EDITOR’S PICK

In women of reproductive age, polycystic ovary syndrome (PCOS) is one of the most common abnormalities, and obesity is observed in about 80% of these patients. The relationship between PCOS and obesity is complex, and therefore the study “Selection of Appropriate Tools for Evaluating Obesity in Polycystic Ovary Syndrome Patients” is very welcome. The author concludes that using BMI to diagnose and classify obesity, a high fat content, or fat distribution of android type in PCOS patients with normal weight can be overlooked.

Prof Joep Geraedts

SELECTION OF APPROPRIATE TOOLS FOR EVALUATING OBESITY IN POLYCYSTIC OVARY SYNDROME PATIENTS

*Yang Xu

Reproductive and Genetic Medical Center, Peking University First Hospital; OB/GYN Department, Peking University First Hospital, Beijing, China

*Correspondence to xuyangm@126.com

Disclosure: The author has declared no conflicts of interest.
Received: 02.05.17  Accepted: 06.07.17
Citation: EMJ Repro Health. 2017;3[1]:48-52.

ABSTRACT

Patients with polycystic ovary syndrome (PCOS) have unique endocrine and metabolic characteristics, whereby the incidence and potentiality of obesity, as well as the accompanying risk of metabolic and cardiovascular diseases, are significantly increased. Currently, BMI is widely used to diagnose and classify obesity. However, body fat is not accounted for in BMI calculations, and the missed diagnosis rate of obesity is nearly 50%. Since PCOS patients with normal weight are also characterised by a high content of fat or fat distribution of android type, some of these patients are often overlooked if an inappropriate diagnostic tool for obesity is selected, which affects the therapeutic effect. Herein, we have reviewed the mechanism and diagnostic methods of PCOS-related obesity and suggested that not only body weight and circumference alone, but also the body fat percentage and fat distribution, should be considered for the evaluation of obesity in PCOS patients.

Keywords: Polycystic ovary syndrome (PCOS), obesity, normal weight obesity, body fat percentage, body composition.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common endocrine disease in women of childbearing age. It is characterised by chronic anovulation and hyperandrogenism, and commonly manifests as irregular menstruation, infertility, hirsutism, and obesity. The pathophysiological changes of PCOS involve abnormalities in the neuroendocrine system, glucose metabolism, lipid metabolism, protein metabolism, and local ovarian regulatory factors. It affects a woman’s reproductive function and causes long-term complications, such as Type 2 diabetes, cardiovascular disease (CVD), and endometrial cancer, which pose a serious threat to a woman’s health.

Due to the heterogeneity of clinical manifestations of PCOS, its definition and diagnosis remain controversial. The clinical practice guidelines issued by the Endocrine Expert Working Group in the USA and Europe in 2013 recommended the use of criteria published in 2003 by the European
Society of Human Reproduction and Embryology and American Society for Reproductive Medicine (ESHRE/ASRM): a patient can be diagnosed with PCOS if two of the following three criteria are met: oligoovulation or anovulation; clinical and/or biochemical signs of hyperandrogenism; polycystic ovaries and exclusion of other aetiologies, such as congenital adrenal hyperplasia, androgen-secreting tumours, and Cushing's syndrome.

Obesity is a common clinical manifestation of PCOS, with an incidence of 50–80%, which differs with respect to race and geographical factors. Obesity refers to an increase in body weight due to an increase in the volume of body fat and/or an increase in the number of adipocytes, or an abnormal increase in the percentage of body fat (PBF). Additionally, in obesity, body fat is excessively accumulated in certain locations. In the diagnosis and treatment guidelines for PCOS, weight loss and lifestyle changes are considered as the first-line treatment option for overweight or obese patients, but it is believed that PCOS patients with normal weight cannot benefit from weight loss.

Obesity further increases the secretion of androgens, affecting the metabolic and reproductive functions. In PCOS, the levels of low-density lipoprotein, triglycerides, and cholesterol are increased, while the level of high-density lipoprotein is decreased, with an increased risk of arteriosclerosis and changes in vascular endothelial function. Additionally, PCOS also increases the risk of CVD as well as the related complications. Obese PCOS patients have a higher incidence of menstrual disorders and long-term anovulation than patients with normal weight and, thus, show a poorer effect after receiving ovulation stimulation.

**MECHANISM OF POLYCYSTIC OVARY SYNDROME OBESITY**

The pathogenesis of obesity is influenced by genetic and environmental factors, such as diet and lifestyle. Adipose tissue is not only an ‘energy warehouse’, but also an important endocrine organ. It can secrete numerous cytokines and hormones, and plays an important role in regulating body metabolism, inflammation, and immune response. Normal content and distribution of fat are essential for maintaining body functions and fertility potential in females. Gynoid fat distribution begins in adolescence, where an adequate fat content is conducive to triggering and maintaining a regular and ovulatory menstrual cycle. A significant decrease in adipose tissue in adulthood will lead to secondary amenorrhoea. Peripheral adipose tissue is an important site for the synthesis of oestrogen outside the ovary, where the androgen transforms into oestrogen through the aromatisation effect.

There could be several mechanisms of obesity in PCOS. PCOS patients have a significant increase in intake of food rich in carbohydrates, high in glycemic index, and high in saturated fat. They also have an excessively high intake of total energy and sedentary lifestyles, which is particularly common in individuals with genetic and environmental susceptibility. As compared to age and body weight matched controls, the basal metabolic rate and postprandial calorogenesis were found to be lower in PCOS patients. Due to the abnormal endocrine levels, PCOS patients have a retarded perception of satiety, which manifests as gluttony and food craving. Mouse models have revealed that excessive androgen increases appetite and the frequency of eating, as well as promoting the accumulation of abdominal fat. At the onset of adolescence, obesity is associated with excessive androgen. Thus, it is possible to control the progression of PCOS and even prevent it in adulthood by controlling the excessive androgen prior to adolescence. Veilleux et al. showed us that adipocyte hyperplasia (the proliferation and differentiation of preadipocytes) is predominant in the subcutaneous adipose tissue, whereas adipocyte hypertrophy (the enlargement of existing adipocytes) is present both in subcutaneous and omental adipose tissue depots. The key point is that the hypertrophic adipocytes are associated with dyslipidaemia and insulin resistance. Thus, obesity in PCOS not only exacerbates the existing characteristics but also affects the therapeutic results.

**COMMON DIAGNOSTIC METHODS FOR OBESITY**

- BMI: In 1842, the Belgian mathematician Quetelet found that body weight was proportional to the square of height. Currently, BMI is often used for the diagnosis and classification of obesity, as well as for the prediction and assessment of disease risk in epidemiological studies due to its ease of use, safety, and low cost. However, BMI does not consider the body fat, which is very important, and is unable to distinguish fat, lean body weight, or bone. If BMI alone is used...
to diagnose obesity, individuals with an increase in muscle mass will be mistakenly included as obese, while individuals with a high content of fat and low lean body weight will be considered to have normal BMI. In addition, with the same BMI, PBF may be different due to differences in sex, age, and race.\textsuperscript{38}

- Waist circumference (WC), waist-to-hip ratio, and waist-to-height ratio: The waist-to-hip ratio can be used to indirectly measure the body fat distribution. The WC, alone or in combination with BMI, has a stronger correlation with an increased health risk than BMI alone.\textsuperscript{19} The WC reflects the abdominal or visceral fat, and has no correspondence with BMI. Hip circumference reflects different body compositions at the gluteofemoral area, such as muscle, bone, and fat. A recent study indicated that women with central obesity with BMI <25 kg/m\textsuperscript{2} are 2.03-times (95\% confidence interval of adjusted odds ratio: 1.62–2.54) more likely to have at least one CVD factor when compared with normal weight women without central obesity.\textsuperscript{20}

- Body composition analysis: It measures the body fat, fat-free body weight, overall body water, and basal metabolic rate, and calculates PBF. The main methods for measuring body fat include bioelectrical impedance, hydrostatics plethysmography, isotope dilution technique, dual-energy X-ray absorptiometry, and skin-fold thickness measurement.\textsuperscript{21} A high PBF is associated with insulin resistance even in patients with normal body weight.\textsuperscript{22} Thus, PBF is a good predictor of obesity,\textsuperscript{23} and is increasingly used for its value in the diagnosis of obesity.\textsuperscript{24}

Based on the different racial characteristics, the World Health Organization (WHO)\textsuperscript{25} and the International Diabetes Federation (IDF)\textsuperscript{26} have determined the cut-off values of BMI and WC for the diagnosis of obesity. For adult women in China, a BMI of 24 to <28 kg/m\textsuperscript{2} is defined as overweight, and BMI \textgeq 28 kg/m\textsuperscript{2} is defined as obese;\textsuperscript{4} a WC of \textgeq 80 cm is defined as central obesity. Studies collected data from 13,601 adults to detect the accuracy of BMI in the diagnosis of obesity and found that if patients with a BMI \textgeq 30 kg/m\textsuperscript{2} were diagnosed as obese, bioelectrical impedance was used to calculate the body fat. BMI calculations showed a specificity of up to 97\% but had a sensitivity of only 42\% in detecting obesity, whereby 50\% of the obese population diagnosed by PBF were missed by BMI.\textsuperscript{27,28} Therefore, in the diagnosis and classification of obesity, it is necessary to refer to the content and distribution of body fat, rather than body weight and BMI alone. Nevertheless, there is a lack of consensus on the cut-off value of PBF for the diagnosis of obesity. Currently, it is recommended that the cut-off value of PBF for the diagnosis of obesity in women is 30–35\%.\textsuperscript{29} In addition, our previous study found that, at a cut-off point of 29\%, PBF has a sensitivity of 88.2\% and a specificity of 57.7\% in diagnosis of PCOS, suggesting that PBF can be used to screen PCOS due to its increased sensitivity.\textsuperscript{30}

Combining BMI, PBF, and various metabolic indicators, obesity can be divided into four phenotypes:\textsuperscript{9} a) normal weight obese (NWO), b) metabolically obese normal weight (MONW), c) metabolically healthy obese, and d) metabolically unhealthy obese. Among them, body measurement data of NWO are described as BMI: 22.6±1.9, WC: 72.3±4.9, and PBF: 34.9±5.0, while those of MONW are described as: BMI: 22.5±2.0, WC: 77.5±0.3, and PBF: 31.8±5.9. A common feature of the two obese groups is that both BMI and WC are in the normal range. Kang et al.\textsuperscript{31} found that the blood pressure and fasting blood glucose level are significantly increased in NWO individuals, along with dyslipidaemia. When compared to individuals with less body fat, the mortality due to CVD is increased by 2.2-times in NWO individuals.\textsuperscript{32} MONW individuals also have a high risk of diabetes.\textsuperscript{33} These two groups of high-risk patients are often excluded from the obese category if their diagnosis is solely based on body weight, BMI, or WC.

### NORMAL WEIGHT OBESITY

Ruderman et al.\textsuperscript{34} found that normal weight individuals may suffer from Type 2 diabetes mellitus, premature coronary heart disease, hypertension, and hyperlipidaemia if they have insulin resistance. Occurrence of metabolic abnormalities may be associated with the fat distribution. For normal weight patients with metabolic abnormalities, their metabolic indicators can be improved after controlling their diet and energy as well as exercising.\textsuperscript{35} In 2006, De Lorenzo et al.\textsuperscript{36} proposed the concept of NWO in individuals with a normal BMI (<25 kg/m\textsuperscript{2}) but a high content of fat (PBF >30\%). This type of obesity shows an incidence of 2–28\% in women,\textsuperscript{37} but there is a lack of data in PCOS patients. The NWO is highly correlated to subclinical vascular inflammation and cardiovascular metabolic disease,\textsuperscript{38} and is also associated with mortality of coronary heart disease.\textsuperscript{39}
There are significant differences in body composition and fat distribution between lean PCOS patients and lean controls. With matching body weights, the body fat is significantly increased and the lean body weight is significantly lower in lean PCOS patients as compared to the controls. The healthy controls show gynoid fat distribution, while majority of the lean PCOS patients (70%) show non-gynoid fat distribution, and 50% of them exhibit android fat distribution. This distribution of fat is characterised by an increase in visceral fat and the degree of insulin resistance. Lean PCOS women show the same metabolic characteristics as obese PCOS women. As compared to patients with gynoid fat distribution in which the fat is peripherally distributed, the risk of cardiovascular metabolic disease is significantly increased in patients with abdominal fat or androgenic obesity.

CONCLUSION

In summary, PCOS patients with normal body weight or BMI may have adverse reproductive and health outcomes due to increased fat content or abnormal fat distribution. Presumably, if the lean PCOS patients are further classified by the diagnostic criteria of PBF, a considerable number of patients will be classified as NWO or MONW and may have been easily overlooked if inappropriate diagnostic tools are selected, which could affect their therapeutic options; for example, they would still benefit from controlling their body fat. Therefore, we propose that in addition to body weight and circumference, the total body fat and fat distribution should also be considered in evaluating obesity in PCOS patients.

In view of the issues mentioned, much work is still needed in the future. The methods and criteria for evaluating PCOS obesity need to be re-defined and incidences of NWO and MONW in PCOS patients need to be summarised using epidemiological statistics to facilitate early intervention and delay the progression and improve the outcome of PCOS and save medical resources.

REFERENCES

21. Cornier MA et al.; American Heart Association Obesity Committee of the Council on Nutrition; Physical Activity and Metabolism; Council on Arteriosclerosis;


