# RESEARCH

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# Association between triglyceride glucose index and depression in polycystic ovary syndrome

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# Abstract

**Objective** The relationship between the triglyceride glucose (TyG) index and the incidence of depression in populations with polycystic ovary syndrome (PCOS) remains unclear. This study aims to investigate the relationship between the TyG index and depression incidence in PCOS populations.

**Methods** We conducted a study on 725 women aged 18 to 45 who visited our hospital from January 2021 to December 2023. Demographic and anthropometric data were collected, and serum assays were performed. The Center for Epidemiologic Studies Depression Scale (CES-D) was used to assess the past week's feelings and determine depression status. Statistical methods such as binary logistic regression analysis were used to analyze the relationship between the TyG index, Homeostatic model assessment insulin resistance index(HOMA-IR), and depression in PCOS patients. The TyG index, HOMA-IR, was tested for its ability to predict depression using receiver operating characteristic (ROC) curves.

**Results** In logistic regression models, a significant positive association was observed between the TyG index and depression after the adjusted analysis ( $4.552(2.975 \sim 6.966)$ , P < 0.001). Compared to HOMA-IR( $1.224(1.122 \sim 1.336)$ , P < 0.001), the TyG index was a more significant risk factor for depression. ROC analysis showed that the AUC of the TyG index(0.724,  $0.684 \sim 0.765$ ) was higher than the HOMA-IR(0.698,  $0.656 \sim 0.74$ ).

**Conclusions** A high TyG index was associated with higher odds of having depression in the population with PCOS. This indicated that the TyG index may be an independent predictor of depression development.

Clinical trial number Not applicable.

Keywords Polycystic ovary syndrome (PCOS), Triglyceride glucose (TyG) index, Depression, Insulin resistance(IR)

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# Introduction

Polycystic ovary syndrome(PCOS) is a common gynecological endocrine disorder that affects women of childbearing age worldwide. Its typical symptoms include menstrual abnormalities, hyperandrogenism, and polycystic ovary-like changes detected by ultrasound [1]. At the same time, patients often present with infertility, obesity, insulin resistance(IR), and dyslipidemia, which are associated with an increased risk of type 2 diabetes, cardiovascular disease, and endometrial cancer [2-4]. In addition, PCOS patients are often affected by various mental health disorders. Studies have shown that the risk of depression in PCOS patients may have been 3-8 times higher than that of normal individuals [5]. Depression is significantly associated with decreased function and quality of life, as well as increased mortality, posing a significant challenge to clinical and public health [6, 7]. It is estimated that depression will become the leading cause of disability burden globally by 2030 [8]. Therefore, actively identifying and early screening of PCOS patients at risk of depression, as well as timely intervention to address risk factors, are crucial for reducing the incidence of depression and alleviating the global healthcare burden.

IR [9] is the pathophysiological core of PCOS, and metabolic dysfunction is one of the consequences. Its pathogenesis may be related to low-grade inflammation [10], oxidative stress [11, 12], DNA methylation [13], and abnormal glucose and lipid metabolism. Some studies [14–16] also indicate that IR itself is an independent risk factor for depression apart from diabetes. The gold standard for evaluating IR in clinical practice is the hyperinsulinemic-euglycemic clamp (HEC). Although HEC is the gold standard for evaluating IR, its complex, expensive, and time-consuming detection method makes it unsuitable for large-scale clinical practice and epidemiological research. In recent years, the TyG index [17, 18] has emerged as a new indicator for assessing IR status and shows strong concordance with the traditional gold standard for assessing IR. The research conducted by Jihoon Oh et al. [19] has revealed a significant association between high triglyceride(TG) levels and depression among adult women. It has also been reported [20] that elevated TyG levels are strongly associated with an increased risk of depression and could serve as a reliable biomarker for assessing depression risk. However, the relationship between the TyG index and depression in patients with PCOS is still unclear. Therefore, this study aims to explore the relationship between the TyG index and depression in patients with PCOS of childbearing age.

# Materials and methods Research subjects

This cross-sectional study was conducted on women who came to the Gynecological Clinic of the People's Hospital of Yuyao in Ningbo, Zhejiang province of the People's Republic of China, from January 2021 to December 2023. According to the inclusion and exclusion criteria, 725 PCOS patients were ultimately selected. The inclusion criteria for PCOS were as follows: 1)Age range of 18 to 45 years old; 2) Diagnosed with PCOS according to the 2003 Rotterdam diagnostic criteria [1]: (1) oligo- or anovulation; (2) clinical and/or biochemical hyperandrogenism; (3) polycystic morphology of the ovary on ultrasound examination (at least 12 follicles 2-9mmin diameter and/or  $\geq 10$  ml volume per ovary); 3)Prior diagnosis of depression but had not taken antidepressants in the past three months were included in the study; 4) The patient agreed to participate in this study and signed an informed consent form. Patients with these conditions excluded: 1) Diagnosed with diabetes in the past, except for those who found diabetes in the Gynecological Clinic for the first time; took insulin sensitizers(rosiglitazone, pioglitazone, metformin, and liraglutide)in the past six months prior; 2) Pregnant or lactating women; 3) comorbid serious physical illnesses: severe hepatic or renal insufficiency, malignant tumors, autoimmune disorders such as systemic lupus erythematosus, ankylosing spondylitis; 4) took drugs in the past three months: such as steroids(Dexamethasone, methylprednisolone, etc.); sedatives(Diazepam, clonazepam, estazolam, lorazepam, etc.), antidepressants(Sertraline, fluoxetine, venlafaxine, etc.), antiepileptic drugs(Maxipine, phenytoin sodium), oral contraceptives, anti-triglyceride drugs: fenofibrate and omega-3, etc.

# Ascertainment of depression

The Center for Epidemiologic Studies Depression Scale (CES-D) was used to assess the depression scale [21] of the past week's feelings and determine depression status. The CES-D is a 20-item instrument with each item rated on a four-point scale: 0 = "not at all or less than one day in the last week," 1 = "1–2 days in the last week", 2 = "3–4 days in the last week", 3 = "5–7 days in the last week". The total score ranges from 0 to 60, and  $\geq$  16 is considered depression [22–24].

# Covariates

The analysis incorporated various covariates, including socioeconomic and demographic factors (age, height, weight, BMI, hirsutism, acne, infertility, annual house-hold income, education level), as well as laboratory test results (serum triglyceride(TG), total cholesterol(TC), high-density lipoprotein cholesterol(HDL-C), low-density lipoprotein cholesterol(LDL-C), and uric acid(UC),

sex hormone levels (estradiol(E<sub>2</sub>), progesterone(P), follicle-stimulating hormone(FSH), luteinizing hormone(LH), testosterone(T), prolactin(PRL)).

Generally, the height and weight of the research subjects were measured by dedicated personnel. The patient measured their height and weight on an empty stomach in the morning, taking off their outer clothing and shoes. Simultaneously calculate BMI: weight (kg)/height<sup>2</sup>  $(m^2)$ . Evaluate nine parts of the body based on the modified Ferriman Gallway score (mF-G score) [25] for Asian women. For Chinese women, a score greater than four will be diagnosed as hirsutism, or a total score of two for three parts, including the upper lip, lower abdomen, and inner thigh, can also be diagnosed. According to the Pillsbury classification system [26] for acne, 0 points indicate no acne, 1-2 points indicate mild acne and 3-5 points indicate moderate cystic acne. A score of 1 or higher is considered positive. Infertility [27] is defined as the failure to achieve a clinical pregnancy after 12 months or more of regularly unprotected sexual intercourse. The sampling time of the subjects was the 2nd to 4th day of the menstrual cycle or when they came to the Gynecological Clinic of the hospital for amenorrhea. Blood samples were collected in the morning after fasting overnight for at least 8 h. Serum concentrations of FSH, LH, E<sub>2</sub>, PRL, T, P, and fasting insulin were determined by using a chemiluminescence immunoassay(Abbott I2000-3, USA). The deglycerin method(LABOSPECT008AS, Japan) was used to determine serum TG levels. TC and UC were determined by using the enzymic method (LABOSPEC-T008AS, Japan). Fasting blood glucose was determined using the Hexokinase method (LABOSPECT008AS, Japan) and direct measurement (LABOSPECT008AS, Japan) of HDL-C and LDL-C. The intra- and inter-assay coefficients of variation (CV) for all these were less than 5%, respectively.

Homeostatic model assessment insulin resistance index( HOMA-IR) [28] = fasting blood glucose level (mmol/L) \* fasting insulin level ( $\mu$ U/mL)/22.5 is calculated. The TyG index [29] was calculated with the formula: Ln [TG(mg/dL) \* fasting glucose (mg/dL)/2].

# Statistical analysis

All data were subjected to statistical analysis using SPSS 26.0. The normality of the variables was assessed using either the Kolmogorov-Smirnov or Shapiro-Wilk test. Represent data that follows a normal distribution as mean±standard deviation was used two independent sample t-tests for inter-group comparisons. Non-normally distributed data was described using median and quartiles [M (P25-P75)], and inter-group comparisons were performed using the non-parametric rank sum test (Mann Whitney U test). Count data were expressed in frequency and percentage (n,%), and the Pearson

chi-square test was used for inter-group comparison. Group comparisons based on variable normality were conducted using Independent t-tests or Mann-Whitney U-tests. Statistical methods such as binary logistic regression analysis were used to analyze the relationship between the TyG index, HOMA-IR, and depression in PCOS patients. Multivariate logistic regression models were adopted to investigate the independent association between the TyG index, HOMA-IR, and depression in PCOS patients. The first model (model 1) adjusted for infertility, acne, hirsutism, age, BMI, education, and annual family income, and the second (model 2) adjusted for infertility, acne, hirsutism, age, BMI, education, annual family income, HDL-C, LDL-C, UC, and TC.

Variables significantly associated with depression in univariate logistic regression were included in multivariate logistic regression. Six independent predictive factors were identified: TyG index, infertility, acne, hirsutism, HOMA-IR, and annual family income. The collinearity test results indicated that all variables had variance inflation factors less than 2, which suggests that collinearity can ignored. TyG index and HOMA-IR were tested for their ability to predict depression using receiver operating characteristic (ROC) curves. All statistical tests were evaluated using a two-sided test, and a *P*-value  $\leq 0.05$  was considered statistically significant for the difference being tested.

## Results

This study finally included 725 PCOS patients, 213 of whom were assessed as depressed by CES-D, and the incidence rate of depression was about 29.4%. The basic sociodemographic characteristics of all participants are shown in Table 1. The average age of the two groups was around 28, and there was no significant difference between the two groups. Women with depression had higher BMI, fasting insulin, HOMA-IR, UC, and the TyG index, and the differences were statistically significant (P<0.05). However, HDL-C was higher in patients without depression (P<0.05). There were significant differences in education level and annual household income (P<0.05). The two groups had no significant differences in E<sub>2</sub>, P, T, PRL, LH, FSH, LDL-C, and TC levels(P>0.05).

The results of the univariate analysis are presented in Table 2. We found that symptoms of infertility, hirsutism, and acne in PCOS were associated with depression, while BMI, education level, annual household income, fasting blood glucose, fasting insulin, the TyG index, HOMA-IR, HDL-C, TC, and UC levels were associated with depression also. Among these variables, education level, annual household income, and HDL-C negatively correlated with depression. The association between TyG index, HOMA-IR, HOMA-IR, and depression is shown in Table 3. Our study revealed that a higher TyG index was associated

| Table 1 | Sociodemo | ographic cha | aracteristics o | of the PCOS | women with | and without | depression |
|---------|-----------|--------------|-----------------|-------------|------------|-------------|------------|
|---------|-----------|--------------|-----------------|-------------|------------|-------------|------------|

| Characteristics                    | Depression(n=213)     | Non depression(n=512) | Pvalue  |
|------------------------------------|-----------------------|-----------------------|---------|
| Age(year)                          | 27(23, 31)            | 28(24, 31)            | 0.296   |
| Height(m)                          | 1.60(1.57, 1.63)      | 1.60(1.57, 1.64)      | 0.151   |
| Weight(kg)                         | 65.00(56.00, 70.00)   | 60.00(52.55, 70.00)   | < 0.001 |
| BMI(kg/m <sup>2</sup> )            | 25.26(22.00,29.30)    | 23.28(20.86,26.96)    | < 0.001 |
| Acne                               |                       |                       |         |
| No                                 | 72(33.8%)             | 263(51.4%)            | < 0.001 |
| Yes                                | 141(66.2%)            | 249(48.6%)            |         |
| Hirsutism                          |                       |                       | 0.009   |
| No                                 | 90(42.3%)             | 271(52.9%)            |         |
| Yes                                | 123(57.7%)            | 241(47.1%)            |         |
| Infertility                        |                       |                       | 0.010   |
| No                                 | 122(57.3%)            | 346(67.6)             |         |
| Yes                                | 91(42.7%)             | 166(32.4)             |         |
| Annual household income (RMB yuan) |                       |                       | 0.024   |
| <30,000                            | 79(37.1)              | 141(27.5)             |         |
| 30, 000-100, 000                   | 69(32.4)              | 187(36.5)             |         |
| >100,000                           | 65(30.5)              | 184(35.9)             |         |
| Education                          |                       |                       | 0.008   |
| Less than university               | 69(32.4)              | 131(25.6)             |         |
| University                         | 117(54.9)             | 276(53.9)             |         |
| More than university               | 27(12.7)              | 105(20.5)             |         |
| E <sub>2</sub> (pmol/L)            | 134.00(111.10,167.00) | 131.00(106.00,167.00) | 0.517   |
| P(nmol/L)                          | 0.81(0.60,1.10)       | 0.90(0.60,1.10)       | 0.860   |
| FSH(IU/L)                          | 5.01(4.13,6.10)       | 4.92(4.13,5.90)       | 0.575   |
| LH(IU/L)                           | 7.68(5.58,11.60)      | 8.20(5.56,11.70)      | 0.185   |
| T(nmol/L)                          | 1.74(1.39,2.22)       | 1.78(1.38,2.16)       | 0.884   |
| PRL(ug/L)                          | 13.90(10.00,17.60)    | 13.40(10.20,17.80)    | 0.528   |
| Fasting blood glucose(mg/dl)       | 90.72(85.32,98.64)    | 89.82(84.60,95.94)    | 0.073   |
| Fasting insulin(µIU/mI)            | 13.70(9.50,20.85)     | 10.20(7.24,14.60)     | < 0.001 |
| HOMA-IR                            | 3.19(1.97,4.87)       | 2.26(1.55,3.35)       | < 0.001 |
| TG(mg/dl)                          | 142.65(104.55,198.02) | 102.78(73.76,138.22)  | < 0.001 |
| TyG index                          | 8.78(8.42~9.12)       | 8.47(8.08~8.77)       | < 0.001 |
| HDL-C(mmol/L)                      | 1.29(1.05,1.55)       | 1.38(1.15,1.68)       | < 0.001 |
| LDL-C(mmol/L)                      | 2.86(2.30,3.34)       | 2.73(2.26,3.29)       | 0.517   |
| TC(mmol/L)                         | 4.74(4.13,5.33)       | 4.70(4.12,5.34)       | 0.962   |
| UC(µmol/l)                         | 329.00(272.00,388.00) | 310.00(259.75,369.25) | 0.029   |

BMI, Body mass index; E<sub>2</sub>, Estradiol; P, Progesterone; FSH, Follicle-stimulating hormone; LH, Luteinizing hormone; T, Testosterone; PRL, Prolactin; HOMA-IR, Homeostatic model assessment insulin resistance index; TG, Triglycerides; TyG index, triglyceride glucose index; HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; TC, Total cholesterol; UC, Uric acid. Values are reported as median (25th percentile, 75th percentile) or number (%). The Mann-Whitney U test for continuous variables and x<sup>2</sup> test for categorical variables analyzed data

with an elevated risk of depression in populations with PCOS. This association was statistically significant in adjusted model 1 (OR =  $3.965(2.692 \sim 5.840)$ , *P*<0.001) and fully adjusted model 2 (OR = 4.552 (2.975 ~ 6.966), *P*<0.001). Compared to HOMA-IR in corrected model 1( $1.228(1.129 \sim 1.336)$ , *P*<0.001) and fully corrected model 2(1.224 ( $1.122 \sim 1.336$ ), *P*<0.001), the TyG index was a more significant risk factor for depression.

Figures 1 and 2, along with Table 4, presented the ROC curve and its characteristics for TyG index, HOMA-IR, and multi-factor in the prediction of depression in PCOS. The area under the ROC curve (AUC) of the predictive model for depression with TyG index was

 $0.687(0.644 \sim 0.73)$ , with sensitivity equal to 61.5% and specificity equal to 66.8%(Fig. 1. A; Table 4). We combined other predictors with the TyG index using multiple logistic regression analysis to compare its performance. It found that the AUC improved to  $0.724(0.684 \sim 0.765)$ , with sensitivity equal to 58% and specificity equal to 77.3%. (Fig. 1. B; Table 4). The AUC of HOMA-IR(0.634,  $0.588 \sim 0.68$ ) was lower than the TyG index, with sensitivity equal to 58.2% and specificity equal to 66.4%(Fig. 2.C; Table 4). Combined with other predictive factors, the AUC of HOMA-IR ( $0.698, 0.656 \sim 0.74$ ) was still lower than the TyG index, with sensitivity equal to 60.6% and specificity equal to 60.6% and specificity equal to 69.7%. (Fig. 2.D; Table 4).

| Tabl | <b>e 2</b> Univariate ana | lysis of | fvarious | parameters and | d c | depression in | patients wit | h F | PC | 0 | S |
|------|---------------------------|----------|----------|----------------|-----|---------------|--------------|-----|----|---|---|
|------|---------------------------|----------|----------|----------------|-----|---------------|--------------|-----|----|---|---|

| Variable                | β-coefficient | OR (95% CI)          | Р       |
|-------------------------|---------------|----------------------|---------|
| Infertility             | 0.441         | 1.555(1.119~2.159)   | 0.008   |
| Acne                    | 0.727         | 2.068(1.483~2.885)   | < 0.001 |
| Hirsutism               | 0.43          | 1.537(1.113~2.122)   | 0.009   |
| BMI                     | 0.061         | 1.063(1.03~1.098)    | < 0.001 |
| Education               |               |                      |         |
| Less than university    |               | 1.0                  | 0.024   |
| University              | -0.217        | 0.805(0.560~1.157)   | 0.241   |
| More than university    | -0.717        | 0.488(0.292~0.816)   | 0.006   |
| Annual household income |               |                      |         |
| <30,000                 |               | 1.0                  | 0.039   |
| 30, 000-100, 000        | -0.418        | 0.659(0.446~0.973)   | 0.036   |
| >100,000                | -0.461        | 0.631(0.425~0.936)   | 0.022   |
| Fasting blood glucose   | 0.216         | 1.241(1.007~1.53)    | 0.043   |
| Fasting insulin         | 0.055         | 1.057(1.037 ~ 1.077) | 0.000   |
| TG                      | 0.005         | 1.005(1.003 ~ 1.007) | < 0.001 |
| HOMA-IR                 | 0.226         | 1.254(1.162~1.353)   | < 0.001 |
| TyG idex                | 1.426         | 4.162(2.898~5.977)   | < 0.001 |
| HDL-C                   | -0.684        | 0.505(0.324~0.786)   | 0.002   |
| LDL-C                   | -0.006        | 0.994(0.967~1.022)   | 0.669   |
| TC                      | 0.005         | 1.005(0.847 ~ 1.193) | 0.953   |
| UC                      | 0.002         | 1.002(1.000~1.004)   | 0.016   |

BMI, Body mass index; TG, Triglycerides; HOMA-IR, Homeostatic model assessment insulin resistance index; TyG index, triglyceride glucose index; HDL-C, Highdensity lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; TC, Total cholesterol; UC, Uric acid

 Table 3
 Association between triglyceride glucose index and depression in PCOS

| Variable  | Model 1                  | Р          | Model 2            | Р       |
|-----------|--------------------------|------------|--------------------|---------|
|           | OR(95%CI)                |            | OR(95%CI)          |         |
| TyG index | 3.965(2.692~5.840)       | < 0.001    | 4.552(2.975~6.966) | < 0.001 |
| HOMA-IR   | 1.228(1.129~1.336)       | < 0.001    | 1.224(1.122~1.336) | < 0.001 |
| TC        | terration and the second | the states |                    |         |

TyG index, triglyceride glucose index; HOMA-IR, Homeostatic model assessment insulin resistance index. Model 1: Infertility, acne, hirsutism, age, BMI, education, and annual family income were adjusted. Model 2:Infertility, acne, hirsutism, age, BMI, education, annual family income, HDL-C, LDL-C, UC, and TC were adjusted

# Discussion

This study showed a positive association between the TyG index and the incidence of depression in the PCOS populations. A higher TyG index can elevate the risk of depressive disorders. TyG index was an independent predictor of depression in patients with PCOS, and its predictive performance was better than HOMA-IR. In a systematic review and meta-analysis conducted by Hongzheng [30], the prevalence of depression in women with PCOS in the Chinese Mainland was 37% (95% CI, 29 -44%). Damone AL et al. [31] found that the incidence rate of depression in PCOS patients was 27.5%, and Mehrukh Zehravi et al. [32] mentioned in the review that the incidence rate of depression in PCOS patients ranged from 28 to 64%. The incidence rate of depression in our study is 29.4%, which is consistent with other studies.

The TyG index [33] has been directly associated with glucose-lipid metabolism as an indirect marker of IR in

recent years. Jihoon Oh [19] found in a nationwide survey on effective measurement of depression conducted in South Korea that high serum TG levels are associated with depression in adult women (there is a significant association between high levels of TG ( $\geq 150 \text{ mg/dl}$ ) and depression in adult women). A two-sample Mendelian randomization analysis by So HC [34] suggested that high TG levels may be a causal risk factor for depression and its associated features. In a large sample study of American adults by Erin Hoare et al. [35], it was found that the higher the fasting blood sugar in women, the more severe the symptoms of depression after controlling for other population and lifestyle behavioral risk factors. In our study, the serum TG of the depression group was significantly higher than that of the non-depression group, but the difference in fasting blood glucose between the two groups was not significant. Possible factors include differences in race and the scales used to assess depression. Possible factors include differences in age, race, and the scales used to assess depression. A nationwide cross-sectional study conducted by Shi [18] found that individuals with higher TyG index were more likely to experience depressive symptoms among American adults. A study conducted by Nan et al. [36] found that the TyG index was an independent risk factor for depression in patients with coronary atherosclerotic heart disease(OR = 6.604 (3.007~14.505), P< 0.001). Jeong Kyung Ko [37] also conducted a national health and nutrition examination survey on a representative sample of South Korea and



Fig. 1 ROC curves of single-factor and multi-factor validation models. Figure A shows the ROC curve of the TyG index. Figure B shows the ROC curve of the TyG index and multi-factor prediction model



Fig. 2 ROC curves of single-factor and multi-factor validation models. Figure C shows the ROC curve of the HOMA-IR. Figure D shows the ROC curve of the HOMA-IR and multi-factor prediction model

| Table 4 Ability of the Ty | vG index. HOMA-IR | and multi-factor to | predict depression anal | vsis based on Roc curves |
|---------------------------|-------------------|---------------------|-------------------------|--------------------------|
|                           |                   |                     |                         |                          |

| Variable                             | AUC   | Cut-off | OR(95%CI)   | Sensitivity | Specificity | Р       |  |
|--------------------------------------|-------|---------|-------------|-------------|-------------|---------|--|
| TyG index                            | 0.687 | 8.67    | 0.644~0.73  | 61.5%       | 66.8%       | < 0.001 |  |
| HOMA-IR                              | 0.634 | 2.75    | 0.588~0.68  | 58.2%       | 66.4%       | < 0.001 |  |
| TyG index + other predictive factors | 0.724 | 0.36    | 0.684~0.765 | 58%         | 77.3%       | < 0.001 |  |
| HOMA-IR + other predictive factors   | 0.698 | 0.31    | 0.656~0.74  | 60.6%       | 69.7%       | < 0.001 |  |

TyG index, triglyceride glucose index; HOMA-IR, Homeostatic model assessment insulin resistance index. Other predictive factors: infertility, acne, hirsutism, and annual family income

found that high TG levels and elevated fasting blood glucose levels may lead to adult suicide risk and depression symptoms. Lee et al. [38] found a significant association between depression and TyG index in a national health and nutrition examination survey of 4688 adults in South Korea. Zhang Xin et al. [39] found that it had a 32% increase in depression risk per unit elevation in the TyG index among the hypertensive population in the United States.

The specific mechanism of the relationship between the TyG index and depression in PCOS patients is unclear. Firstly, IR may play an important role in the associations between the TyG index and depressive disorders. Rodent models of impaired insulin signaling show dysregulated energy and glucose homeostasis, as well as anxiety-like and depressive behaviors [40]. Kleinridders A. et al. [41] study discovered that mice with a brain-specific knockout of the insulin receptor (NIRKO mice) develop agerelated depressive-like behaviors. IR in the brain induces mitochondrial and dopaminergic dysfunction, leading to depressive-like behaviors. Multiple studies [15, 33]have reported that there is a significant association between IR and depression, which can increase the risk of depression. Li J's research [34] on people without diabetes found that moderate-to-severe depression significantly increased the odds of IR (OR = 1.65, 95% CI: 1.04-2.61, p = 0.035), and the use of antidepressants also reduced this association. Erensoy's findings [42] suggest that metformin decreases IR and improves mood both in adolescent and adult women with PCOS. Greenwood et al. [35] conducted a study on 738 PCOS patients, which showed that HOMA-IR was associated with a 1.23-fold increased risk of depression, suggesting that IR can independently affect the onset of depression. In this study, it was found that when IR increases, the risk of depression symptoms in PCOS increases by 25%. These studies suggested a complex interplay between IR and depression, warranting additional investigation.

Secondly, inflammation may play an important role between the two. The TyG index is positively correlated with the levels of pro-inflammatory factors such as white blood cells and C-reactive protein, while proinflammatory factors are positively correlated with the severity of depression. Antidepressants can reduce the levels of pro-inflammatory cytokines in patients with depression. Another possible mechanism is oxidative stress(OS) [43–45]. In previous studies, oxidative stress [46] has been identified as an important cause of depression, and the involvement in the pathogenesis of depression is clear. Reactive oxygen species(ROS) play a crucial role in normal brain function and the pathogenesis of neurological disorders [47]. The brain is more susceptible to OS due to its higher oxygen consumption, higher lipid content, and weaker antioxidant defense ability [48]. Oxidative stress may also damage the structure and function of mitochondria, causing mitochondrial DNA damage or abnormal mitochondrial protein function, reduced ATP synthesis, and disrupted cellular energy metabolism. These changes exacerbate the generation and toxic effects of intracellular reactive oxygen species, thereby exacerbating the occurrence of depression [49–52]. The increase in the TyG index exacerbates the body's prooxidative state, producing a large number of free radicals; oxidative stress damages brain tissue and ultimately leads to depression [39, 53, 54].

To our knowledge, this is the first study to investigate the relationship between the TyG index and depression among individuals with PCOS. This study contributes to our attention on blood lipids and glucose in depression and offers a reference for the clinical prevention and treatment of PCOS with comorbid depression. However, our study still has some limitations. First, the study population in this research is limited, as it is only from China and does not exclude patients with diabetes. Second, our study was a cross-sectional observational study and cannot determine the causal relationship between the TyG index and depression. Therefore, more research, such as prospective cohort studies and the long follow-up period, is needed to validate and expand existing findings in the future. In addition, due to the inability to include sufficiently adjusted covariates, it is impossible to avoid the bias caused by this situation.

# Conclusions

A high TyG index is associated with higher odds of having depression in PCOS after adjustment for potential confounders. This finding indicated that the TyG index may be an independent predictor of depression development.

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#### Author contributions

Guili Chen and Lin Zhu are co-first authors. Guili Chen: Project development and research design, manuscript writing– original draft. Lin Zhu: Data curation, manuscript writing– original draft. Weirong Mao and Lanying Wang: Data collection, input and correction. Yingyun Wu and Ying Lou: Data statistics and analysis. Jianting Ma made critical revisions to the manuscript for important intellectual content and contributed to the study concept, design, and implementation. All the authors discussed the first draft of the paper and put forward suggestions for revision. All authors read and approved the final manuscript.

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## Data availability

Data is provided within the manuscript or supplementary information files. Sequence data that support the findings of this study have been deposited in the Science Data Bank. The online version contains supplementary material available at https://www.scidb.cn/anonymous/TmZNM1ly.

#### Declarations

#### Ethics approval and consent to participate

The study was approved by the Ethics Committee of Yuyao People's Hospital (protocol code: 2022-03-014), and informed consent was obtained from participants. The Protocol of the current study was performed in accordance with the Declaration of Helsinki standards.

## **Consent for publication**

Not applicable.

#### **Competing interests**

The authors declare no competing interests.

#### Supplementary information

The online version contains supplementary material available at https://www.scidb.cn/anonymous/TmZNM1ly.

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# References

- Revised. 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Human Reproduction. 2004;19(1):41–7.
- Alvarez YR, Pico M, Ashokprabhu N, Abou-Amro K, Bailey S, Pung E, et al. Polycystic ovarian syndrome: a risk factor for cardiovascular disease. Curr Atheroscler Rep. 2023;25(12):1003–11.
- Osibogun O, Ogunmoroti O, Michos ED. Polycystic ovary syndrome and cardiometabolic risk: opportunities for cardiovascular disease prevention. Trends Cardiovasc Med. 2020;30(7):399–404.
- Teede HJ, Tay CT, Laven J, Dokras A, Moran LJ, Piltonen TT, et al. Recommendations from the 2023 international Evidence-based guideline for the assessment and management of polycystic ovary syndrome. Fertil Steril. 2023;120(4):767–93.
- Cooney LG, Lee I, Sammel MD, Dokras A. High prevalence of moderate and severe depressive and anxiety symptoms in polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod. 2017;32(5):1075–91.
- Kessler RCBE. The epidemiology of depression across cultures. Annu Rev Public Health. 2013;34:119–38.
- Depression. and Other common mental disorders, global health estimates. World Health Organization; 2017.
- Santomauro DF, Mantilla Herrera AM, Shadid J, Zheng P, Ashbaugh C, Pigott DM, et al. Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. Lancet. 2021;398(10312):1700–12.
- Anju E, Joham RJN, Elisabet Stener-Victorin RS, Legro S, Franks LJ, Moran. Jacqueline Boyle, Helena J Teede. Polycystic ovary syndrome. Lancet Diabetes Endocrinol. 2022;10(9):668–80.
- Wu H, Ballantyne CM. Metabolic inflammation and insulin resistance in obesity. Circul Res. 2020;126(11):1549–64.
- Yaribeygi H, Sathyapalan T, Atkin SL, Sahebkar A. Molecular mechanisms linking oxidative stress and diabetes mellitus. Oxidative Med Cell Longev. 2020;2020:1–13.
- Yaribeygi H, Butler AE, Barreto GE, Sahebkar A. Antioxidative potential of antidiabetic agents: A possible protective mechanism against vascular complications in diabetic patients. J Cell Physiol. 2018;234(3):2436–46.
- Willmer T, Goedecke JH, Dias S, Louw J, Pheiffer C. DNA methylation of FKBP5 in South African women: associations with obesity and insulin resistance. Clin Epigenetics. 2020;12(1).
- Behnoush AH, Mousavi A, Ghondaghsaz E, Shojaei S, Cannavo A, Khalaji A. The importance of assessing the triglyceride-glucose index (TyG) in patients with depression: a systematic review. Neurosci Biobehav Rev. 2024;159:105582.
- Lee J-H, Park SK, Ryoo J-H, Oh C-M, Mansur RB, Alfonsi JE, et al. The association between insulin resistance and depression in the Korean general population. J Affect Disord. 2017;208:553–9.
- Kan CSN, Golden SH, Rajala U, Timonen M. A systematic review and metaanalysis of the association between depression and insulin resistance. Diabetes Care. 2013;36(2):480–9.

- Nabipoorashrafi SA, Seyedi SA, Rabizadeh S, Ebrahimi M, Ranjbar SA, Reyhan SK, et al. The accuracy of triglyceride-glucose (TyG) index for the screening of metabolic syndrome in adults: A systematic review and meta-analysis. Nutr Metabolism Cardiovasc Dis. 2022;32(12):2677–88.
- Shi Y-Y, Zheng R, Cai J-J, Qian S-Z. The association between triglyceride glucose index and depression: data from NHANES 2005–2018. BMC Psychiatry. 2021;21(1).
- Oh J, Kim T-S. Serum lipid levels in depression and suicidality: the Korea National health and nutrition examination survey (KNHANES) 2014. J Affect Disord. 2017;213:51–8.
- Xu Z-Y, Zheng H, Pan Z-J, Hu S-Y, Wang Y-X, Su W-J. Association between triglyceride-glucose (TyG) index and risk of depression in middle-aged and elderly Chinese adults: evidence from a large National cohort study. Biomolecules Biomed. 2025.
- 21. Radloff LS, The CES-D, Scale A. Self-Report depression scale for research in the general population. Appl Psychol Meas. 1977;1(3):385–401.
- Li H, Zheng D, Li Z, Wu Z, Feng W, Cao X et al. Association of depressive symptoms with incident cardiovascular diseases in Middle-Aged and older Chinese adults. JAMA Netw Open. 2019;2(12).
- Jiang LWY, Zhang Y, Li R, Wu H. The reliability and validity of the center for epidemiologic studies depression scale (CES-D) for Chinese university students. Front Psychiatry. 2019;10:315.
- 24. Fu H, Si L, Guo R. What is the optimal Cut-Off point of the 10-Item center for epidemiologic studies depression scale for screening depression among Chinese individuals aged 45 and over?? An exploration using latent profile analysis. Front Psychiatry. 2022;13.
- Bayhan G, Demirkol MBT, Ertem, A M, Yalinkaya, A, C Erden. A comparative study of a gonadotropin-releasing hormone agonist and finasteride on idiopathic hirsutism. Clin Exp Obstet Gynecol. 2000;27(3–4):203–6.
- Colonna L, Pacifico V, Lello S, Sorge R, Raskovic D, Primavera G. Skin improvement with two different oestroprogestins in patients affected by acne and polycystic ovary syndrome: clinical and instrumental evaluation. J Eur Acad Dermatol Venereol. 2011;26(11):1364–71.
- 27. Handelsman DJ, Cong J, Li P, Zheng L, Tan J. Prevalence and risk factors of infertility at a rural site of Northern China. PLoS ONE. 2016;11(5).
- 28. Luo LHJ, Huang R, Kong D. The association between dietary inflammation index and depression. Front Psychiatry. 2023;14:1131802.
- Liu C, Liang D. The association between the triglyceride–glucose index and the risk of cardiovascular disease in US population aged ≤ 65 years with prediabetes or diabetes: a population-based study. Cardiovasc Diabetol. 2024;23(1).
- Hong Z, Wu P, Zhuang H, Chen L, Hong S, Qin J. Prevalence of depression among women with polycystic ovary syndrome in Mainland China: a systematic review and meta-analysis. BMC Psychiatry. 2024;24(1).
- Damone AL, Joham AE, Loxton D, Earnest A, Teede HJ, Moran LJ. Depression, anxiety and perceived stress in women with and without PCOS: a community-based study. Psychol Med. 2018;49(09):1510–20.
- Zehravi M, Maqbool M, Ara I. Depression and anxiety in women with polycystic ovarian syndrome: a literature survey. Int J Adolesc Med Health. 2021;33(6):367–73.
- Nam K-W, Kwon H-M, Jeong H-Y, Park J-H, Kwon H, Jeong S-M. High triglyceride-glucose index is associated with subclinical cerebral small vessel disease in a healthy population: a cross-sectional study. Cardiovasc Diabetol. 2020;19(1):53.
- So H-C, Chau CK-I, Cheng Y-y, Sham PC. Causal relationships between blood lipids and depression phenotypes: a Mendelian randomisation analysis. Psychol Med. 2020;51(14):2357–69.
- Hoare E, Dash S, Varsamis P, Jennings G, Kingwell B. Fasting plasma glucose, Self-Appraised diet quality and depressive symptoms: A US-Representative Cross-Sectional study. Nutrients. 2017;9(12).
- Guan J, Wang Y, Dong C, Chen Y, Li B, Zhou Y, et al. The impact of the Triglyceride-Glucose index on the development of depression in patients with coronary atherosclerotic heart disease. Neuropsychiatr Dis Treat. 2024;20:2105–13.
- Ko J-K, Han K-M, Shin C, Lee S-H, Han C, Kim Y-K, et al. Association of metabolic syndrome and its components with suicidal ideation and depression in adults: A nationally representative sample of the Korean population. J Affect Disord. 2019;249:319–26.
- Lee JW, Park SH. Association between depression and nonalcoholic fatty liver disease: contributions of insulin resistance and inflammation. J Affect Disord. 2021;278:259–63.

- Zhang X, Zhao D, Guo S, Yang J, Liu Y. Association between triglyceride glucose index and depression in hypertensive population. J Clin Hypertens. 2024;26(2):177–86.
- 40. Rawlinson S, Andrews ZB. Hypothalamic insulin signalling as a nexus regulating mood and metabolism. J Neuroendocrinol. 2021;33(4).
- Kleinridders A, Cai W, Cappellucci L, Ghazarian A, Collins WR, Vienberg SG et al. Insulin resistance in brain alters dopamine turnover and causes behavioral disorders. Proceedings of the National Academy of Sciences. 2015;112(11):3463-8.
- Erensoy HNM, Ghafarzadeh S, Aghamohammadzadeh N, Nader ND. A pilot trial of Metformin for insulin resistance and mood disturbances in adolescent and adult women with polycystic ovary syndrome. Gynecol Endocrinol. 2019;35(1):72–5.
- MH HMCYC. Pro-inflammatory cytokines and cognitive dysfunction among patients with bipolar disorder and major depression. Psychiatry Clin Neurosci. 2022;76(9):450–8.
- 44. Ryan KM, McLoughlin DM. Peripheral blood inflammatory markers in depression: response to electroconvulsive therapy and relationship with cognitive performance. Psychiatry Res. 2022;315.
- 45. Carr AL, Sluiman AJ, Grecian SM, Forster R, McLachlan S, Strachan MWJ, et al. Depression as a risk factor for dementia in older people with type 2 diabetes and the mediating effect of inflammation. Diabetologia. 2020;64(2):448–57.
- Liu LLM, Xiu J, Zhang B,Hu H. Stimuli-responsive nanoparticles delivered by a nasal-brain pathway alleviate depression-like behavior through extensively scavenging ROS. Acta Biomater. 2023;171:451–65.
- Hassan W, Noreen H, Rehman S, Kamal MA, da Rocha JBT. Association of oxidative stress with neurological disorders. Curr Neuropharmacol. 2022;20(6):1046–72.

- Bhatt S, Nagappa AN, Patil CR. Role of oxidative stress in depression. Drug Discovery Today. 2020;25(7):1270–6.
- Chen H, Lu M, Lyu Q, Shi L, Zhou C, Li M et al. Mitochondrial dynamics dysfunction: unraveling the hidden link to depression. Biomed Pharmacother. 2024;175.
- Czarny P, Wigner P, Galecki P, Sliwinski T. The interplay between inflammation, oxidative stress, DNA damage, DNA repair and mitochondrial dysfunction in depression. Prog Neuropsychopharmacol Biol Psychiatry. 2018;80:309–21.
- 51. Tobe E. Mitochondrial dysfunction, oxidative stress, and major depressive disorder. Neuropsychiatr Dis Treat. 2013.
- Ying Xu CW, Jonathan J, Klabnik JM, O'Donnell. Novel therapeutic targets in depression and anxiety antioxidants as a candidate treatment. Curr Neuropharmacol. 2014;12:108–19.
- 53. Adams-Huet B, Jialal I. An increasing Triglyceride–Glucose index is associated with a Pro-Inflammatory and Pro-Oxidant phenotype. J Clin Med. 2024;13:13.
- Luca M, Luca A. Oxidative Stress-Related endothelial damage in vascular depression and vascular cognitive impairment: beneficial effects of aerobic physical exercise. Oxidative Med Cell Longev. 2019;2019:1–6.

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