 2.8) |
| Pulse (beats·min$^{-1}$) | 76.47 ± 5.95 (495) | 75.67 ± 6.49 (503) | 0.044 | 0.8 (0 to 1.6) |
| Imaging-PCOM | 439/471 (93.2%) | 443/491 (90.2%) | 0.090 | 3.0 (−0.5 to 6.5) |
| General disease history | | | | |
| Fatty liver | 53/495 (10.7%) | 19/503 (3.8%) | < 0.001 | 6.9 (3.7 to 10.1) |
| Family history | | | | |
| Hypertension | 215/495 (43.4%) | 187/503 (37.2%) | 0.044 | 6.3 (0.2 to 12.3) |
| Genital system neoplasms | 41/495 (8.3%) | 19/503 (3.8%) | 0.003 | 4.5 (1.6 to 7.5) |
| Pregnancy complication | 9/495 (1.8%) | 0/503 (0) | 0.002 | 1.8 (0.6 to 3.0) |
| Reproductive history | | | | |
| Prior delivery | 20/496 (4.0%) | 35/504 (6.9%) | 0.043 | −2.9 (−5.7 to −0.1) |
| Prior full-term birth | 12/496 (2.4%) | 26/504 (5.2%) | 0.023 | −2.7 (−5.1 to −0.4) |
| Treatment history | | | | |
| Previous CC | 121/482 (25.1%) | 159/471 (33.8%) | 0.003 | −8.7 (−14.4 to −2.9) |
| Previous acupuncture | 57/494 (11.5%) | 64/479 (13.4%) | 0.39 | −1.8 (−6.0 to 2.3) |
| Medication to adjust menstrual cycle | 350/495 (70.7%) | 326/503 (64.8%) | 0.046 | 5.9 (0.1 to 11.7) |
| Exercise | | | < 0.001 | |
| Every day | 68/493 (13.8%) | 69/503 (13.7%) | | |
| Every week | 62/493 (12.6%) | 116/503 (23.1%) | | |
| 1–3 times a month | 85/493 (17.2%) | 121/503 (24.1%) | | |
| Never | 278/493 (56.4%) | 197/503 (39.2%) | | |
| Laboratory | | | | |
| Free T (pg·mL$^{-1}$) | 2.38 ± 0.75 (465) | 2.20 ± 0.91 (490) | 0.001 | 0.2 (0.1 to 0.3) |
| SHBG (nmol·L$^{-1}$) | 37.51 ± 26.67 (466) | 47.43 ± 32.97 (488) | < 0.001 | −9.9 (−13.7 to −6.1) |

| Characteristics | Northern China N = 496 | Southern China N = 504 | P value[a] | Absolute difference (95% CI) |
|---|---|---|---|---|
| FAI | 6.39 ± 4.79 (461) | 5.35 ± 4.00 (488) | < 0.001 | 1.0 (0.5 to 1.6) |
| E2 (pmol·L$^{-1}$) | 246.44 ± 252.21 (465) | 291.38 ± 367.58 (493) | 0.028 | −44.9 (−85.1 to −4.7) |
| LH (mIU·mL$^{-1}$) | 9.78 ± 5.43 (464) | 11.15 ± 6.30 (493) | < 0.001 | −1.4 (−2.1 to −0.6) |
| LH/FSH | 1.65 ± 0.88 (463) | 1.91 ± 1.31 (493) | < 0.001 | −0.3 (−0.4 to −0.1) |
| Glucose (mmol·L$^{-1}$) | 5.11 ± 0.87 (467) | 4.98 ± 1.08 (491) | 0.040 | 0.1 (0 to 0.3) |
| Insulin (pmol·L$^{-1}$) | 103.41 ± 83.49 (464) | 89.18 ± 92.18 (493) | 0.013 | 14.2 (3.0 to 25.4) |
| HOMA-IR | 3.50 ± 3.20 (461) | 3.10 ± 4.00 (488) | 0.080 | 0.4 (−0.1 to 0.9) |
| TG (mmol·L$^{-1}$) | 1.60 ± 0.96 (468) | 1.50 ± 0.85 (490) | 0.013 | 0.1 (0 to 0.3) |
| HDL (mmol·L$^{-1}$) | 1.19 ± 0.34 (467) | 1.36 ± 0.38 (491) | < 0.001 | −0.2 (−0.2 to −0.1) |
| APOA (g·L$^{-1}$) | 1.45 ± 0.30 (468) | 1.56 ± 0.32 (490) | < 0.001 | −0.1 (−0.2 to −0.1) |
| APOB (g·L$^{-1}$) | 0.93 ± 0.30 (468) | 0.87 ± 0.27 (489) | 0.006 | 0.1 (0 to 0.1) |
| Metabolic syndrome | 119/495 (24.0%) | 77/504 (15.3%) | < 0.001 | 8.8 (3.9 to 13.7) |

The values in parentheses are total numbers or percentages.

[a] The Kruskal–Wallis test was used to compare the differences between two groups.

## 4.2. BMI 增加导致干预效果减弱

令人关注的是，虽然克罗米芬对活产的有效性在 PCOSAct 中的中国女性（4个治疗周期28%）和 PPCOS I 中 BMI<30 的美国女性（6个治疗周期36.8%）类似，但是在 PCOSAct 的中国女性中克罗米芬的有效性显著高于 PPCOS I 中全部美国女性（不考虑BMI）（4个治疗周期28% vs. 6个治疗周期22.5%）。在 PCOSAct 中，中国 PCOS 女性（平均BMI为24.2）在每个治疗周期的排卵率为66.0% [11]。在 PPCOS I 中，一组平均BMI小于30.0的白种人每个治疗周期的排卵率为61.0% [20]，平均BMI为35.1的白种人排卵率为49.0% [19]。印度的另一项研究表明，印度 PCOS 女性（平均BMI为26.5）的排卵率为56.2% [22]。综上所述，所有这些研究表明，PCOS 女性的排卵反应与临床表型一致，受BMI影响，但不受种族影响。

PCOSAct 试验发现，BMI是临床结局的重要因素。随着BMI增加，排卵率、受孕率、妊娠率和活产率均降低。这与美国239 127个IVF周期的鲜胚IVF队列研究一致，该研究表明，BMI增加组的妊娠结局出现进展性恶化且具有统计学意义[23]。最近，对 PCOS 女性而言，在不孕治疗前通过改变生活方式减重很有好处[24]。因此，如果BMI较高的 PCOS 女性想要怀孕，则建议减重。

然而，在 PCOSAct 试验中，不同BMI组之间的流产率没有明显差异，这与中国的另一项研究相似[25]。先前有一项研究表明，流产率受BMI影响极大[26]，并且已经证明肥胖是与不良妊娠结局（包括自然流产）相关的独立因素[27]。PCOSAct 试验中正常BMI组和超重组相比较，超重组的妊娠早期流产率和总流产率显著增加，但超重组和肥胖组之间或正常BMI组和肥胖组之间没有差异。这可能表明超重 PCOS 女性的流产风险较高。

## 4.3. 不同生活方式导致不同的 BMI 和表型

中国南北方气候的显著差异可能促使中国女性的 PCOS 表型不同。总体而言，中国北方女性比中国南方女性有更严重的表型和更差的治疗结局。我们发现中国北方人的平均体型较大，这可部分归因于饮食结构和生活方式。由于气候寒冷，北方饮食结构的特点是面食、肉类和家禽摄入较多，而大米、鱼、绿色蔬菜和新鲜水果的摄入量较低；南方饮食模式的特点是大量摄入米饭，少量摄入面食[28,29]。中国北方女性可能因气候寒冷而较少锻炼，这导致普通型肥胖和中心性肥胖的风险升高。本研究结果表明，BMI增加与 PCOS 表型的加重密切相关，包括更严重的胰岛素抵抗、高血压、血脂异常以及不同类型的代谢综合征。中国北方和南方 PCOS 女性的表型差异与BMI分类一致，因此，这两者之间的差异可能归因于BMI差异，同时有些差异可能是文化因素造成的。

本文的一个局限是，本文是二次分析，而不是以流行病学调查为主要设计的研究。另一个局限是存在人口流动性，在当地研究中心登记的患者可能不是出生在本地的。此外，由于对中医的接受程度不同，因此北方和南方研究中心的 PCOS 患者人群可能不具有同质性。

本文提供了规模最大的基于医院的 PCOS 女性队列研究的数据，描述了中国各地 PCOS 女性的典型表型特

**表5** 按地理分布的临床结局

| Outcomes[a] | Northern China | Southern China | Total | P value[b] | Absolute difference (95% CI) | Rate ratio (95% CI) |
|---|---|---|---|---|---|---|
| Ovulations/total no. of women | 371/496 (74.8%) | 409/504 (81.2%) | 780/1000 (78.0%) | 0.015 | −6.4 (−11.5 to −1.2) | 0.9 (0.9 to 1.0) |
| Ovulations/total no. of treatment cycles | 777/1661 (46.8%) | 852/1710 (49.8%) | 1629/3371 (48.3%) | 0.080 | −3.0 (−6.4 to 0.3) | 0.9 (0.9 to 1.0) |
| Conceptions/total no. of women | 153/496 (30.8%) | 167/504 (33.1%) | 320/1000 (32.0%) | 0.440 | −2.3 (−8.1 to 3.5) | 0.9 (0.8 to 1.1) |
| Pregnancies/total no. of women | 109/496 (22.0%) | 109/504 (21.6%) | 218/1000 (21.8%) | 0.890 | 0.3 (−4.8 to 5.5) | 1.0 (0.8 to 1.3) |
| Live births/total no. of women | 102/496 (20.6%) | 103/504 (20.4%) | 205/1000 (20.5%) | 0.960 | 0.1 (−4.9 to 5.1) | 1.0 (0.8 to 1.3) |
| Pregnancy loss/total no. of women who conceived | 47/149 (31.5%) | 63/166 (38.0%) | 110/315 (34.9%) | 0.230 | −6.4 (−16.9 to 4.1) | 0.8 (0.6 to 1.1) |
| Pregnancy loss in the first trimester/total no. of women who conceived | 41/149 (27.5%) | 60/166 (36.1%) | 101/315 (32.1%) | 0.100 | −8.6 (−18.9 to 1.6) | 0.8 (0.5 to 1.1) |
| Pregnancy loss in the second or third trimester/total no. of women who conceived | 6/149 (4.0%) | 3/166 (1.8%) | 9/315 (2.9%) | 0.320 | 2.2 (−1.5 to 6.0) | 2.2 (0.6 to 8.8) |
| Biochemical factor/total no. of women who conceived | 31/149 (20.8%) | 49/166 (29.5%) | 80/315 (25.4%) | 0.080 | −8.7 (−18.2 to 0.8) | 0.7 (0.5 to 1.0) |

[a] Live birth was defined as the delivery of a live-born infant ≥ 20 weeks' gestation. Conception was defined as any positive serum level of human chorionic gonadotropin. Pregnancy was defined as an intrauterine pregnancy with fetal heart motion as determined by ultrasonography. Ovulation was defined as a serum progesterone level according to the standard of the local site laboratory (minimum value of luteal phase). Biochemical factor was defined as a positive urine or serum human chorionic gonadotropin test, but no fetus or gestational sac was visible on ultrasound.

[b] The chi-square test was used to compare the differences between three groups.

征和地理特征。在PCOS女性中，肥胖加剧生殖和代谢障碍，降低生育能力。不同的地域和表型特征可能主要归因于BMI差异以及BMI和不同临床结局之间的关系。

## 致谢

## Compliance with ethics guidelines

Jingshu Gao, Hongli Ma, Yu Wang, Xinming Yang, Yijuan Cao, Bei Zhang, Conghui Han, and Xiaoke Wu declare that they have no conflict of interest or financial conflicts to disclose.

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