

Polycystic ovary syndrome in Singapore

Thomas FJ King^{1,2} *FRCP (Edin)*

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in young women, affecting approximately 10% of women. It is a heterogeneous condition that can present with a wide spectrum of signs and symptoms, including acne, hirsutism, obesity, menstrual irregularities and infertility. It is a complex trait that is thought to arise from the interaction of genetic and environmental factors. The underlying pathophysiology is a combination of both ovarian hyperandrogenism and insulin resistance, which in itself is linked to other long-term cardiometabolic consequences.

Standardised diagnostic criteria are important to allow appropriate identification of patients for clinical management and for screening of associated complications. The diagnostic criteria have evolved over the years, and this evolution has led to some diagnostic differences and even difficulty among healthcare providers, which can translate to mixed messages and patient confusion. The first diagnostic criteria stemmed from a meeting at the US National Institutes of Health (NIH) in 1990, which recommended that the diagnosis be made on the basis of chronic anovulation (CA) and clinical or biochemical hyperandrogenism (H), but without reference to polycystic ovary morphology (PCOm) on ultrasound.¹

In 2003, a joint meeting of the European Society for Human Reproduction and Embryology and American Society for Reproductive Medicine (ESHRE/ASRM) was held in Rotterdam, the Netherlands to update the diagnostic criteria.² These revised criteria proposed that the presence of 2 of the 3 features, namely, CA, H and PCom, would be sufficient for diagnosis of PCOS.

In terms of the specifics of the 3 criteria, CA is defined as less than 8 menstrual cycles per year, or more than 35 days between cycles. Hyperandrogenism is defined by clinical features (hirsutism, acne and androgenic alopecia), or an elevated serum testosterone level. Ultrasound features are classified as more than 12 antral follicles (measuring 2–9mm in diameter) or an ovarian volume of greater than 10cm³ in either ovary. Before confirming a diagnosis of PCOS, other conditions such

as thyroid dysfunction, hyperprolactinaemia, congenital adrenal hyperplasia, androgen-secreting tumours and Cushing's syndrome should be excluded.²

From the diagnostic selection of 2 out of 3 of the clinical features emerge 4 distinct potential phenotypes: H-CA, H-PCOm, CA-PCOm and all 3 features in H-CA-PCOm. A phenotype-based approach can help to tailor the management to a patient's specific needs, which is particularly useful in a heterogeneous condition that is managed by many disciplines. In Singapore, PCOS is generally managed by primary care, endocrinology, gynaecology and reproductive medicine, and each discipline has its own strengths that can be tailored to the patient's phenotype and specific needs. Regardless of the managing discipline, screening for associated conditions such as endometrial hyperplasia, metabolic syndrome, type 2 diabetes, subclinical cardiovascular disease, obstructive sleep apnoea, anaemia, vitamin D deficiency, depression and anxiety should be considered.³

In 2006, the Androgen Excess and PCOS (AE-PCOS) Society suggested a compromise between the 2 sets of diagnostic criteria, proposing that PCOS is mainly a hyperandrogenic disorder, and hyperandrogenism is essential for the diagnosis.⁴

The 2003 Rotterdam diagnostic criteria have been the mainstay in medical education and clinical practice, and they are useful for standardisation for clinical research. However, there are some caveats with their use.

With the development of high-resolution transvaginal ultrasonography, features that fit the diagnostic criteria set out in 2003 may be seen in more than 50% of normal young ovulatory women.⁵ In 2018, updated joint guidelines from ESHRE/ASRM revised the ultrasound criteria, specifically that for >8MHz transvaginal scans, a cut-off of >20 follicles per ovary should be applied.⁶ They also highlight the diagnostic difficulties in adolescents, where menstrual irregularity and multifollicular ovaries are common, and that scanning may be deferred until 8 years post-menarche.

Hirsutism may be graded based on the modified Ferriman-Gallwey score, but this is still relatively

¹ Department of Endocrinology, Changi General Hospital, Singapore

² Department of Reproductive Medicine, KK Women's and Children's Hospital, Singapore

Correspondence: Dr Thomas FJ King, Department of Endocrinology, Changi General Hospital, 2 Simei St 3, Singapore 529889.

Email: thomas.king@singhealth.com.sg

subjective. It is also important to bear in mind normal ethnic differences in hair distribution. While a score of ≥ 8 is taken to be abnormal in Caucasian women, scores of 3–6 may be more appropriate cut-offs for East Asian populations, and possibly higher values for South Asian populations.⁷ Furthermore, hirsutism may be less severe in adolescence and it is often self-treated before the patient presents to her doctor.

The measurement of testosterone is subject to clinical and assay variation. The majority of circulating testosterone is bound to sex hormone binding globulin (SHBG) and albumin, so conditions that affect these levels will affect the interpretation of the total testosterone result.

Biochemical assessment can be made using total testosterone, calculated free testosterone, calculated bioavailable testosterone or free androgen index. Where necessary, free testosterone may be measured by liquid chromatography-tandem mass spectrometry, but the currently available direct immunoassays for free testosterone are of limited value.⁶

In this issue of the *Annals*, Teoh et al. noted the complications in diagnosis, and the wide spectrum of clinicians treating PCOS in Singapore.⁸ This is because there is a spectrum of patient profiles, and those presenting with menstrual irregularities or infertility may be seen by a gynaecologist, while those with hyperandrogenism and glucose intolerance may be seen by an endocrinologist. The authors also noted a lack of studies in Southeast Asia, and an absence of a systemic referral system specific to PCOS. Hence their aim was to study clinicians treating PCOS, primarily with regard to knowledge of clinical features and diagnostic criteria, and secondarily to assess physician knowledge of complications and management of PCOS. A web-based survey was sent to all clinicians involved in the care of PCOS patients in Singapore, throughout disciplines in the public and private sector. Respondents had to identify modalities

for diagnosis that aligned with guidelines including those from NIH 1990, Rotterdam 2003, AE-PCOS 2006 and ESHRE 2018. Along with the 4 core diagnostic criteria (CA, PCOM, clinical hyperandrogenism and biochemical hyperandrogenism), peripheral criteria such as luteinising hormone to follicle-stimulating hormone ratio, anti-Müllerian hormone and SHBG were included.

Data from 160 participants were included in the analysis, around half of whom were specialists. Almost all physicians from gynaecology and endocrinology reported using diagnostic criteria, of which the 2003 Rotterdam were the most commonly used (66.3%). This is consistent with data on current physician practice in Europe and North America—71% chose at least 1 incorrect modality to diagnose PCOS, and only 39.5% could identify the correct clinical features, of whom a significant majority were gynaecologists. The majority (over 95%) recognised type 2 diabetes and infertility as complications of PCOS, but only about one third of respondents recognised other complications such as depression and anxiety. Endocrinologists were most concerned about non-alcoholic steatohepatitis, and gynaecologists were most concerned about endometrial cancer. Gynaecologists were most likely to have a standardised protocol at their workplace (62%). The majority of respondents expressed that the provision of standardised educational materials would help them care for patients.

In summary, care for patients with PCOS in Singapore could be improved in a number of areas. Investigating patient experiences and satisfaction levels would complement the findings of the current study. Singapore clinical practice guidelines could help to streamline referral pathways, harmonise diagnosis and management, improve screening for complications, and lead to overall better patient satisfaction and long-term outcomes.

Table 1. Summary of 3 diagnostic criteria for polycystic ovary syndrome

National Institutes of Health consensus criteria 1990 ¹ (all required)	Rotterdam ESHRE/ASRM 2003 ² (2 out of 3 required)	AE-PCOS definition 2008 ⁴ (all required)
Clinical and/or biochemical signs of hyperandrogenism	Clinical and/or biochemical signs of hyperandrogenism	Clinical and/or biochemical signs of hyperandrogenism
Oligo- or anovulation	Oligo- or anovulation	Ovarian dysfunction: oligo/anovulation and/or polycystic ovary morphology on ultrasound
Polycystic ovary morphology on ultrasound		

AE-PCOS: Androgen Excess and PCOS Society; ESHRE/ASRM: European Society for Human Reproduction and Embryology/American Society for Reproductive Medicine; PCOS: polycystic ovary syndrome

Superscript numbers: Refer to numbers in REFERENCES

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