

PCOS and Infertility: An Evidence-Based Approach

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No Disclosures

- I have no relevant financial relationships to disclose.

Objectives

- Review diagnostic criteria for PCOS
- Understand mechanisms underlying anovulation and infertility in PCOS patients
- Describe ovulation induction and methods of monitoring for ovulation
- Discuss the current literature on treatment of infertility related to PCOS

Quick Review – What is PCOS?

- Most common endocrine disorder in women
- Prevalence: 6-12% of reproductive-aged women
- Reproductive and metabolic disorder
- Diagnosis by NIH or Rotterdam criteria



Clinical Features

- Hyperandrogenism (clinical **or** biochemical)
 - Hirsutism
 - Acne
- Chronic anovulation (oligomenorrhea)
- Metabolic syndrome
- Obesity
- Increased risk for DM, CAD, endometrial cancer



Diagnostic Criteria

- NIH criteria
- Rotterdam criteria (2003)
 - Expanded definition
 - More patients fit criteria



What is PCO morphology?

- Ultrasound imaging in PCOS patients usually reveals enlarged ovaries
- 12 or more antral follicles (2-9 mm) per ovary
- Increased ovarian volume (> 10 cm³)
- **Note: Cannot diagnose PCO morphology in the presence of a cyst larger than 10 mm (i.e. a dominant follicle)**

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Important Points re: PCO morph

- Ultrasound should **not** be used for the diagnosis of PCOS in those with a gynecological age of < 8 yrs (< 8 yrs since menarche)
- If dominant follicle or cyst > 1 cm is present, must repeat the US during ovarian quiescence for accurate AFC

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What is PCO morphology?

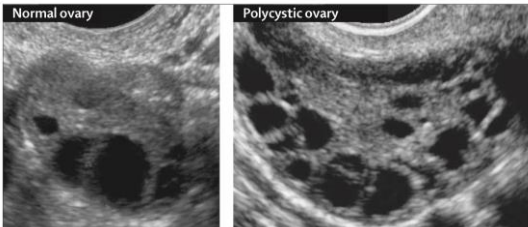


Figure: Normal and polycystic ovary shown by transvaginal ultrasonography during the follicular phase of a menstrual cycle

Norman et al. The Lancet 2007

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Pathophysiology - anovulation

- Excess androgen production
- Alteration of ovarian morphology (increased size)
- Increased LH pulse frequency
- Arrested antral follicle development
- Abnormal interaction of insulin and LH on granulosa cells



Ovulation induction

- Clomiphene vs. letrozole?
- Gonadotropins?
- Ovulation monitoring



First-line treatment for infertility

- **Letrozole should be considered first-line treatment for ovulation induction in patients with PCOS**
- Higher pregnancy rates with letrozole vs. clomiphene (PPCOS II trial)

Legro, NEJM 2014
ASRM Practice Comm. 2018



Letrozole

- Dosing: 5-10 mg
 - If ovulation achieved, no benefit to increasing dose
- Safety
- Counsel regarding off-label use
- Risk of multiple gestation



Metformin in PCOS

- Typical dose in PCOS: 1500-2000 mg/day in divided doses
- Who needs metformin?
 - Impaired glucose tolerance
 - Diabetes



Should you prescribe metformin?

- There is little additional benefit to the addition of metformin above lifestyle therapy alone for weight loss.
- No data to support improvement in hirsutism with metformin.
- Insufficient data to recommend metformin for prevention of diabetes in women with PCOS.

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Metformin and infertility

- Clomiphene is 3x more effective at achieving live birth compared with metformin
- Meta-analysis suggests possible increased PR in obese PCOS women who take metformin in addition to clomiphene
- *Bottom line:* Do not prescribe metformin for fertility purposes alone.

ACOG 2018
Cochrane 2014



In vitro fertilization

- Per-cycle pregnancy rates much higher than with oral medications
- Increased risk of OHSS in PCOS patients
- May be considered earlier in the treatment algorithm if coexisting infertility factors (tubal, male, etc.)



Obstetric considerations

- Patients with PCOS and obesity are at increased risk for obstetric complications
 - Greater risk in women diagnosed by more classic (NIH) criteria vs. non-hyperandrogenic women
- Lifestyle interventions **prior** to conception are critical to reduce risk

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Conclusions

- Letrozole first line for OI
- Lifestyle interventions are important
- Counsel about obstetric risks
