

The Association Between Triglyceride-Glucose Index and Its Combination with Obesity Indicators and Lower Extremity Peripheral Artery Disease in Patients with Type 2 Diabetes Mellitus: A Cross-Sectional Study

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Background: Lower extremity peripheral artery disease (LEAD) is a significant chronic complication of type 2 diabetes mellitus (T2DM) that significantly contributes to disability and mortality. The subtle presentation of LEAD symptoms often leads to under-recognition and misdiagnosis. Therefore, identifying simple and effective evaluation indicators is essential for the early detection and management of LEAD. Insulin resistance is closely associated with diabetes and its complications. However, the specific relationship between insulin resistance—measured by the triglyceride-glucose (TyG) index—and obesity indicators in relation to LEAD remains unclear.

Objective: This study aims to investigate the association between the TyG index and its combination with obesity indicators in participants with T2DM and LEAD.

Methods: We performed a univariate analysis on 3176 T2DM patients to identify risk factors for LEAD. Patients were then divided into quartiles based on the TyG index combined with various obesity indicators. The chi-square test was used to compare the prevalence of LEAD across these groups. Logistic regression analysis was conducted to examine the association between the TyG index, in combination with different obesity indicators, and the occurrence of LEAD. Finally, we assessed the predictive ability of the TyG index combined with obesity indicators for LEAD by comparing the area under the ROC curve (AUC).

Results: The study included 3176 T2DM patients (1691 males and 1485 females) with a mean age of 56.16±10.60 years. Among them, 106 individuals had LEAD. The prevalence of LEAD varied significantly across quartiles of the TyG index, TyG-WC, and TyG-WHR (Q4 > Q3 > Q2 > Q1; P < 0.05). Multiple logistic regression analysis showed that the TyG index, TyG-WC, and TyG-WHR were positively associated with the risk of LEAD in T2DM patients. ROC curve analysis identified the best cutoff values for predicting LEAD: 9.8059 for the TyG index (sensitivity: 49.1%, specificity: 67.9%, AUC: 0.583), 808.8397 for TyG-WC (sensitivity: 70.8%, specificity: 47.8%, AUC: 0.603), and 8.8543 for TyG-WHR (sensitivity: 75.5%, specificity: 44.6%, AUC: 0.607).

Conclusion: In T2DM patients, the TyG index, TyG-WHR, and TyG-WC are positively associated with the occurrence of LEAD. TyG-WHR and TyG-WC exhibit a stronger correlation with LEAD compared to the TyG index alone, indicating their superior diagnostic value.

Keywords: type 2 diabetes mellitus, lower extremity peripheral artery disease, TyG-WC, TyG-WHR, insulin resistance

Introduction

The International Diabetes Federation (IDF) estimated that in 2019, 463 million people worldwide had diabetes mellitus (DM), and this number is projected to reach 700 million by 2045.¹ Peripheral arterial disease (PAD) stands out as one of the major chronic complications of DM.² Specifically, PAD refers to a vascular disease resulting from structural and functional abnormalities of the aorta and its branches due to atherosclerosis and thrombosis. Primarily affecting the arteries of the lower extremities, PAD often manifests with symptoms such as intermittent claudication. The relationship between diabetes and PAD is significant, with diabetes serving as a notable risk factor. Diabetic individuals are 2 to 4 times more likely to develop PAD compared to non-diabetic populations,^{2,3} and 20% to 35% of PAD patients also have DM.⁴ Importantly, atherosclerotic vascular disease, encompassing PAD, coronary heart disease (CHD), and cerebrovascular disease, stands as the leading cause of disability and mortality in type 2 diabetes mellitus (T2DM).^{5,6} Despite this, PAD has historically received less attention than CHD or stroke among the various pathological consequences of atherosclerosis.⁷ This article primarily focuses on lower extremity PAD, specifically referred to as LEAD.

Sarcopenia and LEAD have musculoskeletal consequences that directly impair patients' quality of life and prognosis. Although PAD is primarily a vascular disease, all etiological factors of sarcopenia identified so far are present in PAD. Indeed, both sarcopenia and PAD are accompanied by oxidative stress, skeletal muscle mitochondrial impairments, inflammation, inhibition of specific pathways regulating muscle synthesis or protection (ie IGF-1, RISK, and SAFE), and activation of molecules associated with muscle degradation.⁸ Symptoms of LEAD in diabetic patients often remain hidden. Only 10% display typical intermittent claudication symptoms, while 50% present with other lower limb symptoms, and the remaining 40% are asymptomatic.^{9–11} Diabetic LEAD frequently coexists with diabetic peripheral neuropathy, where some patients exhibit diminished pain perception, obscuring the symptoms and severity of LEAD. Consequently, diabetic LEAD shows a higher prevalence of asymptomatic or atypical symptoms compared to non-diabetic LEAD.² Asymptomatic diabetic LEAD patients face a similar risk of cardiovascular death as symptomatic patients.¹² These differences highlight the necessity for early screening and treatment in diabetic patients. Regular assessment of LEAD risk markers and early preventive measures are crucial for managing the disease in diabetic patients.

Metabolic diseases characterized by insulin resistance (IR), including hyperglycemia and obesity, are independent risk factors for cardiovascular disease.¹³ These conditions pose a significant public health challenge that necessitates urgent intervention and control. IR acts as a crucial link in metabolic disorders, serving as the common pathophysiological basis for initiating both metabolic and cardiovascular diseases, and it stands as the major cause and independent prognostic factor of atherosclerosis.¹⁴ It is also one of the underlying mechanisms of T2DM and a key factor contributing to the progression of the disease.¹⁵ Atherosclerotic vascular disease, the most prevalent complication of T2DM, is closely associated with IR.¹⁶ However, direct methods for measuring IR, such as the hyperinsulinemic-euglycemic clamp test and insulin suppression test, are invasive, complex, expensive, and not conducive to widespread clinical application and rapid detection. In recent years, some researchers have proposed using the triglyceride-glucose (TyG) index as a simple indicator to assess IR. Previous studies have explored the relationship between the TyG index and the coexistence of diabetes and atherosclerotic vascular disease.¹⁷ However, the association between the TyG index, combined with various obesity indices, and the coexistence of T2DM and LEAD remains unexplored.

This study investigated the association between TyG index, combined with various obesity indices, and the coexistence of T2DM and LEAD through a cross-sectional analysis. The findings provide a theoretical foundation for the early detection and prevention of LEAD in patients with T2DM.

Methods

Study Participants

Figure 1 illustrates the process of selecting study subjects from the National Metabolic Management Center (MMC) database. Following the application of inclusion and exclusion criteria, a total of 3176 T2DM patients, aged between 18 and 80 years, were identified from the Department OF Endocrinology and Metabolism at the Affiliated Hospital of Southwest Medical University. This selection occurred between September 2017 and January 2024. The patients were

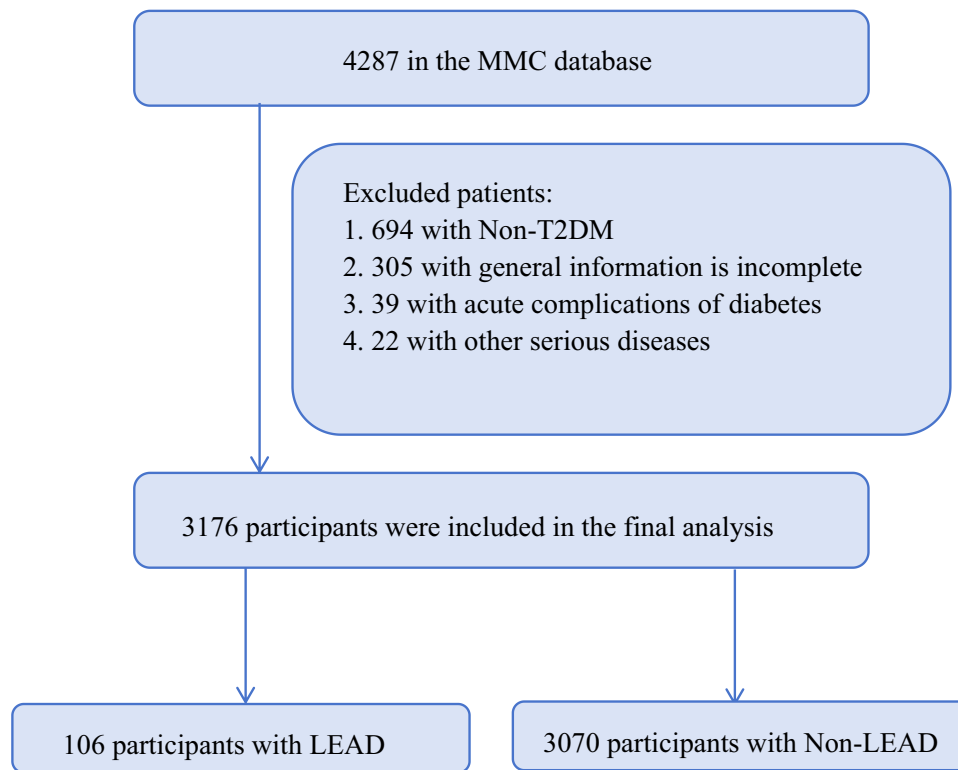


Figure 1 Flowchart for the selection of the participants from the MMC database.

part of the MMC, which offers standardized management for metabolic diseases under the leadership of Ruijin Hospital, Shanghai. They underwent a comprehensive assessment that included standardized questionnaires, physical examinations, laboratory tests, and screening for diabetes-related complications. All patients were confirmed to have T2DM based on the American Diabetes Association's "Standards of Medical Care in Diabetes" (2020 version): fasting plasma glucose (FPG) ≥ 7.0 mmol/L, and/or oral glucose tolerance test (OGTT) 2-hour post-load plasma glucose ≥ 11.1 mmol/L, and/or hemoglobin A1c (HbA1c) $\geq 6.5\%$ and/or self-reported medical history.¹⁸ Additionally, the diagnosis of T2DM with LEAD was based on the standard criteria recommended by the American Heart Association: a resting ABI ≤ 0.9 , or imaging methods including duplex ultrasound, computed tomography angiography, or digital subtraction angiography showing stenosis or thrombosis in the lower extremity peripheral arteries.¹⁹

The inclusion criteria for participants were as follows: (1) Age 18 years or older; (2) Diagnosis in accordance with the American Diabetes Association's "Standards of Medical Care in Diabetes" (2020 version); (3) Completion of ankle-brachial index (ABI) examination. Conversely, the exclusion criteria encompassed: (1) Presence of type 1 diabetes; (2) Presence of other specific types of diabetes; (3) Presence of gestational diabetes; (4) Acute complications of DM, including diabetic ketoacidosis, hyperglycemic hyperosmolar state, hyperosmolar coma, and hypoglycemia; (5) Concurrent severe diseases such as tumors, liver failure, renal failure, etc.; (6) Incomplete or missing demographic or clinical data.

Data Collection

Researchers, equipped with professional training, gathered demographic, lifestyle, and medical history data from participants. In assessing medical history, considerations included hypertension, CHD, liver diseases, kidney diseases, and other relevant conditions. Additionally, the medication status of participants was documented, encompassing antidiabetic drugs, antihypertensive medications, antihypertensive drugs, and antiplatelet medications. Physical examinations were conducted before breakfast, participants' weight and height were measured with lightweight clothing and no shoes, and body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. Circumferences of the

head, neck, waist, and hips were measured. The waist-to-hip ratio (WHR) was calculated as the waist circumference (WC) divided by the hip circumference, and the waist-to-height ratio (WtHR) was calculated as the waist circumference divided by height. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured on the right arm using an Omron blood pressure monitor, with three readings taken and the average calculated.

Morning venous blood samples were collected from each participant after an overnight fast of at least 8 hours. These samples were used to measure fasting plasma glucose (FPG), 2-hour postprandial glucose (2hPG), triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), uric acid (UA), glycated hemoglobin A1c (HbA1c).

ABI Measurements

The ankle-brachial index (ABI) is a cost-effective and reliable method for assessing lower extremity hemodynamics. It is determined by dividing the highest systolic pressure in each leg—measured at the dorsalis pedis and posterior tibial arteries using a Doppler probe—by the higher of the systolic pressures in the right or left brachial artery.

Definitions

The TyG index, TyG-WC, TyG-BMI, TyG-WHR, and TyG-WtHR were computed using the following formulas: (1) TyG index = \ln [triglycerides (mg/dl) \times glucose (mg/dl)/2];¹⁷ (2) TyG-WC = TyG index \times WC (cm); (3) TyG-BMI = TyG index \times BMI; (4) TyG-WHR = TyG index \times WHR; (4) TyG-WtHR = TyG index \times WtHR. Insulin resistance was evaluated using the HOMA method with the equation: HOMA-IR = [Fasting insulin (μ U/mL) \times FPG (mmol/L)] / 22.5.²⁰

Participants were categorized into four groups (Q1, Q2, Q3, Q4) based on the quartiles of the TyG index, TyG-WC, TyG-BMI, TyG-WHR, and TyG-WtHR, respectively, with the Q1 group serving as the reference group.

Statistical Analysis

Participant characteristics were presented as mean (standard deviation) or median (interquartile range) for continuous variables, depending on their distribution, while categorical variables were expressed as count (proportion). Comparisons of continuous variables were conducted using Student's *t*-test, Mann–Whitney *U*-test, Kruskal–Wallis *H*-test, or one-way ANOVA, based on the normality of the data. Chi-square tests were used for between-group comparisons of categorical variables. The relationship between the TyG index and its combination with obesity indices and LEAD in patients with T2DM was analyzed using logistic regression models, with results presented as odds ratios (OR) and 95% confidence intervals (CI). All statistical analyses were two-tailed, with significance set at $p < 0.05$. Statistical analyses were performed using SPSS (version 26.0), and Forest plots were generated using GraphPad Prism (version 9.0.0).

Results

Clinical Characteristics

The study included 3176 T2DM patients (1691 males and 1485 females) with a mean age of 56.16 \pm 10.60 years. Among the participants, 106 individuals exhibited LEAD. The clinical characteristics of the subjects, categorized by LEAD, are detailed in [Table 1](#). Significant differences were observed in age, BMI, Neck circumference, WC, WHR, WtHR, SBP, HOMA-IR, TG, TC, LDL-C, UA, LABI, RABI, TyG index, TyG-WC, TyG-WHR, TyG-WtHR, TyG-BMI, and Hypertension, with statistically significant differences ($p < 0.05$).

Prevalence of LEAD

Comparing the prevalence of LEAD among T2DM patients stratified by quartiles of different indices reveals ([Table 2](#)): Among individuals grouped by quartiles of TyG index, TyG-WC, and TyG-WHR, the prevalence of LEAD is highest in the Q4 group, followed by Q3, Q2, and Q1 groups, with statistically significant differences ($P < 0.05$). Among individuals grouped by quartiles of TyG-WtHR, the prevalence of LEAD is higher in the Q4 and Q3 groups compared to the Q2 and Q1 groups, with statistically significant differences between groups ($P < 0.05$). There were no statistically significant differences in the prevalence of LEAD among individuals grouped by quartiles of TyG-BMI ($P > 0.05$).

Table 1 Clinical Characteristics of Participants with and without LEAD

| Variables | All | LEAD | Non-LEAD | p-value |
|-------------------------|--------------------------|--------------------------|--------------------------|---------|
| Male(%) | 1691(53.20%) | 53(50.00%) | 1638(53.40%) | 0.280 |
| Age(years) | 56.16±10.60 | 61.05±11.31 | 56.00±10.54 | <0.001 |
| Height(cm) | 160.59±8.57 | 159.18±8.76 | 160.64±8.57 | 0.084 |
| Weight(kg) | 63.90±12.03 | 64.63±12.31 | 63.88±12.02 | 0.525 |
| BMI(kg/m ²) | 24.68±3.64 | 25.50±4.42 | 24.65±3.60 | 0.018 |
| Head circumference(cm) | 56.00(55.00,57.00) | 56.00(55.00,58.00) | 56.00(55.00,57.00) | 0.676 |
| Neck circumference(cm) | 37.00(34.00,39.00) | 37.75(35.00,40.00) | 37.00(34.00,39.00) | 0.031 |
| WC(cm) | 86.16±10.20 | 89.15±10.88 | 86.06±10.16 | 0.002 |
| Hip circumference (cm) | 90.68±7.64 | 92.00±8.94 | 90.63±7.59 | 0.069 |
| WHR | 0.95±0.07 | 0.97±0.08 | 0.95±0.07 | 0.006 |
| WtHR | 0.54±0.06 | 0.56±0.07 | 0.54±0.06 | <0.001 |
| SBP (mmHg) | 135.25±20.58 | 146.85±22.91 | 134.86±20.38 | <0.001 |
| DBP(mmHg) | 79.00±11.44 | 79.70±12.48 | 78.97±11.40 | 0.526 |
| FPG(mmol/L) | 9.76±3.44 | 10.25±3.69 | 9.74±3.43 | 0.137 |
| 2hPG(mmol/L) | 14.52±4.85 | 15.38±5.01 | 14.49±4.85 | 0.065 |
| HOMA-IR | 3.11(1.77,5.66) | 9.94(5.95,18.90) | 3.06(1.76,5.56) | 0.018 |
| HbA1c (%) | 9.76±2.57 | 9.95±2.36 | 9.75±2.58 | 0.450 |
| TG (mmol/l) | 1.76(1.20,2.73) | 2.16(1.35,3.41) | 1.74(1.19,2.71) | 0.007 |
| TC (mmol/l) | 4.85±1.90 | 5.30±1.90 | 4.84±1.90 | 0.013 |
| HDL-C (mmol/l) | 1.16±0.35 | 1.12±0.31 | 1.16±0.35 | 0.188 |
| LDL-C (mmol/l) | 2.87±1.06 | 3.15±1.16 | 2.86±1.05 | 0.006 |
| UA (μmol/L) | 326.45(266.68,406.23) | 385.50(306.10,476.60) | 324.90(265.35,403.60) | <0.001 |
| LABI | 1.13(1.08,1.18) | 0.88(0.75,1.01) | 1.13(1.08,1.19) | <0.001 |
| RABI | 1.13(1.07,1.18) | 0.87(0.81,0.97) | 1.13(1.08,1.18) | <0.001 |
| LBAPWV | 1692.00(1458.00,1975.00) | 1599.00(1402.00,1944.00) | 1693.00(1459.00,1976.00) | 0.080 |
| RBAPWV | 1693.00(1458.50,1957.00) | 1728.50(1451.75,1958.50) | 1690.00(1459.00,1957.00) | 0.671 |
| TyG index | 9.48(9.00,9.99) | 9.73(9.16,10.26) | 9.48(9.00,9.99) | 0.004 |
| TyG-WC | 818.31(731.68,909.11) | 867.41(779.44,949.52) | 816.37(730.42,907.68) | <0.001 |
| TyG-WHR | 9.01(8.30,9.79) | 9.49(8.85,10.18) | 8.99(8.28,9.78) | <0.001 |
| TyG-WtHR | 5.08(4.61,5.63) | 5.47(4.95,5.96) | 5.07(4.60,5.62) | <0.001 |
| TyG-BMI | 232.80(206.54,261.43) | 241.87(220.96,269.37) | 232.54(205.94,261.24) | 0.010 |
| Hypertension(%) | 1707(53.70%) | 84(79.20%) | 1623(52.90%) | <0.001 |
| Smoking(%) | | | | 0.621 |
| Never | 1967(62.00%) | 61(57.50%) | 1906(62.10%) | |
| Ever | 663(20.90%) | 24(22.60%) | 639(20.80%) | |
| Current | 545(17.20%) | 21(19.80%) | 524(17.10%) | |
| Drinking(%) | | | | 0.502 |
| Never | 1779(56.00%) | 65(61.30%) | 1714(55.90%) | |
| Ever | 272(8.60%) | 7(6.60%) | 265(8.60%) | |
| Current | 1123(35.40%) | 34(32.10%) | 1089(35.50%) | |

Abbreviations: BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; WtHR, waist-to-height ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; 2hPG, postprandial 2-hour plasma glucose; HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; HbA1c, glycated hemoglobin A1c; TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; UA, uric acid; LABI, left ankle-brachial index; RABI, right ankle-brachial index; LBAPWV, left brachial-ankle pulse wave velocity; RBAPWV, right brachial-ankle pulse wave velocity; TyG index, triglyceride-glucose index.

Multivariate Analysis of Determinants of LEAD in Study Subjects

Logistic regression analysis was conducted using the presence of LEAD as the dependent variable (yes=1, no=0), stratified by quartiles of TyG index, TyG-WC, TyG-WHR, and TyG-WtHR, respectively (Figure 2). The results are as follows:

In the unadjusted model (Table 3, Model 1), the adjusted odds ratios (ORs) (95% confidence intervals, CIs) among individuals grouped by quartiles of TyG index were 1.520(0.801,2.883), 1.978(1.073,3.646), and 2.245(1.232,4.090) in

Table 2 Comparison of the Occurrence of LEAD Among Subjects Grouped by Different Quartiles of TyG Index and Its Combination with Different Obesity Indices

| Indicators | LEAD | Q1 | Q2 | Q3 | Q4 | χ^2 | p-value |
|------------|---------|-------------|-------------|-------------|-------------|----------|---------|
| TyG index | Yes (%) | 16(15.10%) | 24(22.60%) | 31(29.20%) | 35(33.00%) | 8.175 | 0.043 |
| | No(%) | 779(25.40%) | 769(25.00%) | 763(24.90%) | 759(24.70%) | | |
| TyG-WC | Yes(%) | 14(13.20%) | 22(20.80%) | 32(30.20%) | 38(35.80%) | 13.234 | 0.004 |
| | No(%) | 780(25.40%) | 772(25.10%) | 762(24.80%) | 756(24.60%) | | |
| TyG-WHR | Yes(%) | 14(13.20%) | 23(21.70%) | 33(31.10%) | 36(34.00%) | 11.751 | 0.008 |
| | No(%) | 780(25.40%) | 771(25.10%) | 761(24.80%) | 758(24.70%) | | |
| TyG-WtHR | Yes(%) | 18(17.00%) | 12(11.30%) | 35(33.00%) | 41(38.70%) | 22.057 | <0.001 |
| | No(%) | 776(25.30%) | 782(25.50%) | 759(24.70%) | 753(24.50%) | | |
| TyG-BMI | Yes(%) | 17(16.00%) | 25(23.60%) | 31(29.20%) | 33(31.10%) | 6.051 | 0.109 |
| | No(%) | 777(25.30%) | 769(25.00%) | 763(24.90%) | 761(24.80%) | | |

Notes: "Q1" for the first quartile, "Q2" for the second quartile, "Q3" for the third quartile, and "Q4" for the fourth quartile.

the Q2, Q3, and Q4 groups, respectively, compared to the Q1 group. The differences between the Q3 and Q4 groups and the Q1 group were statistically significant ($P < 0.05$). Similarly, among individuals grouped by quartiles of TyG-WC, the adjusted ORs (95% CIs) were 1.588(0.806,3.126), 2.340(1.239,4.419), and 2.800(1.505,5.210), respectively, compared to the Q1 group, with statistically significant differences observed between the Q3 and Q4 groups and the Q1 group ($P < 0.05$). In addition, among individuals grouped by quartiles of TyG-WHR, the adjusted ORs (95% CIs) were 1.662 (0.849,3.254), 2.416(1.283,4.550), and 2.646(1.416,4.945), respectively, compared to the Q1 group, with statistically significant differences between the Q3 and Q4 groups and the Q1 group ($P < 0.05$). Lastly, among individuals grouped by quartiles of TyG-WtHR, the adjusted ORs (95% CIs) were 0.662(0.317,1.383), 1.988(1.116,3.541), and 2.347 (1.337,4.122), respectively, compared to the Q1 group, with statistically significant differences observed between the Q3 and Q4 groups and the Q1 group ($P < 0.05$).

After adjusting for age (Table 3, Model 2), the adjusted odds ratios (ORs) (95% confidence intervals, CIs) among individuals grouped by quartiles of TyG index were 1.587(0.835,3.017), 2.237(1.209,4.137), and 2.847(1.552,5.224) in the Q2, Q3, and Q4 groups, respectively, compared to the Q1 group. Statistically significant differences were observed between the Q3 and Q4 groups and the Q1 group ($P < 0.05$). Similarly, among individuals grouped by quartiles of TyG-WC, the adjusted ORs (95% CIs) were 1.595(0.809,3.146), 2.311(1.221,4.374), and 3.094(1.658,5.773), respectively, compared to the Q1 group, with statistically significant differences observed between the Q3 and Q4 groups and the Q1 group ($P < 0.05$). Additionally, among individuals grouped by quartiles of TyG-WHR, the adjusted ORs (95% CIs) were 1.599(0.815,3.136), 2.483(1.316,4.686), and 2.783(1.486,5.212), respectively, compared to the Q1 group, with

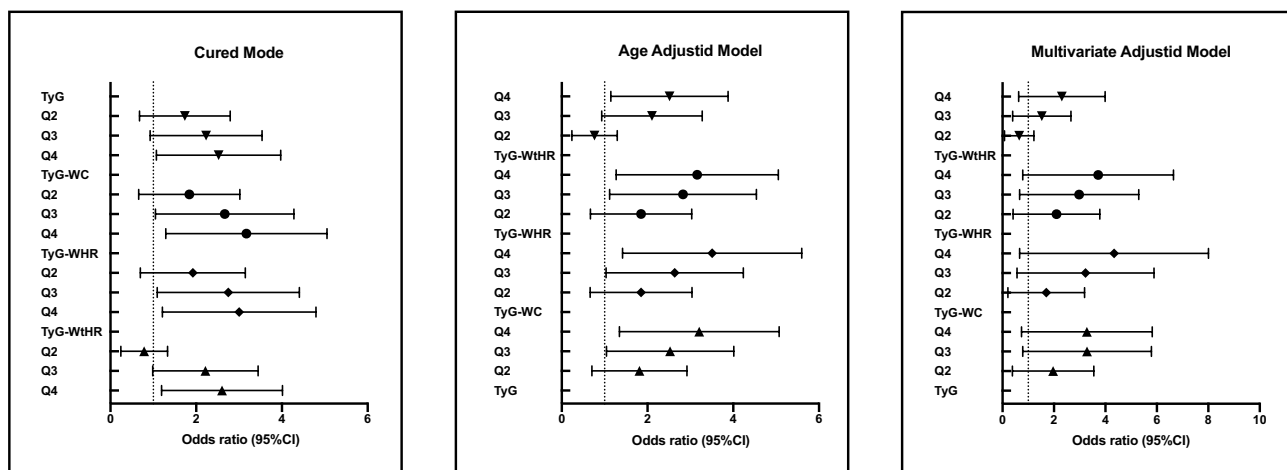


Figure 2 Forest plots for logistic regression analysis of different indexes on the risk of LEAD in T2DM patients.

Table 3 Logistic Regression Analysis of Different Indexes on the Risk of LEAD in T2DM Patients

| Indicators | Groups | Model 1 | | Model 2 | | Model 3 | |
|------------|--------|--------------------|-------|--------------------|--------|--------------------|-------|
| | | OR (95% CI) | P | OR (95% CI) | P | OR (95% CI) | P |
| TyG index | Q1 | Reference | | Reference | | Reference | |
| | Q2 | 1.520(0.801,2.883) | 0.200 | 1.587(0.835,3.017) | 0.159 | 1.542(0.639,3.721) | 0.335 |
| | Q3 | 1.978(1.073,3.646) | 0.029 | 2.237(1.209,4.137) | 0.010 | 2.652(1.164,6.043) | 0.020 |
| | Q4 | 2.245(1.232,4.090) | 0.008 | 2.847(1.552,5.224) | 0.001 | 2.626(1.133,6.085) | 0.024 |
| TyG-WC | Q1 | Reference | | Reference | | Reference | |
| | Q2 | 1.588(0.806,3.126) | 0.181 | 1.595(0.809,3.146) | 0.178 | 1.264(0.476,3.358) | 0.638 |
| | Q3 | 2.340(1.239,4.419) | 0.009 | 2.311(1.221,4.374) | 0.010 | 2.494(1.007,6.177) | 0.048 |
| | Q4 | 2.800(1.505,5.210) | 0.001 | 3.094(1.658,5.773) | <0.001 | 3.299(1.294,8.414) | 0.012 |
| TyG-WHR | Q1 | Reference | | Reference | | Reference | |
| | Q2 | 1.662(0.849,3.254) | 0.138 | 1.599(0.815,3.136) | 0.172 | 1.647(0.684,3.963) | 0.266 |
| | Q3 | 2.416(1.283,4.550) | 0.006 | 2.483(1.316,4.686) | 0.005 | 2.379(1.022,5.538) | 0.044 |
| | Q4 | 2.646(1.416,4.945) | 0.002 | 2.783(1.486,5.212) | 0.001 | 2.949(1.250,6.956) | 0.014 |
| TyG-WtHR | Q1 | Reference | | Reference | | Reference | |
| | Q2 | 0.662(0.317,1.383) | 0.272 | 0.643(0.307,1.345) | 0.241 | 0.477(0.178,1.284) | 0.143 |
| | Q3 | 1.988(1.116,3.541) | 0.020 | 1.887(1.057,3.369) | 0.032 | 1.246(0.559,2.775) | 0.591 |
| | Q4 | 2.347(1.337,4.122) | 0.003 | 2.265(1.286,3.988) | 0.005 | 1.900(0.869,4.155) | 0.108 |

Notes: Model 1: Unadjusted; Model 2: Adjusted for age; Model 3: Adjusted for age, SBP, TC, LDL-C, UA, Neck circumference, and Hypertension.

statistically significant differences observed between the Q3 and Q4 groups and the Q1 group ($P < 0.05$). Lastly, among individuals grouped by quartiles of TyG-WtHR, the adjusted ORs (95% CIs) were 0.643(0.307,1.345), 1.887 (1.057,3.369), and 2.265(1.286,3.988), respectively, compared to the Q1 group, with statistically significant differences observed between the Q3 and Q4 groups and the Q1 group ($P < 0.05$).

After further adjustment for SBP, TC, LDL-C, UA, Neck circumference, and Hypertension (Table 3, Model 3), the following associations were observed: (1) Among individuals grouped by quartiles of TyG index, the adjusted odds ratios (ORs) (95% CIs) were 1.542(0.639,3.721), 2.652(1.164,6.043), and 2.626(1.133,6.085) in the Q2, Q3, and Q4 groups, respectively, compared to the Q1 group, with statistically significant differences observed between the Q3 and Q4 groups and the Q1 group ($P < 0.05$). (2) Among individuals grouped by quartiles of TyG-WC, the adjusted ORs (95% CIs) were 1.264(0.476,3.358), 2.494(1.007,6.177), and 3.299(1.294,8.414), respectively, compared to the Q1 group, with statistically significant differences observed between the Q3 and Q4 groups and the Q1 group ($P < 0.05$). (3) Among individuals grouped by quartiles of TyG-WHR, the adjusted ORs (95% CIs) were 1.647(0.684,3.963), 2.379(1.022,5.538), and 2.949 (1.250,6.956), respectively, compared to the Q1 group, with statistically significant differences observed between the Q3 and Q4 groups and the Q1 group ($P < 0.05$). (4) Among individuals grouped by quartiles of TyG-WtHR, the adjusted ORs (95% CIs) were 0.477(0.178,1.284), 1.246(0.559,2.775), and 1.900(0.869,4.155), respectively, compared to the Q1 group, with no statistically significant differences observed.

Predictive Value of TyG Index and Its Combination with Obesity Indicators in Screening for LEAD Presence in T2DM Patients

To explore the predictive value of the TyG index and its combination with obesity indicators for LEAD, we analyzed the ROC curves (Figure 3). Our results revealed specific optimal cutoff values for different predictors: TyG index had a cutoff value of 9.8059 (sensitivity: 49.1%, specificity: 67.9%, and AUC: 0.583), TyG-WC had a cutoff value of 808.8397 (sensitivity: 70.8%; specificity: 47.8%; and AUC: 0.603), and TyG-WHR had a cutoff value of 8.8543 (sensitivity: 75.5%; specificity: 44.6%; and AUC: 0.607).

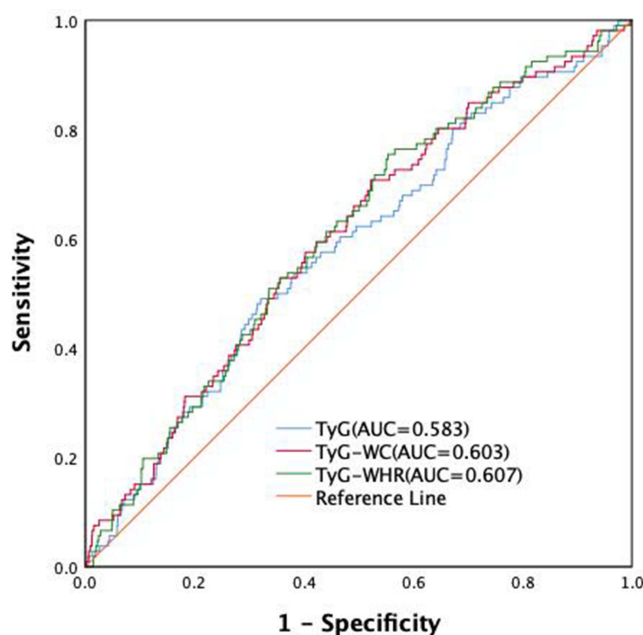


Figure 3 Receiver operating characteristic (ROC) curve analysis of different indexes to indicate LEAD in T2DM patients.

Discussion

In this cross-sectional study involving 3176 adult patients with T2DM, we observed a positive correlation between the TyG index and its combination with obesity indicators and the occurrence of LEAD. Particularly, higher TyG index, TyG-WC, and TyG-WHR groups were associated with an increased risk of LEAD. Among these groups, TyG-WC and TyG-WHR exhibited the strongest correlation with LEAD, demonstrating a more robust association than TyG index alone. The optimal cutoff value for predicting the presence of LEAD was 808.8397 for TyG-WC and 8.8543 for TyG-WHR.

To the best of our knowledge, our study represents the inaugural investigation into the association between the TyG index and its amalgamation with obesity indicators in relation to LEAD. The TyG index, a biomarker derived from fasting glucose and triglyceride levels, has garnered attention as a surrogate for insulin resistance due to its straightforward calculation and high sensitivity and specificity.²¹ Data analysis from the National Health and Nutrition Examination Survey showed that a higher TyG index is significantly associated with an increased risk of PAD.²² Similarly, a study in China found that an elevated TyG index correlates significantly with a higher risk of arterial stiffness and nephric microvascular damage.²³ Additionally, a study in Turkey indicated that the development of chronic limb-threatening ischemia can be predicted using the TyG index, which is easily calculated from routine biochemical parameters, in patients diagnosed with lower extremity peripheral artery disease.²⁴ Furthermore, previous research has indicated a correlation between the TyG index and PAD, with a higher TyG index independently linked to an elevated risk of PAD.^{23,25} Our findings echo this trend, revealing that higher quartiles of the TyG index correlate with an increased risk of LEAD, signifying a significant positive correlation between the TyG index and LEAD. In contrast to prior studies, our research extends its scope by conducting statistical analyses on the interplay between the TyG index combined with various obesity indicators and LEAD. Our results demonstrate that combining the TyG index with central obesity indicators such as WC and WHR yields the strongest correlation with LEAD, suggesting a diagnostic utility surpassing that of the TyG index alone. This enhancement may stem from obesity's direct influence on the development of cardiovascular risk factors, including dyslipidemia, T2DM, hypertension, and sleep disorders.²⁶ Additionally, obesity may independently contribute to cardiovascular disease and cardiovascular disease-related mortality, especially concerning body fat distribution.^{26,27} Moreover, combining the TyG index with obesity indicators may afford a more precise

evaluation of insulin resistance than employing HOMA-IR or the TyG index in isolation.^{28–30} Our findings furnish substantial evidence supporting the significance of the TyG index, TyG-WC, and TyG-WHR as predictors of LEAD risk.

The heightened risk of LEAD in individuals with T2DM may be attributed to elevated levels of the TyG index, TyG-WC, and TyG-WHR, all of which are associated with IR.^{31,32} IR is inherent in T2DM and tends to be higher in individuals with elevated TyG index levels. Primarily, IR can disrupt glucose metabolism and trigger lipotoxicity.³³ Moreover, it frequently intertwines with endothelial dysfunction,³⁴ a pivotal factor in cardiovascular diseases. Endothelial dysfunction encompasses reduced nitric oxide bioavailability, heightened oxidative stress, increased expression of pro-inflammatory and pro-thrombotic factors, and abnormal vasoreactivity, collectively contributing to atherosclerosis.³⁵ Furthermore, various mechanisms such as the release of inflammatory factors, nitric oxide inactivation, activation of the sympathetic nervous system and renin–angiotensin–aldosterone system, and platelet activation can precipitate vascular dysfunction, culminating in an array of cardiovascular diseases.³³ Experimental studies are imperative to validate these mechanisms.

Several limitations affect the interpretation of our findings. Firstly, this study is cross-sectional, and therefore, the causative link between TyG index and its combination with obesity indicators and LEAD cannot be determined. Secondly, the potential mechanism of the association between TyG index and its combination with obesity indicators and LEAD requires further prospective large-scale study. Despite these limitations, the relatively large sample size strengthens the validity of our results. Considering that TyG index and its combination with obesity indicators can be easily calculated from routine indicators, it is readily available for use in clinical practice, particularly in large screening procedures. Given the strong influence of IR and obesity on LEAD, further studies should be performed for evaluating.

Conclusions

In T2DM patients, the TyG index, TyG-WHR, and TyG-WC are positively associated with the occurrence of LEAD. TyG-WHR and TyG-WC show a stronger correlation with LEAD compared to the TyG index alone, indicating their superior diagnostic value.

Ethics Statement

The study was performed in accordance with the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Institutional Review Board of the Affiliated Hospital of Southwest Medical University. All participants provided written informed consent prior to their involvement in the study.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no potential conflicts of interest directly relevant to the content of this article.

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