

Lipid Accumulation Product is Related to Metabolic Syndrome in Women with Polycystic Ovary Syndrome

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Key words

- polycystic ovary syndrome
- metabolic syndrome
- lipid accumulation product

Abstract

Purpose: Metabolic disturbances are common features of polycystic ovary syndrome (PCOS), which possibly enhance the risk of diabetes and cardiovascular disease. Lipid accumulation product (LAP) is an emerging cardiovascular risk factor. The aim of this study was to explore the ability of LAP to identify metabolic syndrome (MS) in PCOS women.

Methods: In a cross-sectional study, anthropometric, biochemical and clinical parameters were measured in 105 PCOS women. Receiver operating characteristic (ROC) analysis was used to find

out the cut-off points of LAP to predict MS. MS was categorized according to International Diabetes Federation (IDF) criteria.

Results: The prevalence of MS was 43.8% in this study. PCOS women with MS had significantly higher LAP levels compared to those without MS. LAP was highly correlated with components of MS. ROC analysis showed that LAP was a significant discriminator for MS in PCOS women, and the optimal cutoff point of LAP to predict MS was 54.2 (93.3% sensitivity, 96.7% specificity).

Conclusions: LAP seems to be associated with MS and has a strong and reliable diagnostic accuracy for MS in PCOS women.

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common female endocrine disorders with a prevalence of 5–10% in women of reproductive age [1]. It is characterized by hyperandrogenemia, chronic anovulation, and polycystic ovary morphology [2,3]. The etiology of PCOS is still not very clear, however, previous studies have shown that insulin resistance (IR) and central obesity are key pathological factors of PCOS [4,5]. PCOS is not only the reproductive endocrine disease, but also metabolic disorder. Patients with PCOS are often accompanied by metabolic abnormalities, such as dyslipidemia, obesity, and glucose intolerance, which are also components of the metabolic syndrome (MS) [6].

MS is a cluster of metabolic disorders associated with increased risk of cardiovascular disease (CVD), and central or abdominal obesity is considered a fundamental pathology for the MS. Many of the anthropometric and metabolic abnormalities of PCOS overlap with components of MS, and PCOS patients are at increased risk of having MS [7]. Adults with MS are at a greater risk of developing CVD [8]. PCOS women with MS may be at even greater risk for CVD because they

are exposed to risk factors at a younger age [9]. Early and accurate identification of high-risk individuals for MS could be important to predict and prevent CVD and type 2 diabetes. There is, therefore, an urgent need to develop a simple, accurate and economic predictor for MS in PCOS. The lipid accumulation product (LAP), which was first described by Kahn [10], is based on a combination of waist circumference (WC) and serum triglycerides (TG) and serves as a simple index for lipid over accumulation in adults. High levels of LAP are associated with CVD, impaired glucose tolerance (IGT) and type 2 diabetes [11,12]. In healthy population, LAP is a powerful marker of MS [13,14], however, to the best of our knowledge, there is currently limited research on the relationship between LAP and MS in women with PCOS. Thus, we aim to investigate the ability of LAP to identify MS in PCOS patients.

Materials and Methods

Patients

From February 2009 to October 2011, 105 patients diagnosed with PCOS at the Department of Endocrinology of the Third Affiliated Hospital

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Table 1 Clinical characteristics of PCOS women with or without MS.

Variables	Without MS (n=60)	With MS (n=45)	P-values
age (years)	24.6±4.6	25.2±5.1	0.478
BMI (Kg/m ²)	22.7±1.7	27.2±2.2	<0.001
waist (cm)	71.2±4.3	85.2±3.6	<0.001
systolic blood pressure (mmHg)	118±8	131±9	<0.001
diastolic blood pressure (mmHg)	72±5	81±9	<0.001
fasting glucose (mmol/L)	5.2±0.4	5.7±0.5	<0.001
postload glucose (mmol/L)	7.4±1.1	8.7±1.5	<0.001
fasting insulin (mIU/L)	18.5±4.1	25.5±4.9	<0.001
HOMA-IR	4.35±1.27	6.62±1.64	<0.001
triglycerides (mmol/L)	2.02±0.65	3.48±0.86	<0.001
total cholesterol (mmol/L)	4.88±0.33	5.18±0.39	<0.05
LDL cholesterol (mmol/L)	2.44±0.27	2.56±0.31	0.065
HDL cholesterol (mmol/L)	1.19±0.12	0.94±0.07	<0.001
luteinizing hormone (mIU/ml)	15.22±2.27	16.32±2.36	<0.05
follicle-stimulating hormone (mIU/ml)	6.57±0.79	6.67±0.68	0.486
total testosterone (ng/ml)	0.94±0.09	0.99±0.12	<0.05
estradiol (pg/ml)	65.22±12.86	61.35±13.66	0.141
LAP	26.8±12.8	95.2±28.9	<0.001

Table 2 The area under ROC for LAP, WC, BMI and TG to identify MS in PCOS women.

Markers	Area under ROC curve	95% Confidence interval	P-values
LAP	0.991±0.006	0.980–1.022	<0.001
WC	0.975±0.015	0.945–1.010	<0.001
BMI	0.939±0.019	0.916–0.971	<0.001
TG	0.908±0.028	0.853–0.962	<0.001

of Suzhou University were enrolled. PCOS was diagnosed according to the criteria of Rotterdam 2003 [15]. The age of patients ranged from 18 to 34 years (average age: 24.8 years), who had no history of drugs affecting sex hormone, glucose and lipid metabolism. Studies were performed on the 2nd to the 5th day of the menstrual cycle in PCOS women with spontaneous menses and arbitrary dates in PCOS women with amenorrhea. This study was conducted with approval from the Ethics Committee of the Third Affiliated Hospital of Suzhou University. Written informed consent was obtained from all participants.

Patients were defined as having MS, based on International Diabetes Federation (IDF) criteria for MS, if they had central obesity (waist circumference ≥80cm) plus 2 or more of the following 4 factors: i) increased concentration of triglycerides (TG): ≥1.7mmol/l, ii) reduced concentration of high-density lipoprotein cholesterol (HDL-C): ≤1.29mmol/l, iii) raised blood pressure: systolic pressure ≥130mmHg or diastolic pressure ≥85mmHg or treatment of previously diagnosed hypertension, and iv) increased fasting glucose (FG) level ≥5.6mmol/l (impaired FG, IFG) or previously diagnosed type 2 diabetes.

Research methods

All PCOS patients underwent anthropometric measurements, including weight, height, waist circumferences (WC), Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and the body mass index (BMI) was calculated. Fasting blood samples were obtained from PCOS patients in order to measure luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol (E2), total testosterone (T), fasting glucose (FBG), fasting insulin (FINS), serum triglycerides (TG), total cholesterol (TC), high density lipoprotein (HDL-C) and low density lipoprotein (LDL-C) levels.

A standard 75-g oral glucose tolerance test was performed for the evaluation of the glucose tolerance status. Insulin sensitivity was assessed by homeostasis model assessment of insulin resistance (HOMA-IR), HOMA-IR=FBG (mmol/L) × FINS (mIU/L)/22.5. LAP was calculated using the formula [waist (cm) – 58] × triglyceride concentration (mmol/l), as previously reported [10].

Statistical analysis

Statistical analysis was performed by using SPSS15.0 statistical software. Results are presented as mean±SD. Prevalence rates are expressed as percentages. Independent samples *t*-test was used for comparison of continuous variables between PCOS women with MS and those without MS. Receiver operating characteristic (ROC) curves analysis was performed for LAP, BMI, TG and WC to identify MS in PCOS women. Areas under the curve (AUC) of the ROC curves and their 95% confidence intervals (CI) were evaluated as a measure of diagnostic accuracy. The correlation between variables was tested using the 2-tailed Spearman rank correlation test, a *P*-values less than 0.05 was considered statistically significant.

Results

Among 105 PCOS women, 45 subjects had MS, and the prevalence of MS was 42.8% in this study. As shown in **Table 1**, women with and without MS were similar in age and did not differ significantly in their levels of LDL-C, FSH and E2. PCOS women with MS had significantly increased BMI, WC, SBP, DBP, FBG, postload glucose (PBG), TG and HOMA-IR compared to those without MS. In addition, HDL cholesterol levels were significantly lower in women with MS. Finally, T and LH was significantly higher in PCOS women with MS compared to those without MS (**Table 1**).

PCOS women with MS had significantly higher LAP levels (95.2±28.9 vs. 26.8±12.8) compared to those without MS (**Table 1**).

There was a significant positive correlation between LAP and WC ($r=0.880$, $p<0.001$), SBP ($r=0.601$, $p<0.001$), DBP ($r=0.564$, $p<0.001$), FBG ($r=0.479$, $p<0.001$), PBG ($r=0.517$, $p<0.001$), TG ($r=0.910$, $p<0.001$), HOMA-IR ($r=0.597$, $p<0.001$) respectively. In addition, there was a significant negative correlation between LAP and HDL-C ($r=-0.691$, $p<0.001$).

The results of LAP, WC, BMI and TG ROC curve analysis showed that each marker is a significant discriminator for MS in PCOS women. The largest AUC was obtained with LAP, indicating that LAP was superior for estimating the MS of PCOS patients in this study (**Table 2**). From the ROC curve analysis, the optimal cut-off points of LAP to predict MS in PCOS were 54.2 (93.3% sensitivity, 96.7% specificity, **Fig. 1**).

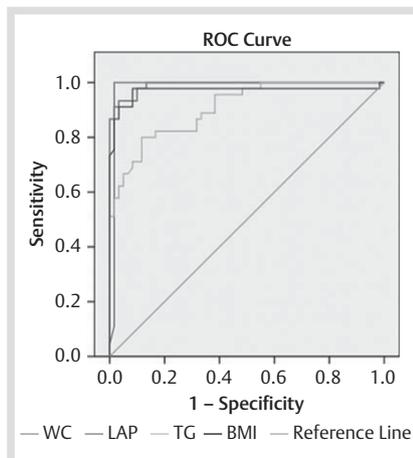


Fig. 1 ROC Curves of LAP, WC, BMI and TG cutoff points to predict MS in PCOS women.

Discussion

PCOS is a condition associated with increased risk for cardiovascular disturbances [16, 17]. PCOS women are at increased risk of having MS, and the prevalence of MS in PCOS patients varies among different ethnicities depends on the definition used [18–20]. In this study, the prevalence of MS, as diagnosed according to IDF criteria, was 42.8% in the studied Chinese PCOS patients. MS itself is a risk for type 2 diabetes and CVD, so early and accurate identification of high-risk individuals for MS is of great importance [21].

Previous studies have evaluated enlarged WC and elevated TG in different populations as a surrogate marker of cardiovascular risk. LAP, an ordinal scale combining WC and TG, could be associated to a dysfunctional and highly lipolytic adipose tissue that is a central abnormality behind MS, CVD and type 2 diabetes [22]. The population-based United States' National Health and Nutrition Examination Survey (NHANES III) concluded that LAP was superior to BMI for recognizing CVD risk and diabetes [10, 11]. In the present study, PCOS women with MS had higher LAP levels in comparison to those without MS. This indicates that high LAP levels are associated with MS in PCOS women. IR plays a central role in both the reproductive and metabolic disturbances observed in women with PCOS [23]. In our study, PCOS women with MS had significantly increased HOMA-IR compared to those without MS. Meantime, we showed that LAP was significantly correlated with HOMA-IR, indicating that LAP may be useful to precociously screen a subset of young women who are susceptible to the development of IR-related comorbidities, including MS, diabetes and CVD. In addition, we demonstrated LAP was highly correlated with WC, SBP, DBP, FBG, PBG, TG and HDL-C, which were components of MS. Therefore, LAP is related to MS and can serve as a reliable marker of MS in PCOS women [24].

Both WC and BMI are shown to be good predictors of the presence of MS [25]. TG, also, is a reliable predictor for these cardiometabolic syndromes. In our study, ROC analysis showed that LAP, WC, BMI and TG were significant discriminators for MS in PCOS women. However, the largest AUC was obtained with LAP, indicating that LAP was superior to WC, BMI and TG for predicting MS of PCOS patients. In addition, ROC curve showed that $LAP \geq 54.2$ had adequate sensitivity and specificity for detecting a state of MS in PCOS women. The high sensitivity and specificity of LAP detected in ROC curve analysis indicate that LAP might be a useful marker to predict MS in PCOS women. The early identi-

fication of PCOS women with MS and introduction of therapeutic interventions may help delay the progression to CVD and T2DM.

Limitations of the present study are the small sample size and the ethnic origin. Therefore, further research should be undertaken in larger sample sizes and different ethnic groups.

In conclusion, our results show that LAP, an easily obtainable measure, has a strong and reliable diagnostic accuracy for MS in PCOS women. Early and accurate identification of high-risk individuals for MS will allow introduction of therapeutic interventions to prevent CVD and type 2 diabetes.

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Declaration of interests: The authors declare no conflicts of interest.

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