Screening for diabetes in women with polycystic ovary syndrome

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Polycystic ovary syndrome is a common hormonal disorder that affects an estimated 5%–10% of women of reproductive age.[1] This condition usually begins in the early teens and is characterized by chronic anovulation and hyperandrogenism; clinical manifestations include oligomenorrhea or secondary amenorrhea, polycystic ovaries, hirsutism, acne, male-pattern hair loss and infertility. Although the etiology of the syndrome is complex and likely multifactorial, major strides in knowledge have been made on its pathogenesis and treatment.

Insulin resistance is now thought to play a major role in the pathophysiology of polycystic ovary syndrome and its associated metabolic abnormalities, predisposing affected women to increased risk for type 2 diabetes, endometrial and breast cancer, and cardiovascular disease. A substantial number of women with the syndrome are overweight or obese; this excess adiposity often exacerbates the underlying reproductive and metabolic abnormalities. With the dramatic increase in the global prevalence of overweight and obesity, polycystic ovary syndrome is increasingly recognized and diagnosed in young women, especially in teenage girls. Primary care professionals are becoming overwhelmed with the high prevalence of this syndrome and the metabolic abnormalities associated with it. Early diagnosis and treatment of these abnormalities will likely reduce long-term risks of diabetes and heart disease.[1,2]

Abnormal glucose homeostasis, at least partly from insulin resistance, is present in 30%–40% of adult women with polycystic ovary syndrome.[1] It is also present at a similar frequency in adolescents in the early stages of polycystic ovary syndrome.[3] Since a considerable number of affected women will subsequently experience type 2 diabetes, screening for diabetes has been advocated for women with the syndrome.[4,5] In this issue, Gagnon and Baillargeon[6] report their examination of the predictive value of the currently recommended fasting glucose cutoff for the screening of abnormal glucose tolerance in a retrospective study of 105 Canadian women with polycystic ovary syndrome assessed at an academic reproductive–endocrine clinic. The authors determined the prevalence of abnormal glucose tolerance and calculated the sensitivity and specificity of the fasting plasma glucose test, as well as likelihood ratios for positive and negative test results. Based on the receiver–operator characteristic curve, the optimal limit for fasting plasma glucose, 5 mmol/L, yielded 79% sensitivity and 66% specificity. Accordingly, only 3 in 4 women with abnormal glucose tolerance were detected. They concluded that all women with polycystic ovary syndrome should undergo an oral glucose tolerance test for proper screening for diabetes. This recommendation is in keeping with several other studies[3,7,8] that have found impaired glucose tolerance to be a better predictor for future diabetes, especially among women with polycystic ovary syndrome.

Hyperglycemia can be assessed by measuring levels of fasting glucose, postprandial or postchallenge glucose, and hemoglobin A_{1C}. All 3 measurements are abnormally high in people who have diabetes. The natural history of diabetes includes an asymptomatic preclinical phase (now recognized as prediabetes), which is estimated to last between 10 and 12 years and can be detected an average of 5–6 years before a clinical diagnosis.[9] In prediabetes and the early stage of diabetes, postprandial hyperglycemia is more common, and affected people remain asymptomatic until their hyperglycemia exceeds the normal renal threshold of 10 mmol/L. Emerging data suggest that a postchallenge glucose level measured 2 hours after a 75-g oral glucose load (the oral glucose tolerance test) is a better predictor than hemoglobin A_{1C} testing for all-cause and cardiovascular mortality.[10]

Early treatment of associated metabolic abnormalities likely reduces risks of diabetes and heart disease.

However, the Canadian and American Diabetes Associations, both of which recognize polycystic ovary syndrome as a risk factor for type 2 diabetes, have recommended screening for diabetes with a fasting plasma glucose test.[4,5] This test is recommended for screening because of its simplicity, reproducibility and low cost. The specificity of a glucose cutoff of 7 mmol/L or more for diabetes is greater than 95%, but its sensitivity is rather poor at about 50%. Strictly speaking, therefore, measuring fasting plasma glucose is not a good screening method because of the test's low sensitivity. If the fasting test result exceeds 5.7 mmol/L (5.6 mmol/L, according to the American Diabetes Association) but is less than 7 mmol/L, a plasma glucose measurement 2 hours after a 75-g oral glucose challenge is recommended as the next step, in order to classify the prediabetes into impaired fasting glucose (5.7–6.9 mmol/L), impaired glucose tolerance (8.0–11.1 mmol/L) or both.[4,5]

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By recommending a screening test for patients with polycystic ovary syndrome that is more sensitive and specific for diabetes, the authors rightly assume that earlier diagnosis of prediabetes and diabetes should lead to better treatment and improved health outcomes. In prediabetes, there is irrefutable evidence to support lifestyle change as well as pharmacological therapy to reduce (or delay) the development of type 2 diabetes by 30%–58%.[11,12] The maintenance of tight glycemic control in people with newly diagnosed type 2 diabetes has also demonstrated benefits in reducing complications and the burden of the disease.[13]

Gagnon and Baillargeon's study has limitations. First, the data were derived from a small sample of women of fairly homogeneous background; the findings may therefore not be representative of a larger and ethnically more diverse population. Second, the cost and simplicity of the oral glucose tolerance test are not trivial, and cost-effectiveness should be taken into consideration. Fasting plasma glucose testing has been shown to be simple and reproducible, and is an inexpensive test for screening for prediabetes and undiagnosed diabetes.[14] Since the women whose glucose tolerance was abnormal in the Gagnon and Baillargeon study were more obese and hypertensive and had higher triglyceride levels, it would be of interest to estimate the odds ratios and relative strength of these risk factors for distinguishing those with and without abnormal tolerance. If stratified by such risk factors, screening guidelines for diabetes in women with polycystic ovary syndrome might be better refined to increase detection accuracy and reduce costs. Until such data are available, the recommendations of the Canadian and American Diabetes Associations, that women with polycystic ovary syndrome be screened for diabetes initially with a fasting plasma glucose test, followed by a 75-g oral glucose challenge when fasting plasma glucose results are abnormal, are logical and should be followed. Importantly, prospective randomized clinical trials designed to attenuate insulin resistance in women with polycystic ovary syndrome may prove to be of great benefit in reducing the risks for diabetes and cardiovascular disease, as well as in the treatment of polycystic ovary syndrome.

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