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Parameters of obesity in polycystic ovary syndrome

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a prevalent female endocrine and metabolic disorder, and is typically presented with menstrual irregularity and an excess of androgen production. Obesity is a common comorbidity with PCOS, and accompanying insulin resistance is proved to be a key pathogenesis of PCOS. Several parameters have been applied to evaluate obesity, including body-mass index (BMI), waist circumference (WC), percentage of body fat (PBF) and lipid accumulation product (LAP) index. Accumulating studies were conducted to analyze the association between the markers of obesity and PCOS, as well as the cut-off level of each marker in order to detect higher risk of cardiovascular diseases or rule out metabolic syndrome. However, standards of obesity parameters to screen or diagnose PCOS are yet to be established. Herein we briefly review the association of obesity measuring methods and its diagnostic value with PCOS, which gives insight into the development of standard criteria for obesity in PCOS.

Obesity and PCOS

Polycystic ovary syndrome (PCOS) is a most common endocrine disorder that affects women of child-bearing age, and its incidence rate in China is about 5.6% among 19 to 45 year-old women[1]. In this epidemiological study, PCOS was diagnosed according to the Rotterdam diagnostic criteria, and the diagnosis was made when two or more of the following three criteria were presented: oligo/amenorrhea, clinical and/or biochemical hyperandrogenism and polycystic ovaries. Oligo/amenorrhea was defined as the absence of menstruation for 35 days or more. Hyperandrogenism included clinical and biochemical hyperandrogenism: The former was defined as an mF-G score of ≥6 with/ without acne, and/or androgenic alopecia; the latter as an androstenedione level of >10.8 nmol/l or total testosterone level of >2.81 nmol/l. The worldwide prevalence of PCOS is between 5%-15%[2]. The incidence rate in China is relatively low, which might result from ethnicity and different criteria that the researchers used to diagnose the disease.

The primary manifestations of PCOS are anovulation and hyperandrogenism[3]. PCOS is strongly associated with obesity, and the comorbidity rate of obesity is 32% according to a population study of 400 subjects from the United States, 223 of whom were black, 166 white, 11 of other races[4]. Patients with PCOS are also at significant risk for metabolic syndrome and cardiovascular complications, including type 2 diabetes and dyslipidemia that are linked to insulin resistance. Obese PCOS women tend to have higher likelihood of metabolic disorders, manifested by increasing levels of fasting glucose, lipid profile and insulin resistance[5]. A

recommended treatment for obese PCOS is mild weight loss, which indicates a decrease of body weight of 5-10%, and it could not only normalize ovulation cycle and raise success rate of pregnancy[6], but also benefit in glucose and lipid metabolism and reduce cardiovascular risk[7,8].

Genetic factors can affect the risk of PCOS and obesity[9]. The polymorphism of insulin receptor substrate-1 (IRS-1) gene was proved to be associated with the risk of PCOS in different ethnicities[10]. Meanwhile, metabolic indices including insulin resistance, fasting insulin and triglycerides were related to genetic variations in insulin signaling, especially IRS-1 gene polymorphism[11, 12]. Myo-inositol supplement was proved a useful treatment for PCOS, which might indicate that insulin signaling and its genetic background played a critical role in the pathogenesis of PCOS[13].

Conventional anthropometric indices of obesity in PCOS

Body-mass index (BMI) and waist circumference (WC) are surrogate markers of obesity, especially visceral adiposity for the latter in normal individuals[14]. Other parameters including percentage of body fat (PBF), waist-height ratio (WHtR) and waist-hip ratio (WHR) show their own advantages in different aspects in detecting obesity. BMI mainly focuses on measuring human density, PBF focuses on quantity of body fat, WC focuses on abdominal width and central obesity, as well as WHtR and WHR. In a large-scale study in Chinese adults, WHtR was a better indicator of cardiovascular risk and the optimal cut-off values were 0.50 and 0.48 for men and women, respectively[15]. However, proper anthropometric indices and their cut-off values for PCOS are under debating and need to be established.

BMI is a most prevalent parameter of obesity in clinical practice, and diverse ethnicity has specific cut-off point to diagnose obesity. In a population-based observational study, 409 PCOS women and 7057 non-PCOS women were followed-up, and mean BMI in PCOS group was significantly higher than control group[16]. Similar result was concluded in a prospective controlled study in Greek population with PCOS, and the significantly higher BMI in PCOS group was also related to elevated fasting plasma glucose, triglyceride and risk of metabolic syndrome (MetS)[17]. It is reported in a prospective cross-sectional study in Indian PCOS women, that the cut-off point of BMI to predict MetS was 22.5kg/m2 in PCOS patients and 23kg/m2 in normal population to start lifestyle intervention[18].

Insulin resistance can result in central obesity, and is a critical pathophysiologic feature relating to PCOS and its metabolic disorder[19]. Since BMI represents a proportional relationship between height and weight, it cannot demonstrate the content and distribution of body fat. WC is a common indicator of central obesity, thus it is facilitated in detecting MetS[20]. The cut-off value of WC to discriminate MetS was 80cm in a study involving 160 Korean PCOS women, and 70cm was proved appropriate to detect visceral adiposity[21]. Toscani *et al*. conducted an observational, cross-sectional study, and revealed that WC and the sum of trunk skinfolds were accurate methods to estimate truncal adiposity and proper methods of clinical screening for insulin resistance in mostly hirsute patients with PCOs[22].

Similar with WC, WHtR and WHR are conventional anthropometric indices of central obesity and insulin resistance. Researchers found that WHtR and WC were more appropriate parameters in evaluating cardiovascular risk and insulin resistance in PCOS patients other than WHR[23]. In terms of the diagnostic value for metabolic syndrome, a cross-sectional study was conducted in 113 Brazilian PCOS women, and WC and WHtR were proved of better accuracy to predict MetS than WHR[24], and the optimal cut-off points to discriminate MetS were 95cm and 0.59, respectively. However, their application and cut-off values for obesity in subjects with PCOS are in need of further study.

PBF is measured and calculated using body composition analyzer based on bioelectrical impedance principle. It is a non-invasive measure to reflect the proportion of body fat with good accuracy and simplicity[25]. In healthy individuals, PBF showed high sensitivity in diagnosis of obesity compared with BMI[26]. Researchers further discovered that PBF was related to risk of insulin resistance, even in those who had normal BMI[27]. PBF was reported significantly increased in PCOS women than healthy controls, and the adipose tissue accumulated mainly in abdomen, waist and upper arms[28]. In obese PCOS women, PBF was associated with possibility of cardiovascular diseases[29].

Dou et al. conducted a comparative study for the conventional parameters of obesity. They analyzed BMI, WC and PBF in 300 reproductive-aged Chinese women with PCOS and 110 age-matched controls, and compared their diagnostic values of PCOS using the receiver operating characteristic (ROC) curve[30]. According to their report, all three parameters were significantly increased in PCOS group, and WC was first recommended for its simplicity. In this study, the cut-off points of WC, BMI and PBF were 80.5cm, 26.6kg/m^2 and 29%, respectively. Comparing with each other, PBF had a better sensitivity of 88.2% and BMI had a better specificity of 98%.

Other obesity parameters and PCOS

Skinfold thickness is a simple parameter to evaluate body fat distribution. In a cross-sectional study involving 49 women with PCOS and 40 controls, obese PCOS group had a more pronounced subcutaneous truncal-abdominal

adiposity than non-obese PCOS and obese control group[31], indicating a specific cut-off value of skinfolds is in need for PCOS patients. Meanwhile, the scale of the studies about skinfold thickness in PCOS patients was relatively small. We expect surveys with large amount of population enrolled to bring about more convincing results.

Lipid accumulation product (LAP) index was reported and defined as [WC(cm)-58] ×TG(mmol/L) by Kahn[32]. In subjects with PCOS, LAP index was found to have the strongest diagnostic accuracy for insulin resistance in comparison with BMI, WC and WHR[33]. In addition, Wiltgen et al. proved that LAP index was beneficial than WC and BMI to identify insulin resistance in PCOS patients due to its simplicity, and high LAP index was a risk factor for cardiovascular disease in PCOS patients[34]. In a case-control study, 392 PCOS and 140 BMI-matched control women were enrolled, and ROC curve analysis revealed that LAP index had higher area under the curve (AUC) to identify impaired glucose tolerance (IGT) comparing with BMI and WC[35].

Visceral adiposity index (VAI) was first described by Amato et al. and was calculated following the formula: Female VAI=[WC/[36.58+(1.89×BMI)]] ×(TG/0.81) ×(1.52/HDL). The concentration of TG and HDL were expressed in mmol/L[36]. The detecting value of VAI was proved in a study of Italian PCOS patients, and this index could distinguish metabolically healthy PCOS from metabolically unhealthy ones[37]. The research team further discovered that VAI was a useful marker of diabetes risk in a cross-sectional study of 241 PCOS subjects[38]. These observations were confirmed by a case-control study in Iranian individuals with PCOS, which indicated that LAP index and VAI were best predictors for insulin resistance in women with PCOS, and WC and VAI were better markers for MetS among PCOS women[39]. In a study including Thai PCOS women, the optimal value of VAI as predictors of MetS was >5.6, and ≥28 kg/m^2 for BMI, ≥0.85 for WHR, ≥0.5 for WHtR using ROC curve analysis, and VAI was of priority than other parameters in detecting MetS[40].

Conclusions

Polycystic ovary syndrome is a common disease that affects women of childbearing age, and can lead to hyperandrogenism, irregular menstruation, infertility and metabolic disorder. Early diagnosis and appropriate intervention to accompanying obesity is critical for metabolic and cardiovascular outcomes. A variety of anthropometric measures including BMI and WC show diagnostic values in identifying obesity in PCOS women, and specific cut-off points for each parameter are validated according to risk of metabolic and cardiovascular aberrations.

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