

Review:

American, European, and Chinese practice guidelines or consensuses of polycystic ovary syndrome: a comparative analysis*

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Abstract: Polycystic ovary syndrome (PCOS) is the most common metabolic and endocrine disorder in women. However, there is no agreement concerning how to diagnose and treat PCOS worldwide. Three practice guidelines or consensuses, including consensus from the European Society of Human Reproduction and Embryology (ESHRE)/the American Society for Reproductive Medicine (ASRM) in Rotterdam, diagnosis criteria and consensus in China, and clinical practice guideline from the Endocrine Society (ES) in the United States are widely recognized. The present paper may provide some guidance for clinical practice based on a comparative analysis of the above three practice guidelines or consensuses.

Key words: Practice guideline; Consensus; Polycystic ovary syndrome

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1 Introduction

Polycystic ovary syndrome (PCOS), as the most common metabolic and endocrine disorder in women, is characterized by oligo-ovulation/anovulation, hyperandrogenism, and polycystic ovaries (Norman et al., 2007). The prevalence of PCOS in Chinese women aged between 12 and 44 years was 7.1%, 11.2%, and 7.4% according to the National Institutes of Health diagnostic criteria (1990), the revised Rotterdam diagnostic criteria for PCOS (2003), and the recommended diagnostic criteria for PCOS by the Androgen Excess Society (2006), respectively. The

prevalence of PCOS increases rapidly from 12 to 14 years of age, peaks between 15 and 24, and decreases gradually thereafter, reaching its lowest point before menopause (Zhuang et al., 2014).

Until now, there has been no agreement concerning how to diagnose and treat PCOS worldwide. However, three practice guidelines or consensuses, including consensus from the European Society of Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) in Rotterdam (The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004a, 2004b; The Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2008a, 2008b; Fauser et al., 2012; The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group, 2012), diagnosis criteria and consensus in China (Endocrinology Group et al., 2008; Chen et al., 2011), and clinical practice guideline from the Endocrine Society (ES) in the United States (Legro et al., 2013), are widely recognized. The

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present paper could provide some guidance for clinical practice based on a comparative analysis of the above practice guidelines and consensuses.

2 Diagnosis of PCOS

As shown in Table 1, the PCOS diagnostic criteria for adults from Rotterdam and ES are similar (The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004a, 2004b; The Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2008a, 2008b; The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group, 2012; Fauser et al., 2012; Legro et al., 2013). In both criteria, androgen excess, ovulatory dysfunction, and polycystic ovaries are equally important for the diagnosis of PCOS in adults. Women who meet any two of three conditions, excluding other disease, e.g. thyroid disease, hyperprolactinemia, congenital adrenal hyperplasia, androgen-secreting tumors, and Cushing's syndrome, could be diagnosed with PCOS. However, in the Chinese diagnostic criteria for PCOS, oligomenorrhea, amenorrhea, or irregular uterine bleeding was required for diagnosis of PCOS (Endocrinology Group et al., 2008; Chen et al., 2011). In other words, women with only hyperandrogenism and polycystic ovaries (but without oligo-/amenorrhea) could not be diagnosed with PCOS in China (Endocrinology Group et al., 2008; Chen et al., 2011). The difference between PCOS diagnosis criteria in China and other countries was probably a result of the distinct PCOS phenotype distribution in China (Li et al., 2013), which is associated with genetic (Cui et al., 2013) and environmental factors (Merkin et al., 2016). As early as 1992, it was found that obesity and hirsutism are associated with some genetic factors (Carmina et al., 1992), and the ethnic background of women with PCOS needs to be considered in studies that investigate its metabolic parameters (Norman et al., 1995). The serum levels of anti-Müllerian hormone (AMH) were also found to be a promising indicator in the diagnosis of PCOS (Laven et al., 2004; Pigny et al., 2006). These genetic and environmental factors should be considered during the initial assessment of PCOS patients.

According to the Rotterdam criteria, only an adolescent girl with oligo-/amenorrhea, hyper-

androgenemia, and polycystic ovaries could be diagnosed with PCOS (The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004a, 2004b; The Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2008a, 2008b; The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group, 2012; Fauser et al., 2012). However, in the ES criteria, confirmation of polycystic ovaries was not a necessary condition, mainly due to technical and interpretive uncertainties. Hyperandrogenism and persistent oligomenorrhea were considered the two main points of evidence of PCOS in adolescents in the ES criteria (Legro et al., 2013). Unfortunately, there was no mention of PCOS diagnosis in adolescents in the diagnostic criteria and consensus in China (Endocrinology Group et al., 2008; Chen et al., 2011). Hence, more attention should be given to PCOS in the Chinese adolescent population. As about one-half of menstrual cycles were anovulatory in the first two years after menarche in adolescent girls (Apter et al., 1993), and there existed some difficulties in the evaluation of polycystic ovary morphology, a more standard diagnosis protocol for the adolescent is urgently needed. As early as 1983 it was found that the measurement of plasma free testosterone before and after administration of dexamethasone appears to be the most sensitive single method for detecting PCOS in adolescents (Moll and Rosenfield, 1983). To test ovarian androgenic function in these adolescents may be of prognostic value, because those adolescents with functional ovarian hyperandrogenism have persistent hyperandrogenism, and glucose tolerance tends to deteriorate (Rosenfield et al., 2015). The ovarian androgenic function test could be considered in designing a specific diagnosis protocol for the adolescent.

Diagnosis of PCOS in perimenopause and menopause was first proposed in the ES criteria (Legro et al., 2013). However, as the ovarian volume and follicle number will gradually decrease with age, polycystic ovaries might present less frequently in menopausal women. As the diagnosis of PCOS in postmenopausal women was problematic, many of them may be diagnosed earlier. Since ethnic background plays an important role in the clinical manifestation of PCOS, an accurate diagnosis in menopausal Asian women needs more in-depth study.

Table 1 Diagnosis in the American, European, and Chinese practice guidelines or consensuses of PCOS

Population	Diagnostic criteria		
	2003 Rotterdam ¹	2011 China ²	2013 ES ³
In adults	At least 2 out of 3 criteria: (1) oligo- or anovulation; (2) clinical and/or biochemical signs of hyperandrogenism; (3) PCO. Exclusion: congenital adrenal hyperplasia, androgen-secreting tumors, or Cushing's syndrome.	Suspected PCOS: (1) oligomenorrhea, amenorrhea, or irregular uterine bleeding; (2) at least 1 out of 2 criteria: (a) clinical and/or biochemical signs of hyperandrogenism; (b) PCO. Definitive PCOS: (1) criteria of suspected PCOS; (2) exclusion: thyroid dysfunction, hyperprolactinemia, delayed adrenocortical hyperplasia, 21-hydroxylase deficiency, Cushing's syndrome, primary premature ovarian insufficiency or premature ovarian failure, ovarian or adrenal androgen-secreting tumors, or functional hypothalamic amenorrhea.	At least 2 out of 3 criteria: (1) androgen excess; (2) ovulatory dysfunction; (3) PCO. Exclusion: thyroid disease, hyperprolactinemia, or nonclassic congenital adrenal hyperplasia.
In adolescents	(1) Oligomenorrhea or amenorrhea present for at least 2 years after menarche (or primary amenorrhea at age 16 years); (2) The diagnosis of PCO on ultrasound includes increased ovarian size (>10 cm ³); (3) Hyperandrogenemia rather than just signs of androgen excess should be documented.		Clinical and/or biochemical evidence of hyperandrogenism (after exclusion of other pathologies), and persistent oligomenorrhea.
In perimenopause and menopause			Well-documented long-term history of oligomenorrhea and hyperandrogenism during the reproductive years. PCO on ultrasound is supportive.

¹ From The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group (2004a, 2004b), The Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group (2008a, 2008b), Fauser et al. (2012), and The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group (2012). ² From Endocrinology Group et al. (2008) and Chen et al. (2011). ³ From Legro et al. (2013). PCOS: polycystic ovary syndrome; ES: the Endocrine Society; ESHRE: the European Society of Human Reproduction and Embryology; ASRM: the American Society for Reproductive Medicine; PCO: polycystic ovary

3 Treatment of PCOS

As shown in Table 2, clinical treatment of PCOS around the world primarily focuses on seven aspects as follows.

3.1 Overweight and obesity

In dealing with the overweight and obesity, all three guidelines/consensuses recommend calorie-restricted diets and exercise (The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004a, 2004b; Endocrinology Group et al., 2008;

The Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2008a, 2008b; Chen et al., 2011; The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group, 2012; Fauser et al., 2012; Legro et al., 2013). Although lifestyle intervention can improve body composition, hyperandrogenism (high male hormones and clinical effects), and insulin resistance in PCOS women, no positive effect of lifestyle intervention on glucose tolerance or lipid profiles was found (Moran et al., 2011). Moreover, the consensus from China recommends quitting smoking or drinking (Endocrinology

Table 2 Treatments in the American, European, and Chinese practice guidelines or consensuses of PCOS

Treatment target	Clinical treatment		
	2003 Rotterdam ¹	2011 China ²	2013 ES ³
Overweight and obesity	Lifestyle modifications are the first-line treatment of obesity in PCOS. Caloric restriction and increased physical activity are recommended. Treatment of adverse lifestyles, including obesity and physical inactivity, should precede ovulation induction. A 5% decrease of body weight might be clinically meaningful.	Adjust lifestyle and quit smoking or drinking. Exercise therapy with calorie-restricted diets.	Exercise therapy, alone or in combination with dietary intervention, in the management of overweight and obesity in PCOS. Perform weight loss strategies begin with calorie-restricted diets for adolescents and women with PCOS who are overweight or obese.
Menstrual irregularity		HCs. Progestin.	HCs are the first-line treatment. Metformin is the second-line treatment.
Hyperandrogenism	Prolonged (>6 months) medical therapy for hirsutism is necessary to document effectiveness. No effective treatment for alopecia is known. Antiandrogens should not be used without effective contraception. Flutamide is of limited value. Drospirenone in some OCs is not antiandrogenic.	HCs e.g. Diane 35 for 3 months (acne) to 6 months (hirsutism).	HCs are the first-line treatment.
Insulin resistance	Diet and lifestyle are first choice for prevention of T2DM. Metformin may be used for IGT and T2DM. Avoid use of other insulin sensitizing agents.	Metformin (for obesity or insulin resistance).	Metformin (for PCOS women with T2DM or IGT who fail lifestyle modification).
Infertility	CC is first choice for induction of ovulation in most anovulatory women with PCOS. Anti-estrogen and aromatase inhibitors appear to be as effective as CC for induction of ovulation. Gonadotropin. Laparoscopic ovarian surgery is an alternative to gonadotropin therapy for CC-resistant anovulatory PCOS. IVF-ET.	CC is first-line. Gonadotrophin: hMG, HP-FSH and r-FSH. Laparoscopic ovarian drilling. IVF-ET.	CC (or comparable estrogen modulators such as letrozole) is first-line. Metformin as an adjuvant therapy for infertility to prevent ovarian hyperstimulation syndrome.
Adolescents			HCs are the first-line treatment in adolescents with suspected PCOS. Lifestyle therapy (calorie-restricted diet and exercise) with the objective of weight loss also is first-line treatment in the presence of overweight/obesity. Metformin as a possible treatment if the goal is to treat IGT/metabolic syndrome. HCs for hyperandrogenism in the presence of advanced pubertal development.

¹ From The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group (2004a, 2004b), The Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group (2008a, 2008b), Fauser et al. (2012), and The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group (2012). ² From Endocrinology Group et al. (2008) and Chen et al. (2011). ³ From Legro et al. (2013). PCOS: polycystic ovary syndrome; ES: the Endocrine Society; HCs: hormonal contraceptives; OCs: oral contraceptives; T2DM: type 2 diabetes mellitus; IGT: impaired glucose tolerance; CC: clomiphene citrate; IVF-ET: in vitro fertilization-embryo transfer; hMG: human menopausal gonadotropin; HP-FSH: highly purified follicle stimulating hormone; r-FSH: recombinant follicle stimulating hormone

Group et al., 2008; Chen et al., 2011), as smoking may worsen the already high risk for metabolic syndrome in women with PCOS (Pau et al., 2013). The importance of training and awareness raising should be emphasized. The consensus in Rotterdam also mentioned the issue of conception and pregnancy while undertaking hypocaloric diets, excessive physical exertion, pharmacologic intervention, or during the period of rapid weight loss after bariatric surgery, as the effects of these interventions on the evolution of early pregnancy are not yet known (Endocrinology Group et al., 2008; Chen et al., 2011). Due to enhanced feelings of well-being, it is possible that high-protein and low-carbohydrate diets may be associated with better compliance and hence be more successful in the long-term treatment of obesity (Galletly et al., 2007). Specific ethnicity-based protocols for calorie-restricted diets and exercise are urgently needed.

3.2 Menstrual irregularity

Menstrual irregularity within the first post-menarchal years can be an early clinical sign of PCOS (Avvad et al., 2001). Both the diagnosis criteria and consensus in China and the clinical practice guideline from the ES recommend hormonal contraceptives (HCs) as the first-line treatment (Endocrinology Group et al., 2008; Chen et al., 2011; Legro et al., 2013). Additionally, the clinical practice guideline from the ES recommends metformin as the second-line treatment, and the consensus in China recommends progestin as another intervention (Endocrinology Group et al., 2008; Chen et al., 2011; Legro et al., 2013). It was recently found that cabergoline can be used as a safe administration in PCOS patients with hyperprolactinemia to improve menstrual cycles and the patient acceptability of this approach is higher due to a shorter treatment duration and lower dosage of metformin (Ghaneei et al., 2015). Treatment with pioglitazone can also improve the irregularities of menses and hirsutism (Stabile et al., 2014). Although menstrual irregularity is the most common symptom of PCOS patients, clinicians should initially conduct a comprehensive analysis of the patient. For patients who cannot or are not willing to receive HCs or other drugs, complementary and alternative medicine, including traditional Chinese medicine and acupuncture, are promising treatments for the menstrual irregularity of PCOS patients (Wu et al., 2016; Qu et al., 2017).

3.3 Hyperandrogenism

Hyperandrogenism is the most constant and prominent diagnostic component of PCOS (Wang et al., 2015), and 60%–80% PCOS women suffer from hyperandrogenism (Norman et al., 2007). Both the consensus in China (Endocrinology Group et al., 2008; Chen et al., 2011) and the clinical practice guideline from the ES (Legro et al., 2013) recommend HCs for the hirsutism/acne of PCOS. Hyperandrogenism is assessed by observation of clinical manifestations (hirsutism/acne), biochemical indexes, or both. PCOS patients present more severe hyperandrogenic and obese phenotypes than patients from the general population (Luque-Ramirez et al., 2015). In PCOS women, the progestin in HCs suppresses luteinizing hormone (LH) secretions and the subsequent androgen synthesis, and the estrogens in HCs increase sex hormone binding globulin, thus reducing bioavailable androgen (Rivera et al., 1999). Generally, patients are advised to take HCs for three months for acne and for six months for hirsutism. Although the ES suggests the androgen-reducing activity of metformin (Legro et al., 2013), it is not very effective in reducing the severity of hirsutism in PCOS (Harborne et al., 2003; Cosma et al., 2008). Therefore, metformin is not recommended to be used for the management of hyperandrogenism (Milewicz, 2013). Moreover, a new *myo*-inositol, monacolin K, and lipoic acid association was recently found to contain appropriate substances to contrast various etiopathogenic elements responsible for the onset of PCOS and the symptoms of hyperandrogenism (Morgante et al., 2015).

3.4 Insulin resistance

PCOS women seem to have peripheral insulin resistance, which is characterised by a 35%–40% decrease in insulin-mediated glucose uptake (Dunaif et al., 1992). A diagnosis of PCOS confers a 5- to 10-fold increased risk of developing type 2 diabetes mellitus (T2DM) (Ehrmann et al., 1999; Legro et al., 1999). It is well-known that weight loss therapy and lifestyle modifications are the first-line therapy for obese PCOS women (Thomson et al., 2009; Harrison et al., 2011). All three guidelines/consensuses consistently recommend metformin as the first-line treatment in women with PCOS who have T2DM or impaired glucose tolerance (IGT), or who fail lifestyle

modification. It was recently found that 12 weeks of carnitine administration can lead to reductions in weight, body mass index (BMI), waist circumference, and hip circumference in PCOS women, and show beneficial effects on glycaemic control; however, it did not affect lipid profiles or free testosterone (Samimi et al., 2016). Chromium picolinate is useful in PCOS to reduce insulin resistance and stimulate ovulation (Ashoush et al., 2016) and 220 mg zinc sulfate supplementation per day for 8 weeks among PCOS women was found to have beneficial effects on metabolic profiles (Foroozanfard et al., 2015).

3.5 Infertility

PCOS women are at increased risk of anovulation and infertility (Norman et al., 2007), and infertility is often the presenting complaint of PCOS women (Goldzieher and Axelrod, 1963). Considering the prevalence of PCOS and the health and economic burden of infertility, strategies to optimize fertility are important (Joham et al., 2015). All three guidelines/consensuses regard clomiphene citrate (CC) as the first choice for induction of ovulation in anovulatory women with PCOS, and both Rotterdam and the ES suggest comparable estrogen modulators, such as letrozole, as an effective therapy for the induction of ovulation in PCOS (The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004a, 2004b; The Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2008a, 2008b; The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group, 2012; Fauser et al., 2012; Legro et al., 2013). It was recently found that letrozole is associated with higher live-birth and ovulation rates among infertile women with PCOS compared with CC (Legro et al., 2014). For treating the infertility resulting from PCOS, aromatase inhibitors are promising; however, longer term studies are necessary to prove their safety (Melo et al., 2015).

The consensuses of Rotterdam and China also suggest gonadotropin therapy as an effective therapy for restoring fertility, and laparoscopic ovarian surgery is an alternative to gonadotropin therapy for CC-resistant anovulatory PCOS (The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004a, 2004b; Endocrinology Group et al., 2008; The Thessaloniki ESHRE/ASRM-Sponsored PCOS Con-

sensus Workshop Group, 2008a, 2008b; Chen et al., 2011; The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group, 2012; Fauser et al., 2012). The clinical practice guideline from the ES states that in clomiphene-resistant women, metformin plus clomiphene lead to higher live-birth rates than clomiphene alone and metformin also leads to higher live birth rates than laparoscopic ovarian drilling (Legro et al., 2013). To sum up, a detailed specific and ethnicity-based strategy is urgently needed. The long-term effects of estrogen modulators and other common interventions of treating the infertility of PCOS women should be explored.

3.6 Adolescents

The clinical practice guideline from the ES pays more attention to adolescents with PCOS (Legro et al., 2013). HCs are recommended as the first-line treatment in adolescents with suspected PCOS, and lifestyle therapy (calorie-restricted diet and exercise) is recommended as the first-line treatment in the presence of overweight/obesity. A higher prevalence of obstructive sleep apnoea and metabolic dysfunction was found in a selected group of obese girls with PCOS referred with sleep-related complaints compared to BMI-matched control girls without PCOS (Nandalike et al., 2012). The related treatment for respiratory and metabolic dysfunctions should also be considered. In addition, yoga was more effective than conventional physical exercises in improving glucose, lipid, and insulin values, including insulin resistance values, in adolescent girls with PCOS independent of anthropometric change (Nidhi et al., 2012). Supplementation with chromium for adolescents with PCOS is also a promising treatment option (Amr and Abdel-Rahim, 2015). Although dietary interventions were beneficial for weight control, it failed to attenuate biochemical hyperandrogenism. Innovative strategies are needed to explore the independent effects of diet on the features of adolescents with PCOS. Traditional Chinese medicine could also be chosen as an alternative treatment for PCOS adolescents.

3.7 Psychological interventions

The ES guideline mentions an increased prevalence of depression and anxiety in women with PCOS, and suggests screening women and adolescents with PCOS for depression and anxiety, and, if identified,

providing appropriate referral and/or treatment (Legro et al., 2013). The Rotterdam consensus indicates that PCOS women are an at-risk group for psychological and behavioral disorders and reduced quality of life, including depression, anxiety, eating disorders, sexual and relationship dysfunction (The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004a, 2004b; The Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2008a, 2008b; The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group, 2012; Fauser et al., 2012). More attention should be paid to psychological intervention in China. Although infertility does not appear to constitute a primary determinant of psychological problems (Tan et al., 2008), excess body hair, obesity, and menstrual abnormalities carry unique risks for adverse psychological symptoms, and menstrual problems may be the most salient of these features and deserve particular concern as a marker for psychological risk among women with PCOS (McCook et al., 2015).

As early as 1983, it was hypothesized that psychological stress and neurotransmitter levels may be linked to some of the hormonal derangements, including inappropriate gonadotropin secretion and elevated adrenal androgen levels in PCOS patients (Lobo et al., 1983). Group counselling sessions focusing on supportive relationships followed by high-intensity aerobic training were found to have beneficial effects on the well-being, health, and exercise behavior of PCOS women (Roessler et al., 2012).

In summary, PCOS represents a major risk factor for psychosocial and emotional problems. PCOS women should undergo psychological screening to improve their long-term prognosis. Due to the high prevalence of depression and anxiety in PCOS women (Bazarganipour et al., 2013), psychological assessment is clearly necessary, which may influence the curative effects of any intervention for PCOS.

4 Conclusions

Considering the wide variation in the clinical presentations associated with PCOS among distinct ethnicities, there is an urgent need for the establishment of ethnicity-specific guidelines for this condi-

tion, which may help to prevent the under- or over-diagnosis of PCOS as well as improve treatment outcomes.

Compliance with ethics guidelines

Fang-fang WANG, Jie-xue PAN, Yan WU, Yu-hang ZHU, Paul J. HARDIMAN, and Fan QU declare that they have no conflict of interest.

This article does not contain any studies with human or animal subjects performed by any of the authors.

References

- Amr N, Abdel-Rahim HE, 2015. The effect of chromium supplementation on polycystic ovary syndrome in adolescents. *J Pediatr Adolesc Gynecol*, 28(2):114-118. <https://doi.org/10.1016/j.jpag.2014.05.005>
- The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group, 2012. Consensus on women's health aspects of polycystic ovary syndrome (PCOS). *Hum Reprod*, 27(1):14-24. <https://doi.org/10.1093/humrep/der396>
- Apter D, Butzow T, Laughlin G, 1993. Hyperandrogenism during Puberty and Adolescence, and Its Relationship to Reproductive Function in the Adult Female. Raven Press, p.265.
- Ashoush S, Abou-Gamrah A, Bayoumy H, et al., 2016. Chromium picolinate reduces insulin resistance in polycystic ovary syndrome: randomized controlled trial. *J Obstet Gynaecol Res*, 42(3):279-285. <https://doi.org/10.1111/jog.12907>
- Avvad CK, Holeuwerger R, Silva VC, et al., 2001. Menstrual irregularity in the first postmenarchal years: an early clinical sign of polycystic ovary syndrome in adolescence. *Gynecol Endocrinol*, 15(3):170-177. <https://doi.org/10.1080/713602836>
- Bazarganipour F, Ziaei S, Montazeri A, et al., 2013. Psychological investigation in patients with polycystic ovary syndrome. *Health Qual Life Out*, 11:141. <https://doi.org/10.1186/1477-7525-11-141>
- Carmina E, Koyama T, Chang L, et al., 1992. Does ethnicity influence the prevalence of adrenal hyperandrogenism and insulin resistance in polycystic ovary syndrome? *Am J Obstet Gynecol*, 167(6):1807-1812. [https://doi.org/10.1016/0002-9378\(92\)91779-A](https://doi.org/10.1016/0002-9378(92)91779-A)
- Chen ZJ, Zhang YW, Liu JY, et al., 2011. Diagnosis criteria for polycystic ovary syndrome. *Natl Health Fam Plan Commission China*, 330:1-7 (in Chinese).
- Cosma M, Swiglo BA, Flynn DN, et al., 2008. Clinical review: insulin sensitizers for the treatment of hirsutism: a systematic review and metaanalyses of randomized controlled trials. *J Clin Endocrinol Metab*, 93(4):1135-1142. <https://doi.org/10.1210/jc.2007-2429>
- Cui LL, Zhao H, Zhang B, et al., 2013. Genotype-phenotype correlations of PCOS susceptibility SNPs identified by GWAS in a large cohort of Han Chinese women. *Hum*

- Reprod*, 28(2):538-544.
<https://doi.org/10.1093/humrep/des424>
- Dunaif A, Segal KR, Shelley DR, et al., 1992. Evidence for distinctive and intrinsic defects in insulin action in polycystic ovary syndrome. *Diabetes*, 41(10):1257-1266.
<https://doi.org/10.2337/diabetes.41.10.1257>
- Ehrmann DA, Barnes RB, Rosenfield RL, et al., 1999. Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. *Diabet Care*, 22(1):141-146.
<https://doi.org/10.2337/diacare.22.1.141>
- Endocrinology Group, Obstetrics and Gynecology Committee, China Medical Association, 2008. Consensus on the diagnosis and treatment for polycystic ovary syndrome. *Chin J Obstet Gynecol*, 43(7):553-555 (in Chinese).
- Fausser BC, Tarlatzis BC, Rebar RW, et al., 2012. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. *Fertil Steril*, 97(1):28-38.
<https://doi.org/10.1016/j.fertnstert.2011.09.024>
- Foroozafard F, Jamilian M, Jafari Z, et al., 2015. Effects of zinc supplementation on markers of insulin resistance and lipid profiles in women with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial. *Exp Clin Endocrinol Diabet*, 123(04):215-220.
<https://doi.org/10.1055/s-0035-1548790>
- Galletly C, Moran L, Noakes M, et al., 2007. Psychological benefits of a high-protein, low-carbohydrate diet in obese women with polycystic ovary syndrome—a pilot study. *Appetite*, 49(3):590-593.
<https://doi.org/10.1016/j.appet.2007.03.222>
- Ghaneai A, Jowkar A, Ghavam MRH, et al., 2015. Cabergoline plus metformin therapy effects on menstrual irregularity and androgen system in polycystic ovary syndrome women with hyperprolactinemia. *Iran J Reprod Med*, 13(2):93-100.
- Goldzieher JW, Axelrod LR, 1963. Clinical and biochemical features of polycystic ovarian disease. *Fertil Steril*, 14(6):631-653.
[https://doi.org/10.1016/S0015-0282\(16\)35047-6](https://doi.org/10.1016/S0015-0282(16)35047-6)
- Harborne L, Fleming R, Lyall H, et al., 2003. Metformin or antiandrogen in the treatment of hirsutism in polycystic ovary syndrome. *J Clin Endocrinol Metab*, 88(9):4116-4123.
<https://doi.org/10.1210/jc.2003-030424>
- Harrison CL, Lombard CB, Moran LJ, et al., 2011. Exercise therapy in polycystic ovary syndrome: a systematic review. *Hum Reprod Update*, 17(2):171-183.
<https://doi.org/10.1093/humupd/dmq045>
- Joham AE, Teede HJ, Ranasingha S, et al., 2015. Prevalence of infertility and use of fertility treatment in women with polycystic ovary syndrome: data from a large community-based cohort study. *J Womens Health*, 24(4):299-307.
<https://doi.org/10.1089/jwh.2014.5000>
- Laven JS, Mulders AGMGJ, Visser JA, et al., 2004. Anti-mullerian hormone serum concentrations in normoovulatory and anovulatory women of reproductive age. *J Clin Endocrinol Metab*, 89(1):318-323.
<https://doi.org/10.1210/jc.2003-030932>
- Legro RS, Kunselman AR, Dodson WC, et al., 1999. Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome: a prospective, controlled study in 254 affected women. *J Clin Endocrinol Metab*, 84(1):165-169.
<https://doi.org/10.1210/jcem.84.1.5393>
- Legro RS, Arslanian SA, Ehrmann DA, et al., 2013. Diagnosis and treatment of polycystic ovary syndrome: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*, 98(12):4565-4592.
<https://doi.org/10.1210/jc.2013-2350>
- Legro RS, Brzyski RG, Diamond MP, et al., 2014. Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. *N Engl J Med*, 371(2):119-129.
<https://doi.org/10.1056/NEJMoa1313517>
- Li R, Zhang Q, Yang D, et al., 2013. Prevalence of polycystic ovary syndrome in women in China: a large community-based study. *Hum Reprod*, 28(9):2562-2569.
<https://doi.org/10.1093/humrep/det262>
- Lobo RA, Granger LR, Paul WL, et al., 1983. Psychological stress and increases in urinary norepinephrine metabolites, platelet serotonin, and adrenal androgens in women with polycystic ovary syndrome. *Am J Obstet Gynecol*, 145(4):496-503.
[https://doi.org/10.1016/0002-9378\(83\)90324-1](https://doi.org/10.1016/0002-9378(83)90324-1)
- Luque-Ramirez M, Alpanes M, Sanchon R, et al., 2015. Referral bias in female functional hyperandrogenism and polycystic ovary syndrome. *Eur J Endocrinol*, 173(5):603-610.
<https://doi.org/10.1530/EJE-15-0646>
- McCook JG, Bailey BA, Williams SL, et al., 2015. Differential contributions of polycystic ovary syndrome (PCOS) manifestations to psychological symptoms. *J Behav Health Serv Res*, 42(3):383-394.
<https://doi.org/10.1007/s11414-013-9382-7>
- Melo AS, Ferriani RA, Navarro PA, 2015. Treatment of infertility in women with polycystic ovary syndrome: approach to clinical practice. *Clinics*, 70(11):765-769.
[https://doi.org/10.6061/clinics/2015\(11\)09](https://doi.org/10.6061/clinics/2015(11)09)
- Merkin SS, Phy JL, Sites CK, et al., 2016. Environmental determinants of polycystic ovary syndrome. *Fertil Steril*, 106(1):16-24.
<https://doi.org/10.1016/j.fertnstert.2016.05.011>
- Milewicz A, 2013. Reimbursement of metformin for polycystic ovary syndrome. *Endokrynol Pol*, 64(5):409-414.
<https://doi.org/10.5603/EP.2013.0025>
- Moll GW, Rosenfield RL, 1983. Plasma free testosterone in the diagnosis of adolescent polycystic ovary syndrome. *J Pediatr*, 102(3):461-464.
[https://doi.org/10.1016/S0022-3476\(83\)80678-7](https://doi.org/10.1016/S0022-3476(83)80678-7)
- Moran LJ, Hutchison SK, Norman RJ, et al., 2011. Lifestyle changes in women with polycystic ovary syndrome.

- Cochrane Database Syst Rev*, 7:CD007506.
<https://doi.org/10.1002/14651858.CD007506.pub3>
- Morgante G, Cappelli V, di Sabatino A, et al., 2015. Polycystic ovary syndrome (PCOS) and hyperandrogenism: the role of a new natural association. *Minerva Ginecol*, 67(5):457-463.
- Nandalike K, Agarwal C, Strauss T, et al., 2012. Sleep and cardiometabolic function in obese adolescent girls with polycystic ovary syndrome. *Sleep Med*, 13(10):1307-1312.
<https://doi.org/10.1016/j.sleep.2012.07.002>
- Nidhi R, Padmalatha V, Nagarathna R, et al., 2012. Effect of a yoga program on glucose metabolism and blood lipid levels in adolescent girls with polycystic ovary syndrome. *Int J Gynaecol Obstet*, 118(1):37-41.
<https://doi.org/10.1016/j.ijgo.2012.01.027>
- Norman RJ, Mahabeer S, Masters S, 1995. Ethnic differences in insulin and glucose response to glucose between white and Indian women with polycystic ovary syndrome. *Fertil Steril*, 63(1):58-62.
[https://doi.org/10.1016/S0015-0282\(16\)57297-5](https://doi.org/10.1016/S0015-0282(16)57297-5)
- Norman RJ, Dewailly D, Legro RS, et al., 2007. Polycystic ovary syndrome. *Lancet*, 370(9588):685-697.
[https://doi.org/10.1016/S0140-6736\(07\)61345-2](https://doi.org/10.1016/S0140-6736(07)61345-2)
- Pau CT, Keefe CC, Welt CK, 2013. Cigarette smoking, nicotine levels and increased risk for metabolic syndrome in women with polycystic ovary syndrome. *Gynecol Endocrinol*, 29(6):551-555.
<https://doi.org/10.3109/09513590.2013.788634>
- Pigny P, Jonard S, Robert Y, et al., 2006. Serum anti-mullerian hormone as a surrogate for antral follicle count for definition of the polycystic ovary syndrome. *J Clin Endocrinol Metab*, 91(3):941-945.
<https://doi.org/10.1210/jc.2005-2076>
- Qu F, Li R, Sun W, et al., 2017. Use of electroacupuncture and transcutaneous electrical acupoint stimulation in reproductive medicine: a group consensus. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)*, 18(3):186-193.
<https://doi.org/10.1631/jzus.B1600437>
- Rivera R, Yacobson I, Grimes D, 1999. The mechanism of action of hormonal contraceptives and intrauterine contraceptive devices. *Am J Obstet Gynecol*, 181(5):1263-1269.
[https://doi.org/10.1016/S0002-9378\(99\)70120-1](https://doi.org/10.1016/S0002-9378(99)70120-1)
- Roessler KK, Glintborg D, Ravn P, et al., 2012. Supportive relationships—psychological effects of group counselling in women with polycystic ovary syndrome (PCOS). *Commun Med*, 9(2):125-131.
- Rosenfield RL, Ehrmann DA, Littlejohn EE, 2015. Adolescent polycystic ovary syndrome due to functional ovarian hyperandrogenism persists into adulthood. *J Clin Endocrinol Metab*, 100(4):1537-1543.
<https://doi.org/10.1210/jc.2014-4290>
- The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004a. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertil Steril*, 81(1):19-25.
<https://doi.org/10.1016/j.fertnstert.2003.10.004>
- The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004b. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). *Hum Reprod*, 19(1):41-47.
<https://doi.org/10.1093/humrep/deh098>
- Samimi M, Jamilian M, Ebrahimi FA, et al., 2016. Oral carnitine supplementation reduces body weight and insulin resistance in women with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial. *Clin Endocrinol*, 84(6):851-857.
<https://doi.org/10.1111/cen.13003>
- Stabile G, Borrielli I, Arsenio AC, et al., 2014. Effects of the insulin sensitizer pioglitazone on menstrual irregularity, insulin resistance and hyperandrogenism in young women with polycystic ovary syndrome. *J Pediatr Adolesc Gynecol*, 27(3):177-182.
<https://doi.org/10.1016/j.jpog.2013.09.015>
- Tan S, Hahn S, Benson S, et al., 2008. Psychological implications of infertility in women with polycystic ovary syndrome. *Hum Reprod*, 23(9):2064-2071.
<https://doi.org/10.1093/humrep/den227>
- The Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2008a. Consensus on infertility treatment related to polycystic ovary syndrome. *Fertil Steril*, 89(3):505-522.
<https://doi.org/10.1016/j.fertnstert.2007.09.041>
- The Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2008b. Consensus on infertility treatment related to polycystic ovary syndrome. *Hum Reprod*, 23(3):462-477.
<https://doi.org/10.1093/humrep/dem426>
- Thomson RL, Buckley JD, Moran LJ, et al., 2009. Comparison of aerobic exercise capacity and muscle strength in overweight women with and without polycystic ovary syndrome. *BJOG*, 116(9):1242-1250.
<https://doi.org/10.1111/j.1471-0528.2009.02177.x>
- Wang F, Pan J, Liu Y, et al., 2015. Alternative splicing of the androgen receptor in polycystic ovary syndrome. *Proc Natl Acad Sci USA*, 112(15):4743-4748.
<https://doi.org/10.1073/pnas.1418216112>
- Wu Y, Robinson N, Hardiman P, et al., 2016. Acupuncture for treating polycystic ovary syndrome: guidance for future randomized controlled trials. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)*, 17(3):169-180.
<https://doi.org/10.1631/jzus.B1500301>
- Zhuang J, Liu Y, Xu L, et al., 2014. Prevalence of the polycystic ovary syndrome in female residents of Chengdu, China. *Gynecol Obstet Invest*, 77(4):217-223.
<https://doi.org/10.1159/000358485>

中文概要

题目：关于美国、欧洲和中国的多囊卵巢综合征临床指南或共识的比较分析

概 要: 通过比较欧洲人类生殖和胚胎学会和美国生殖医学协会联合发表的鹿特丹共识、中国的多囊卵巢综合征诊治标准专家共识和美国内分泌学会的临床实践指南, 分析了不同指南对育龄期、青春期和围绝经期多囊卵巢综合征诊断标准的差异, 概括了多囊卵巢综合征临床治疗的主要方面, 同时提出了一些诊治方面的新进展及今后需要进一步关注的问题。在多囊卵巢综合征的诊断上, 对育

龄期女性的标准三大指南略有不同, 而对青春期和围绝经期女性的标准尚待完善。多囊卵巢综合征的治疗主要围绕肥胖、月经失调、高雄激素血症、胰岛素抵抗、不孕、青春期、心理干预等进行, 各大指南各有侧重。由于不同种族的多囊卵巢综合征的临床表现差异较大, 需要尽早建立具有种族特异性的指南来改善诊疗过度或不足的情况。

关键词: 多囊卵巢综合征; 临床指南; 专家共识