Jacqueline Boyle
Helena J Teede

Polycystic ovary syndrome

An update

Background

Polycystic ovary syndrome (PCOS) is a common condition, present in 12–21% of women of reproductive age. Up to 70% of women with PCOS remain undiagnosed.

Objective

This article summarises the 2011 national PCOS guideline, *Evidence-based guideline for the assessment and management of polycystic ovary syndrome*, for the general practice context, with particular reference to the needs of Indigenous Australian women.

Discussion

Women with PCOS may present with a wide range of symptoms. The Rotterdam criteria are the most widely accepted for diagnosis and the national guideline references these criteria.

Women with PCOS have a higher risk of metabolic syndrome and its cardiovascular sequelae. This is particularly important for Indigenous women who are already at increased baseline risk.

Management of PCOS involves attention to current symptoms, fertility and psychosocial issues, as well as prevention of related future health problems including diabetes.

Resources are available to help guide management and patients may benefit most from a team approach to care.

Keywords

polycystic ovary syndrome; endocrine system diseases; women

CPD

Polycystic ovary syndrome (PCOS) is a common condition, present in 12–21% of women of reproductive age, depending on the criteria used and the population assessed.[1] It causes significant distress to women and accounts for significant healthcare costs; up to $400 million per year in Australia.[2] Changing definitions and a range of symptoms have made the path to diagnosis for many women difficult; up to 70% of women with PCOS in the community remain undiagnosed.[1] In a study of diabetes in urban Indigenous women in Darwin (Northern Territory) of whom 15% had PCOS by the United States National Institutes of Health criteria,[3] none were previously diagnosed with PCOS. Treatment of current symptoms, preventive advice, and management and monitoring for future complications are all important aspects of care.

The 2011 *Evidence-based guideline for the assessment and management of polycystic ovary syndrome* provides valuable advice to general practitioners on evidence based diagnosis and management. Recently developed GP and consumer targeted assessment and management resources have been informed by the guideline and are available online (see *Resources*). This article attempts to summarise recommendations from the guideline[4] with consideration also given to the needs of Indigenous Australian women. (Indigenous in this article refers to the two Indigenous populations of Australia: Aboriginal and Torres Strait Islander people.)

Definitions

While there are a number of definitions of PCOS, the Rotterdam consensus is the most widely accepted across Europe, Asia and Australia and was the definition used for the guideline. It encompasses the National Institutes of Health definition, which generally describes women with a more severe form of PCOS and requires the presence of both hyperandrogenism and oligo/anovulation. The Rotterdam Criteria require the presence of two of the following: oligo/anovulation, hyperandrogenism or polycystic ovaries on ultrasound[5] (*Table 1*).

Presentation

There are a range of symptoms that women may experience and present with if they have PCOS and these can vary with age (*Table 2*).

In younger women, reproductive symptoms predominate. The prevalence of metabolic features increases with age but can also occur in younger women who are overweight.

Hyperandrogenaemia and insulin resistance are pathophysiological features of PCOS. Women are at risk if they have a genetic predisposition, and the onset of symptoms can be triggered by environmental factors, particularly obesity. It is important to be aware that some population groups have a higher risk of PCOS. This is true of Australian Indigenous women, possibly due to higher levels of insulin resistance and higher rates of obesity. In addition, symptoms may vary with population group, for example, southeast Asian women are less likely to have hirsutism.[1,3]

Diagnosis

Diagnosis is dependent on identifying at least two of the following three features, as per the Rotterdam criteria:

- oligo/anovulation is usually seen in women with menstrual cycles greater than 35 days apart or, conversely, with short cycles of less than 21 days. It is important to remember that even women with regular cycles may be anovulatory. For these women a measure of luteal progesterone (day 21 in a 28 day cycle) will determine ovulatory status
- hyperandrogenism. Hirsutism is difficult to assess as most women treat this so it is not obvious on examination. Hyperandrogenaemia is best measured with free testosterone; either calculated free testosterone, free androgen index (FAI) or bioavailable testosterone. Most laboratories will offer at least one of these. Hormonal contraceptive use will affect free testosterone measures. If appropriate, assess after 3 months cessation; alternative contraception should be discussed for this time.[4] If free testosterone is significantly raised or there is evidence of rapid virilisation, further investigations are required to exclude late onset congenital adrenal hyperplasia and virilising tumours
- polycystic ovaries on ultrasound are diagnosed when 10 small antral follicles are seen in each ovary. A unilateral polycystic ovary is rare but still clinically significant.

When assessing women for PCOS, it is important to consider the following points, which are addressed further in the guideline:[4]

- In young women menstrual cycles may take up to 2 years to regulate after menarche. Irregular cycles persisting into the third year postmenarche should be investigated for PCOS. If commencing a young woman on hormonal contraception after 12 months of irregular cycles, consideration should also be given to assessment of PCOS before commencement of the hormonal contraception
- Ultrasound is not reliable in the diagnosis of polycystic ovaries in adolescent and young women. Up to 70% of young women may have polycystic ovaries on ultrasound[6]
- Initial investigations must exclude other causes of the presentation. These include thyroid function tests and prolactin and follicle stimulating hormone (FSH) levels.

Table 1. Diagnostic criteria for Rotterdam diagnosis of polycystic ovary syndrome

Two of the following three criteria are required:

- oligo/anovulation
- hyperandrogenism
  - clinical (hirsutism or less commonly male pattern alopecia) or
  - biochemical (raised FAI or free testosterone)
- polycystic ovaries on ultrasound

Other aetiologies must be excluded such as congenital adrenal hyperplasia, androgen secreting tumours, Cushing syndrome, thyroid dysfunction and hyperprolactinaemia

Table 2. Features of presentation

- Hirsutism and male pattern balding consistent with hyperandrogenism
- Irregular or absent menstrual cycles
- Subfertility or infertility
- Psychological symptoms – anxiety, depression, psychosexual dysfunction, eating disorders
- Metabolic features – obesity, dyslipidaemia, diabetes

Management of PCOS

Management of PCOS requires identification and management of current symptoms, attention to fertility and emotional concerns, as well as preventive activities to minimise the risk of future associated health problems.

The national guideline highlights the key role of obesity in PCOS. Studies consistently show a higher prevalence of PCOS in women who are overweight and obese, and up to 30% of Indigenous women who had a body mass index (BMI) >30 kg/m^2 met PCOS diagnostic criteria.[3] Women with PCOS also have a higher rate of weight gain than those without PCOS – about 1–2 kg/year.[7] A lifestyle program that addresses a healthy diet with caloric restriction, behaviour change support and exercise to aid in weight loss and prevention of future weight gain is the best first line treatment for PCOS.[4] Even a small amount of weight loss (5%) can help restore menstrual cycle regularity and ovulation, assist mental wellbeing, halve the risk of diabetes in high risk groups and help prevent future cardiometabolic risk.[8–11]

No evidence supports any particular exercise regimen as best for women with PCOS. General recommendations include 150 minutes of exercise weekly with 90 minutes of this exercise being aerobic activity at moderate to high intensity.[4] Lifestyle with diet and exercise should always be a core part of management in addition to other treatment measures. Health coaching principles with appropriate education, risk perception and patient driven goal setting may assist with motivation and support in behaviour change. A team approach may also be useful. Anxiety, depression and body image disorders may also impact on the woman's ability to take-up lifestyle advice and these should also be addressed.[4]

Management of current symptoms

Irregular menstrual cycles

The combined oral contraceptive pill (COCP) is effective in achieving menstrual cycle regularity and also provides contraception if this is required. There may be some negative influence on insulin resistance and lipids and a low dose COCP may be preferable.[12,13] Glucose tolerance and lipid levels should be monitored (see screening). In women with oligo/amenorrhoea, intermittent progestin every 3 months may be used to induce a withdrawal bleed and protect the endometrium from hyperplasia.

Hirsutism

The choice of options depends on patient preference, impact on wellbeing and access and affordability.[14]

The best treatment for localised hirsutism is cosmetic therapy (eg. laser and electrolysis) by an experienced operator, but expense and access may be barriers to this treatment for some women.[4,14] Treatment of local facial hair may be augmented in the short term by topical eflornithine, but this is also costly. Generalised hirsutism may benefit from a combined medical and cosmetic approach.[4,14] The COCP is first line medical therapy with no clear evidence to support the benefit of any particular COCP. Overall health risks (smoking, age, weight, metabolic and thromboembolic) need to be taken into consideration when prescribing.[13,15] Metformin may also provide some benefit.[4]

Infertilty

Polycystic ovary syndrome is the most common cause of anovulatory infertility. Increased BMI and age can also contribute to infertility, and women should be counselled about the importance of maintaining a healthy weight (BMI <30 kg/m^2) and optimal timing of family initiation.[4] Fertility in women declines significantly with a BMI >30–32 kg/m^2 and age more than 35 years. In women aged less than 35 years with a BMI >25 kg/m^2 and no other cause of infertility, an intensive lifestyle program addressing weight loss, without any pharmacological treatment for the first 6 months, is recommended.[4] Small amounts of weight loss (~5%) may restore menstrual cycle regularity and ovulation, providing benefit even if pharmacological intervention is subsequently required.[4,10] If lifestyle measures are unsuccessful, then consider referral to a fertility specialist. Referral should be initiated early for women aged more than 35 years and in couples with additional factors contributing to infertility.

If pharmacological treatment is required, the best first line treatment is clomiphene citrate, which has a pregnancy rate of 30–50% after six ovulatory cycles, although in women with a BMI <30–32 kg/m^2, metformin may have a similar efficacy to clomiphene citrate.[4,16]

Table 3. Potential targeted treatment options for polycystic ovary syndrome

Oligomenorrhoea/amenorrhoea

- Lifestyle change (5–10% weight loss + structured exercise)
- Combined oral contraceptive pill (low oestrogen doses, eg. 20 µg may have less impact on insulin resistance)[13]
- Cyclic progestins (eg. 10 mg medroxyprogesterone acetate 10–14 days every 2–3 months)
- Metformin (improves ovulation and menstrual cyclicity)

Hirsutism

- Self administered and professional cosmetic therapy is first line (laser is recommended)
- Eflornithine cream can be added and may induce a more rapid response

Pharmacological therapy

- Consider if there is patient concern or if cosmetic treatment is ineffective/inaccessible/unaffordable
- Should be trialled for at least 6 months before making changes in dose or medication
- Primary therapy is the COCP (monitor glucose tolerance in those at risk of diabetes)
- Anti-androgen monotherapy (eg. aldactone or cyproterone acetate) should not be used without adequate contraception
- Combination therapy – if 36 months of COCP is ineffective, add anti-androgen to COCP (daily spironolactone >50 mg twice daily or cyproterone acetate 25 mg/day, days 1–10 of COCP)

Infertility

- Advise smoking cessation, optimal weight, exercise and folate supplementation
- Advise regarding the age-related decline in fertility to allow optimal timing of family planning
- Infertility therapies may include clomiphene, metformin, gonadotrophins, surgery and in vitro fertilisation

Cardiometabolic risk

- Lifestyle change with a >5% weight loss in those who are overweight reduces diabetes risk by ~50–60% in high risk groups[11]
- Metformin* reduces the risk of diabetes by ~50% in adherent high risk groups[11]

* Metformin and the COCP are not currently approved for use to manage PCOS by many regulatory bodies. The COCP is indicated for contraception and metformin for diabetes. However, their use is supported by evidence and is recommended by international and national specialist societies and is evidence based[18]

Adapted and reproduced with permission from Teede et al[4]

If clomiphene citrate, metformin or a combination of the two is unsuccessful in achieving pregnancy then gonadotrophins are the next pharmacological options.[4]

Laparoscopy with ovarian surgery/drilling (LOS) is a suitable second line treatment if clomiphene citrate with metformin has failed. The pregnancy rate with LOS is as effective as 3–6 cycles of gonadotrophin ovulation induction.[4] If all of the above are unsuccessful or if there are other factors contributing to infertility such as endometriosis or male factors, in vitro fertilisation or intra-cytoplasmic sperm injection is recommended.

Management of current symptoms is further described in *Table 3*.

Screening

Cardiometabolic abnormalities

Women with PCOS have an increase in cardiometabolic risk factors and this is particularly important in Indigenous women who have a higher prevalence of these risk factors and experience diabetes at a younger age than non-Indigenous women.[17] It is important to be aware that around 75% of lean-body women with PCOS will have insulin resistance and ~50% will have metabolic syndrome.[18]

Recommendations

- Assess cigarette smoking and discuss quitting
- Assess body size factors at most visits, as monitoring weight is an evidence based approach to weight management. Body mass index is a guide to overweight and obesity but doesn't reflect fat stores and a waist circumference measurement may be useful. While it is important to screen for eating disorders (see *Table 3* for simple initial screening questions), given that 60% of women with PCOS are overweight and on average increase their weight by 2–3 kg/year compared with an average increase of 0.8 kg/year for other Australian women, weight monitoring and management is vital. This is especially important considering that lifestyle modification remains the first line treatment for PCOS and the implications of excess weight on reproductive and metabolic health
- Measure lipid profile – every 2 years if initially normal and every year if abnormal and/or overweight or obese. The most common abnormalities are low high density lipoprotein-cholesterol (HDL-C) and high triglycerides
- Measure blood pressure annually if BMI <25 kg/m^2, or every visit if BMI >25 kg/m^2
- Assess for prediabetes (impaired fasting glucose and impaired glucose tolerance) and diabetes. The national guideline recommends an oral glucose tolerance test every 2 years in all women and every year in those with additional risks for diabetes (age, ethnicity, parental history of diabetes, history of high glucose levels, smoking, use of anti-hypertensive medications, physical inactivity and waist circumference >80 cm). This is controversial, but if measuring fasting glucose only, up to 80% of prediabetes and 50% of diabetes in young women with PCOS will be missed.[19]

Emotional wellbeing

Women with PCOS are more likely to suffer from depression, anxiety, poor self esteem, disordered eating and psychosexual dysfunction. The national guideline recommends screening and provides 3–5 questions to screen for each of these features[4] (*Table 4*). There is no data on psychosocial features of PCOS in Indigenous women, but anxiety and depression are common problems in the absence of PCOS, so screening is important.[17]

Summary

Polycystic ovary syndrome is a common, lifelong condition that appears to be increasing in prevalence with increasing obesity, and is more

Table 4. Emotional health screening questionnaire*

Depression/anxiety
During the past month, have you often been bothered by feeling down, depressed, anxious or hopeless?
During the past month, have you often been bothered by having little interest or pleasure in doing things?
During the past month, have you often been bothered by feeling excessively worried or concerned?
Body image
Do you worry a lot about the way you look and wish you could think about it less?
On a typical day, do you spend more than 1 hour per day worrying about your appearance?
If so, what concerns do you have and what effect does it have on your life?
Does it make it hard to do your work or be with your friends and family?
Eating disorders
Do you worry you have lost control over your eating?
Do you ever feel disgusted, depressed or guilty about eating?
Have you ever tried fasting or skipping meals in an attempt to lose weight?
Have you tried vomiting, laxatives or diuretics in an attempt to lose weight?
Have you had significant (>5–7%), recurrent fluctuations in body weight?
Sexual dysfunction
During the past few months, have you often been bothered by problems with your sex life such as reduced satisfaction, desire, pain, or any other problems?
Do you feel that PCOS affects your sex life?
Do sexual problems affect your current relationship and/or have sexual problems affected your past relationships?

* If any of the questions in any of the sections are positive, further exploration of that area is required (see guidelines for other tools as needed) and appropriate support and management offered

common in Indigenous and southeast Asian women. The focus for GPs should be on accurate diagnosis, prevention and management of excess weight gain, as well as long term support and management of psychological, metabolic and reproductive health. Concise, evidence based GP assessment and management tools are now readily available to support care (see *Resources*). The national guideline emphasises that a team approach is often required for psychological, nutritional and behavioural support.

Resources

- Jean Hailes for Women's Health: www.managingpcos.org.au
- National Health and Medical Research Council. Evidence-based guideline for the assessment and management of polycystic ovary syndrome: www.nhmrc.gov.au/guidelines/publications/ext0002
- Teede HJ, Misso ML, Deeks AA, et al. Assessment and management of polycystic ovary syndrome: summary of an evidence-based guideline. Med J Aust 2011;195(Suppl)65–112.

Authors

Jacqueline Boyle MBBS, FRANZCOG, MPHTM, PhD, Womens Research Unit and Jean Hailes for Women's Health School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria. jacqueline.boyle@monash.edu

Helena J Teede MBBS, FRACP, PhD, is Director of Research, Education and Translation, Jean Hailes for Women's Health, Melbourne, Victoria.

Conflict of interest: none declared.

References

1. March WA, Moore VM, Willson KJ, Phillips DI, Norman RJ, Davies MJ. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. Hum Reprod 2010;25:544–51.
2. Teede H, Deeks A, Moran L. Polycystic ovary syndrome: a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan. BMC Med 2010;8:41.
3. Boyle JA, Cunningham J, O'Dea K, Dunbar T, Norman RJ. Prevalence of polycystic ovary syndrome in a sample of Indigenous women in Darwin, Australia. Med J Aust 2012;196:62–6.
4. Teede HJ, Misso ML, Deeks AA, et al. Assessment and management of polycystic ovary syndrome: summary of an evidence-based guideline. Med J Aust 2011;195:S65–112.
5. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril 2004;81:19–25.
6. Kristensen S, Ramlau-Hansen CH, Ernst E, et al. A very large proportion of young Danish women have polycystic ovaries: is a revision of the Rotterdam criteria needed? Hum Reprod 2010;25:3117–22.
7. Teede H, Deeks A, Gibson-Helm M, et al. Body mass index as a predictor of polycystic ovary syndromerisk: results of a longitudinal cohort study(abstract no.246). Endocrine Society Annual Meeting. 2010 Jun 19–22 San Diego, California.
8. Pasquali R, Gambineri A, Pagotto U. The impact of obesity on reproduction in women with polycystic ovary syndrome. BJOG 2006;113:1148–59.
9. Norman RJ, Davies MJ, Lord JM, Moran LJ. The role of lifestyle modifications in polycystic ovary syndrome. Trends Endocrinol Metab 2002;13:235–7.
10. Clark AM, Thornley B, Tomlinson L, Galletley C, Norman RJ. Weight loss in obese infertile women results in improvement in reproductive outcome for all forms of fertility treatment. Hum Reprod 1998;13:1502–5.
11. Knowler W, Barrett-Connor E, Fowler S, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393–403.
12. Halperin IJ, Kumar SS, Stroup DF, Laredo SE. The association between the combined oral contraceptive pill and insulin resistance, dysglycemia and dyslipidemia in women with polycystic ovary syndrome: a systematic review and meta-analysis of observational studies. Hum Reprod 2011;26:191–201.
13. Meyer C, McGrath BP, Teede HJ . Effects of medical therapy on insulin resistance and the cardiovascular system in polycystic ovary syndrome. Diabetes Care 2007;30:471–8.
14. Martin KA, Chang RJ, Ehrmann DA, et al. Evaluation and treatment of hirsutism in premenopausal women: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2008;93:1105–20.
15. Lidegaard O, Nielsen LH, Skovlund CW, Skjeldestad FE, Løkkegaard E. Risk of venous thromboembolism from use of oral contraceptives containing different progestogens and oestrogen doses: Danish cohort study, 2001–9. BMJ 2011;343:d6423.
16. Tang T, Lord JM, Norman R, Yasmin E, Balen AH. Insulin-sensitising drugs (metformin, rosiglitazone, pioglitazone, D-chiro-inositol) for women with polycystic ovary syndrome, oligo amenorrhoea and subfertility. Cochrane Database Syst Rev 2012;5:CD003053.
17. Vos T, Barker B, Stanley L, Lopez AD. The burden of disease and injury in Aboriginal and Torres Strait Islander peoples 2003. Brisbane: School of Population Health, The University of Queensland, 2007.
18. Teede H, Hutchison S, Zoungas S. The management of insulin resistance in polycystic ovary syndrome. Trends Endocrinol Metab 2007;18:273–9.
19. Salley KE.S, Wickham EP, Cheang KI, et al. Glucose intolerance in polycystic ovary syndrome: a position statement of the Androgen Excess Society. J Clin Endocrinol Metabol 2007;92:4546–56.

correspondence **afp@racgp.org.au**