Polycystic Ovarian Syndrome: an Evidence-Based Update for Better Osteopathic Patient Management

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Introduction

Polycystic ovarian syndrome (PCOS) is a common and very complex endocrine disorder affecting approximately 8–13 percent of women of reproductive age worldwide. Unfortunately up to 70 percent of women remain undiagnosed. Different diagnostic criteria have in the past posed and unfortunately still pose a challenge to diagnosis. In 2023 the updated recommendations from the International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome have been published. The guidelines underline the importance of applying evidence-based practices when sharing news on diagnosis, treatment and health implications while ascertaining and focusing on patients' priorities. This research update aims to briefly summarise the most important recommendations included in the guidelines.

Overview

Polycystic ovarian syndrome (PCOS) is a common and complex metabolic and most common endocrine disorder affecting approximately 8–13% of women of reproductive age worldwide and as such is causing a significant public health problem. It appears more frequent in South East Asia and Eastern Mediterranean regions. Unfortunately up to 70% of women worldwide remain undiagnosed (Christ and Cedars, 2023; Singh et al., 2023; World Health Organization, 2023).

PCOS is characterised by some or all of the following symptoms: anovulation/menstrual irregularities, infertility and pregnancy complications, obesity, insulin resistance and/or diabetes type II, metabolic syndrome, acne, hirsutism and/or alopecia, polycystic ovaries, anxiety and depression as well as increased risk for cardiovascular conditions, endometrial cancer or sleep apnoea (Davison, 2019; Singh et al., 2023; World Health Organization, 2023).

Symptoms may fluctuate over time while the start of the disease is frequently seen already in adolescence. PCOS is a chronic condition for which there is currently no cure. The exact cause still remains unknown. There exists a significant heterogeneity amongst phenotypic expressions of PCOS and over 30 genes are associated with the development of the disease (Christ and Cedars, 2023). Inherent and environmental factors appear to play an important role in the development of the condition. The pathophysiology appears to be related to chronic low-grade inflammation, hormonal imbalances, insulin resistance as well as hyperandrogenism which all lead to an impaired folliculogenesis. Risk factors for PCOS appear to be environmental pollutants (e.g. heavy metals, endocrine disrupting chemicals, insecticides), genetic factors, lifestyle, cigarette smoking, diet, gut dysbiosis, obesity and genetics as well as vitamin D deficiency (Singh et al., 2023).

Diagnosis

Diagnosis of PCOS still remains an issue due to different diagnostic criteria available (NIH, Rotterdam, AES Criteria). According to *the Recommendations from the 2023 International Evidence-based Guidelines for the Assessment and Management of PCOS* by Teede et al. (2023) the modified Rotterdam Criteria for diagnosing PCOS have been updated. In order to diagnose PCOS **two of three criteria** should be present in the adult after other causes have been excluded while Anti-Mullerian hormone levels can be

used instead of ovarian morphology. A detailed overview of the diagnostic criteria and some relevant definitions can be found in the table below:

Diagnostic criteria in the adult require:

1. *Oligo- or anovulation*
2. *Clinical and /or biochemical hyperandrogenism*
3. *Polycystic ovaries or Anti-Mullerian hormone levels and exclusion of other aetiologies*

Diagnostic criteria for the adolescent require:

1. *Oligo- or anovulation* ***and***
2. *Clinical and /or biochemical hyperandrogenism*

Irregular menstrual cycles are defined as:
Normal in the first year after menarche
>1 year to <3 years post menarche: <21 or >45 days
> 3 years post menarche till menopause: < 21 or >35 days or < 8 cycles per year
>1 year post menarche: > 90 days for any one cycle

Oligo-amenorrhea is defined as:
Cycles >35 days apart or <8 menses a year

Ultrasound criteria:
Follicle number per ovary: ≥ 20 follicles in at least one ovary or
Ovarian volume: ≥10 ml or follicle number per section in at least one ovary

The transvaginal ultrasound is considered more accurate than the transabdominal ultrasound.
Ultrasound assessment in adolescents is not recommended as there are no defined criteria to define the morphology of polycystic ovaries at this age.
Serum AMH levels should not be used as a single test for the diagnosis of PCOS, can however be used instead of PCO morphology

Biochemical hyperandrogenism:
Total and/or free testosterone levels should be used Androstenedione and or dehydroepiandrosterone sulphate (DHEAS) can be considered although they have less specificity.
Women on the combined oral contraceptive pill should be stopped for at least three months before measurement can be done.
NOTE: very high levels of testosterone might be a sign of an androgen secreting tumour!

Clinical hyperandrogenism:
A modified Ferriman Gallway Score should be used to assess hirsutism taking into account ethnicity and self-treatment. Acne and or alopecia alone are poor predictors of biochemical hyperandrogenism.

Further Diagnosis

Women with PCOS should be considered at higher risk of cardiovascular disease and therefore screened for cardiovascular disease risk factors. Also, glycaemic status should be reassessed every one to three years due to the increased risk for impaired fasting glucose, impaired glucose tolerance and type II diabetes. The 75g oral glucose tolerance test (OGTT) is considered the most accurate test for assessing glycaemic status in PCOS. If an OGTT cannot be performed, the fasting plasma glucose or the HbA1c can be considered although they do have significantly reduced accuracy.
Due to the higher prevalence of obstructive sleep apnoea independent of BMI women should be assessed for symptoms such as snoring combined with unrefreshed sleep or daytime sleepiness or fatigue.
Furthermore, screening for depression and anxiety using validated screening questionnaires is recommended due to the higher prevalence of moderate to severe depression in women and poor body image due PCOS.
Last but not least practitioners should be aware that women with PCOS have a markedly higher risk of developing endometrial hyperplasia and cancer. However, as the overall risk remains very low routine screening is not recommended (Teede et al., 2023).

PCOS and Fertility

Women with PCOS might have more difficulties to become pregnant however they should be reassured that natural pregnancy or with assistance can often be achieved successfully. Women should be informed about the adverse effects of excessive weight on pregnancy, miscarriage and live-birth rates and time should be spent on preconception care including diet, sleep, folate supplementation, mental health, etc. For ovulation induction Letrozole is the first line of treatment. Also Metformin or Clomiphene citrate can be used to improve ovulation, clinical pregnancy as well as livebirth rates. Also, in certain situations gonadotropins can be considered as a second-line pharmacological treatment. If first or second-line treatments have failed in vitro fertilisation or intracytoplasmic sperm injection can be considered (Teede et al., 2023).

PCOS and Pregnancy

Women with PCOS have a higher risk for pregnancy complications such as higher gestational weight gain

and hypertension and diabetes, miscarriage, preeclampsia, intrauterine growth restriction/small for gestational age babies/low birth weight, preterm-delivery and caesarean section. Appropriate monitoring and interventions should be offered as early as possible. Metformin can be considered in certain situations (preterm-birth risk reduction and risk of excessive weight gain). Long-term consequences of metformin use in pregnancy still remain unclear (Teede et al., 2023).

General Management

Primary management should be focused on lifestyle- and behavioural changes including healthy diet and regular physical exercise, achieving healthy body weight and abstaining from tobacco smoking.
However treatment should always be tailored to the specific needs of the patient while acknowledging that women affected by PCOS often experience weight stigma. The negative impact of this should be taken into account.
Although, according to the PCOS guidelines there is not one diet that can be recommended over another, according to Sing et al. (2023) healthy diet should focus on sugar reduction as it is suspected to alter gut flora inducing chronic inflammation and increasing insulin resistance. Also low glycaemic index meals are known to reduce fasting insulin, weight circumference as well as total testosterone level.
Physical exercise for the prevention of weight gain and maintenance of health should involve 150-300 minutes of moderate-intensity activities or 75-150 minutes of high-intensity aerobic activities per week or an equivalent combination of both plus muscle strengthening activity on two non-consecutive days of the week.
Pharmacological treatments in form of the oral contraceptive pill is recommended but frequently off-label. The combined oral contraceptive pill (COCP) can be used for cycle regulation and hirsutism while progestins only could be used for endometrial protection. However, there is limited evidence.
Metformin could be used in adults with a BMI of ≥ 25 Kg/m2 for metabolic outcomes however, evidence is modest. All pharmacological interventions should be offered by shared decision and possible risks and benefits should be discussed with the patient. Women presenting with associated depression, anxiety, low self-esteem and or eating disorders should be offered psychological, pharmacological and or cognitive behavioural therapy.
Inositol has limited clinical benefits in terms of ovulation, hirsutism and body weight, it can however be offered based on patient's preference.
Hirsutism can also be managed by oral antiandrogens (only recommended if there is suboptimal response to COCP) or cosmetic therapy (Teede, et al.2023).

Conclusion

PCOS is a common and very complex endocrine disorder. Unfortunately the condition remains still underdiagnosed. In clinical practice the presence of different diagnostic criteria complicate the diagnostic process while the management is often still not evidence-based. This research update aimed to briefly review the main aspects of the condition and to give a summary of the newly updated *International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome* published in 2023.

Think about:
From an osteopathic perspective how could you support female patients with PCOS? What anatomic regions would consider assessing and treating?

References

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