SciMedCentral

Journal of Endocrinology, Diabetes & Obesity

Research Article

# Prognostic Utility of the Triglyceride-Glucose Index in Type 1 Diabetes: Evidence from the NHANES Cohort

**Ruochen Li and Xinhua Xiao***

*Department of Endocrinology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, China*

***Corresponding author**

Xinhua Xiao, Department of Endocrinology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, 100730, China, Tel: +86 139 1183 0085

**Submitted:** 25 August, 2026
**Accepted:** 29 October, 2026
**Published:** 30 October, 2026

**ISSN:** 2333-6692

**Copyright**

© 2026 Li R, et al.

OPEN ACCESS

**Keywords**

• Type 1 diabetes mellitus; Triglyceride-glucose index; Insulin resistance; Chronic kidney disease; Mortality

**Abstract**

**Background:** Insulin resistance is common in type 1 diabetes mellitus (T1DM), but established insulin-based indices are unsuitable for insulin-deficient populations.

**Methods:** We evaluated a modified triglyceride-glucose (TyG) index calculated using glycated hemoglobin-derived mean blood glucose in adults with T1DM. Data from the 1999-March 2020 National Health and Nutrition Examination Survey were analyzed using the complex survey design. Survey-weighted logistic regression assessed prevalent chronic kidney disease (CKD), and survey-weighted Cox proportional hazards models assessed all-cause and cardiovascular mortality. TyG was compared descriptively with estimated glucose disposal rate (eGDR), the triglyceride-to-high-density lipoprotein cholesterol ratio (TG/HDL-C), and the metabolic score for insulin resistance (METS-IR) using receiver operating characteristic (ROC) curves.

**Results:** The study included 269 adults classified as having T1DM, representing approximately 1.09 million United States adults; 250 had linked mortality data. After full adjustment, each 1-unit increase in TyG was associated with higher odds of prevalent CKD (odds ratio 1.70; 95% confidence interval [CI] 1.02-2.81), all-cause mortality (hazard ratio [HR] 1.45; 95% CI 1.04-2.03), and cardiovascular mortality (HR 1.76; 95% CI 1.17-2.66). In ROC analysis, TyG demonstrated predictive performance superior to eGDR for all-cause mortality (area under the curve [AUC], 0.689 vs 0.662; P<0.001) and cardiovascular mortality (AUC 0.664 vs 0.583; P<0.001), as well as other indices. No statistically significant non-linearity was detected.

**Conclusion:** The TyG index is an effective and independent predictor of CKD, all-cause mortality, and cardiovascular mortality among adults with T1DM.

## ABBREVIATIONS

CKD: Chronic Kidney Disease; CVD: Cardiovascular Disease; eGDR: Estimated Glucose Disposal Rate; eGFR: Estimated Glomerular Filtration Rate; HbA1c: Glycated Hemoglobin A1c; HR: Hazard Ratio; IR: Insulin Resistance; MBG: Mean Blood Glucose; METS-IR: Metabolic Score For Insulin Resistance; NHANES: National Health and Nutrition Examination Survey; OR: Odds ratio; RCS: Restricted cubic spline; ROC: Receiver operating characteristic; T1DM: Type 1 diabetes mellitus; TG/HDL-C: Triglyceride-To-High-Density Lipoprotein Cholesterol Ratio; TyG: Triglyceride-Glucose Index

## INTRODUCTION

Type 1 diabetes mellitus (T1DM) affects approximately 9.15 million people worldwide and accounts for about 2% of all diabetes cases [1,2]. Improvements in medical care have prolonged survival, and approximately 19% of people with T1DM worldwide are now older than 60 years [3,4]. Consequently, long-term management and prevention of chronic complications have become increasingly important.

Although T1DM is characterized by autoimmune beta-cell destruction and absolute insulin deficiency, insulin resistance (IR) is also common [5,6]. Previous studies using euglycemic clamps have demonstrated impaired hepatic and peripheral insulin sensitivity early after T1DM diagnosis, with further deterioration during follow-up [7-9]. IR has also been associated with insulin-antibody titers after adjustment for confounders [10].

The coexistence of T1DM and metabolic features associated with type 2 diabetes mellitus (T2DM) has been described as “double diabetes” [11,12]. Proposed features include obesity, dyslipidemia, hypertension, a

family history of type 2 diabetes, metabolic syndrome, and IR [11-13]. Greater IR in T1DM has been associated with macrovascular and microvascular complications, cardiovascular events, and mortality, sometimes despite intensive glycemic control [14-17]. Reliable assessment of IR may therefore identify risk not fully captured by glycemic control alone.

The hyperinsulinemic-euglycemic clamp is the reference method for measuring IR but is invasive, expensive, and technically demanding [18]. Epidemiologic indices, such as the homeostatic model assessment and quantitative insulin sensitivity check index, require endogenous fasting insulin and are thus inapplicable for T1DM. Estimated glucose disposal rate (eGDR) is the most established surrogate for T1DM, but it was derived from a small group with poor glycemic control, and the inclusion of hypertension may limit its sensitivity in younger patients [19-21].

The triglyceride-glucose (TyG) index is a non-insulin-based surrogate that has been associated with diabetic foot disease, retinopathy, kidney disease, cardiovascular disease, and mortality in general or T2DM populations [22-26]. Likewise, Angelino et al. found that TyG-defined insulin resistance was common among adults with T1DM and was associated with poorer glycol-metabolic parameters and higher insulin requirements [27]. In insulin-treated T1DM, replacing fasting glucose with mean blood glucose (MBG) derived from glycated hemoglobin A1c (HbA1c) may provide a more stable modified TyG measure. Lei et al., reported an association between this modified index and diabetic kidney disease in T1DM [28]. Given that evidence regarding mortality and comparison with other IR surrogates remains limited, this study aimed to examine the associations of the TyG index with chronic kidney disease (CKD), all-cause mortality, and cardiovascular mortality in a nationally representative T1DM population. We also aimed to compare TyG with other IR surrogates and assess for potential effect modification and nonlinear associations.

## MATERIALS AND METHODS

We used data from 10 survey cycles of the United States (US) National Health and Nutrition Examination Survey (NHANES), covering 1999 through March 2020. NHANES uses a stratified, multistage probability-sampling design and combines household interviews with standardized examinations and laboratory testing. The National Center for Health Statistics Research Ethics Review Board approved each survey cycle, and participants provided written informed consent. Public data are available at https://www.cdc.gov/nchs/nhanes/.

### Study Design and Population

NHANES does not directly record diabetes type. Participants likely to have T1DM were identified using the treatment-based algorithm developed by Mosslemi et al. [29]. The criteria included self-reported diabetes diagnosed outside pregnancy, current insulin use, initiation of insulin within 1 year of diagnosis, and no current oral glucose-lowering medication. Among 7,359 participants with diabetes, 399 met these criteria. After excluding participants aged younger than 20 years or 80 years or older (n = 84) and those without the required examination or laboratory data (n = 46), 269 adults remained for baseline and prevalent CKD analyses; 250 had linked mortality data (Figure 1).

### Baseline Characteristics and Covariates

Demographic information was collected during NHANES household interviews and included age, sex (female or male), and race/ethnicity (non-Hispanic White or other race/ethnicity). Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Obesity was defined as BMI ≥30 kg/m$^2$. Ever smoking was defined as having smoked at least 100

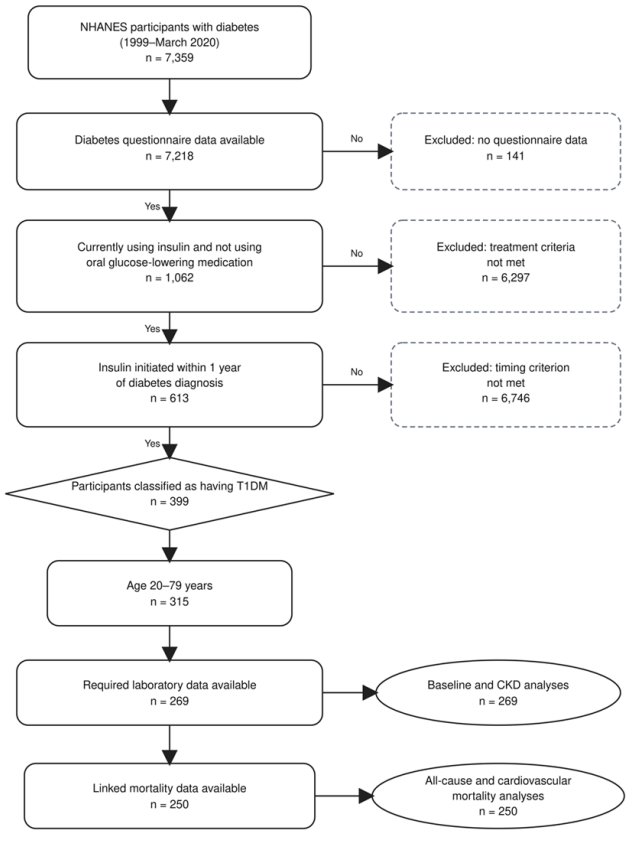


**Figure 1** Participant flowchart.

cigarettes during the participant's lifetime [30]. Diabetes duration was calculated as current age minus age at diagnosis. Laboratory variables included HbA1c, serum creatinine, total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), urinary albumin, and urinary creatinine. Elevated total cholesterol and TG were defined as >200 mg/dL and >150 mg/dL, respectively [31]. The urinary albumin-to-creatinine ratio (UACR) was calculated as urinary albumin (mg/L) divided by urinary creatinine (g/L). Estimated glomerular filtration rate (eGFR) was calculated using the 2021 race-free Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation [32]. CKD was defined as eGFR <60 mL/min/1.73 $m^2$ or UACR >30 mg/g [33]. Because CKD was assessed at one survey examination, it was treated as prevalent CKD rather than confirmed chronic disease.

### Insulin-Resistance Surrogates

Mean blood glucose (MBG) was estimated from HbA1c as MBG (mmol/L) = 1.5944 × HbA1c (%) - 2.594 and was then converted to mg/dL [34]. The modified TyG index was calculated as follows [35]:

$$TyG = \ln\left[\frac{TG(mg/dL) \times MBG(mg/dL)}{2}\right].$$

The estimated glucose disposal rate (eGDR) was calculated as 21.158 - (0.09 × waist circumference in cm) - (3.407 × hypertension status) - (0.551 × HbA1c [%]), where hypertension was coded as 1 if present and 0 if absent [20,36]. The triglyceride-to-high-density lipoprotein cholesterol ratio (TG/HDL-C) was calculated as TG divided by HDL-C [37]. The metabolic score for insulin resistance (METS-IR) was modified by substituting MBG for fasting plasma glucose [38]:

$$METS\text{-}IR = \frac{\ln[2 \times MBG(mg/dL) + TG(mg/dL)] \times BMI(kg/m^2)}{\ln[HDL\text{-}C(mg/dL)]}.$$

### Mortality Outcomes

NHANES records were linked to the National Death Index through December 31, 2019, using a probabilistic matching algorithm [39]. Cardiovascular mortality included deaths attributed to heart disease or cerebrovascular disease in the public-use underlying-cause recode. In cause-specific Cox analyses, deaths from other causes were censored [39].

### Statistical Analysis

Analyses were conducted using Stata MP version 18.0 and incorporated NHANES sampling weights, strata, and primary sampling units according to NHANES guidance for combined survey cycles [40]. Participants were stratified at the survey-weighted medians of TyG (9.14) and eGDR (5.85). Continuous variables are presented as weighted means with standard deviations or weighted medians with interquartile ranges. Categorical variables are presented as unweighted counts with weighted percentages. Survey-adjusted tests appropriate to variable type were used for group comparisons. Spearman coefficients were used to describe correlations among the insulin-resistance surrogates.

Logistic regression and cox proportional hazards models with survey weights were developed to evaluate IR indices association with CKD or mortality. The unadjusted model contained no covariates. Model 1 adjusted for age, sex, and race/ethnicity; Model 2 additionally adjusted for BMI, smoking, and diabetes duration. Indices were standardized as z scores for direct comparison of estimates per 1-standard-deviation increase.

Receiver operating characteristic (ROC) curves were used to compare the four indices. Areas under the curve (AUCs) for TyG and eGDR were compared using z tests, and the Youden index was used to identify exploratory cutoffs, sensitivity, and specificity. Kaplan-Meier curves and log-rank tests compared mortality between groups defined by the weighted medians of TyG and eGDR. Subgroup analyses were conducted by sex, obesity, age, race/ethnicity, and smoking status; multiplicative interactions were tested using Wald tests in Model 1. Restricted cubic spline (RCS) models with three knots evaluated nonlinearity after truncating the lowest and highest 5% of TyG values. The ROC-derived cutoff was used as the reference value, and nonlinearity was tested using the second spline term. Tests were two-sided, with $P<0.05$ considered statistically significant.

## RESULTS

### Participant Characteristics

The 269 participants represented approximately 1.09 million US adults after weighting (Figure 1). Women comprised 41.6% of the study population; the weighted mean age was 48.2 years, and the mean diabetes duration was 19.5 years. Baseline characteristics are presented in Table 1 according to the survey-weighted TyG median of 9.14. Compared with the lower-TyG group, the higher-TyG group was older at interview and diagnosis but had a similar diabetes duration. The higher-TyG group also had higher BMI, waist circumference, HbA1c, total cholesterol, and TG and more frequently had obesity, hypertension, and CKD. Weighted CKD prevalence was 23.5% in the higher-TyG group and 6.2% in the lower-TyG group (**Table S1**). Among the 250 participants with linked mortality data, 85 all-cause deaths and 39 cardiovascular deaths occurred during a median follow-up of 7.1 years. Both all-cause and cardiovascular mortality were higher in the higher-TyG group (Table 2).

**Table 1:** Survey-weighted baseline characteristics by TyG group

| Characteristic | Overall, n = 269; weighted N = 1,093,150 | Lower TyG, n = 108; weighted N = 525,671 | Higher TyG, n = 161; weighted N = 567,479 | *P* value |
|---|---|---|---|---|
| Age, years (SD) | 48.2 (14.4) | 44.2 (12.5) | 52.3 (15.0) | 0.001 |
| Age at diagnosis, years (SD) | 28.7 (17.2) | 23.3 (13.8) | 34.3 (18.7) | <0.001 |
| Diabetes duration, years (SD) | 19.5 (13.9) | 20.9 (10.8) | 18.0 (15.1) | 0.182 |
| Female sex, n (%) | 119 (41.6%) | 38 (37.5%) | 81 (45.9%) | 0.311 |
| Non-Hispanic White race/ethnicity, n (%) | 134 (75.8%) | 60 (83.7%) | 74 (67.5%) | 0.006 |
| BMI, kg/m$^2$ (SD) | 30.1 (7.1) | 27.7 (5.2) | 32.6 (8.3) | <0.001 |
| Waist circumference, cm (SD) | 102.8 (18.3) | 96.4 (13.9) | 110.0 (20.5) | <0.001 |
| Ever smoked >=100 cigarettes, n(%) | 149 (53.8%) | 60 (46.7%) | 74 (61.2%) | 0.112 |
| HbA1c, % (SD) | 8.0 (1.9) | 7.5 (1.3) | 8.6 (2.2) | 0.003 |
| Elevated total cholesterol, n (%) | 83 (30.6%) | 20 (20.8%) | 63 (40.8%) | 0.003 |
| Elevated triglycerides, n (%) | 109 (31.1%) | 1 (0.4%) | 108 (63.1%) | <0.001 |
| eGFR, mL/min/1.73 m$^2$ (SD) | 84.4 (31.1) | 93.4 (26.0) | 74.2 (33.3) | 0.001 |
| Obesity, n (%) | 139 (43.0%) | 38 (29.6%) | 101 (57.0%) | 0.003 |
| Chronic kidney disease, n (%) | 47 (14.7%) | 14 (6.2%) | 33 (23.5%) | 0.003 |
| Hypertension, n (%) | 168 (53.5%) | 54 (41.2%) | 114 (65.6%) | 0.013 |

Values are unweighted n (weighted %) or weighted mean (SD). Abbreviations: BMI: Body Mass Index; CKD: Chronic Kidney Disease; eGFR: Estimated Glomerular Filtration Rate; HbA1c: Glycated Hemoglobin A1c; TyG: Triglyceride-Glucose Index.

**Table 2: Mortality events by TyG groups**

| Outcome | Overall, n=250; weighted N=1,034,858 | Lower TyG, n=99; weighted N=521,689 | Higher TyG, n=151; weighted N=513,169 | *P* value |
|---|---|---|---|---|
| All-cause mortality | 85 (27.2%) | 25 (16.7%) | 60 (37.9%) | 0.006 |
| Cardiovascular mortality | 39 (15.4%) | 9 (6.8%) | 30 (24.1%) | 0.011 |

Values are unweighted n (weighted %). Abbreviation: TyG: Triglyceride-Glucose Index.

## Modified TyG and Prevalent CKD

Each 1-unit increase in TyG was associated with 96% higher unadjusted odds of prevalent CKD (odds ratio [OR], 1.96; 95% confidence interval [CI], 1.26-3.05), and the association remained significant after full adjustment (OR, 1.70; 95% CI, 1.02-2.81) (Figure 2). Compared with the lower-TyG group, the higher-TyG group had an unadjusted OR of 4.62; adjusted ORs were 2.95 in Model 1 and 2.80 in Model 2. On their original measurement scales, TyG, eGDR, and METS-IR were associated with prevalent CKD before adjustment,whereasTG/HDL-Cwasnot(Figure3;**TableS2**). After full adjustment, only TyG remained statistically significant. In ROC analysis, eGDR had the largest descriptive AUC for prevalent CKD (0.727), followed by TG/HDL-C (0.701), METS-IR (0.700), and TyG (0.676). The TyG Youden cutoff was 9.356, with sensitivity of 0.735 and specificity of 0.659 (Table 3; Figure 4). Race/ethnicity modified the TyG-CKD association (P for interaction = 0.02), with a stronger estimate among non-Hispanic White participants (Figure 5). RCS analysis did not detect statistically significant nonlinearity (P for nonlinearity = 0.071) (Figure 6).

## Modified TyG and Mortality

For all-cause mortality, each 1-unit increase in TyG was associated with an unadjusted hazard ratio (HR) of

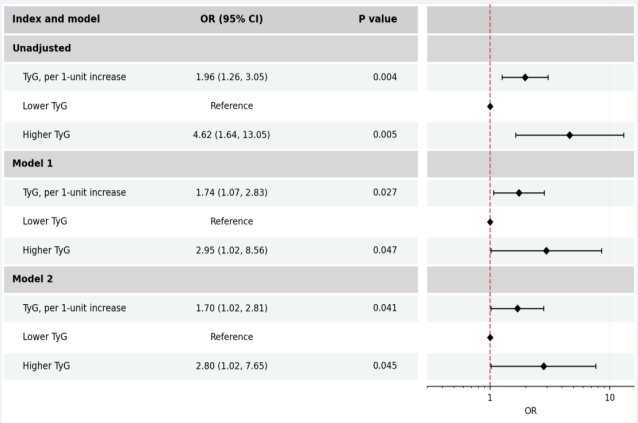


**Figure 2** Association of TyG with CKD. ORs and 95% CIs were estimated using survey-weighted logistic regression. Model 1 adjusted for age, sex, and race/ethnicity; Model 2 additionally adjusted for BMI, smoking, and diabetes duration.

**Table 3: ROC analysis of TyG and eGDR for chronic kidney disease**

| Metric | TyG | eGDR |
|---|---|---|
| AUC | 0.676 | 0.727 |
| 95% CI | 0.674-0.677 | 0.725-0.728 |
| *P* value for AUC comparison | <0.001 | |
| Youden cutoff | 9.356 | 3.611 |
| Sensitivity | 0.735 | 0.644 |
| Specificity | 0.659 | 0.765 |

Abbreviation: AUC: Area Under the Curve; eGDR: Estimated Glucose Disposal Rate; ROC: Receiver Operating Characteristic; TyG: triglyceride-glucose index.

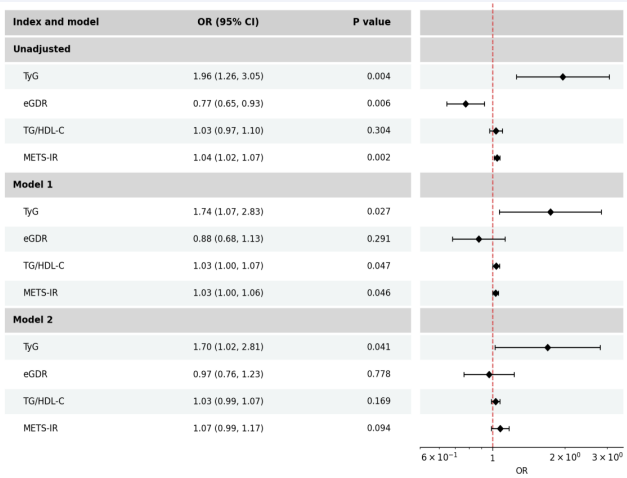


**Figure 3** Original-scale associations of four insulin-resistance surrogates with prevalent CKD. ORs and 95% CIs are reported per 1-unit increase in each index. Model 1 adjusted for age, sex, and race/ethnicity; Model 2 additionally adjusted for BMI, smoking, and diabetes duration.

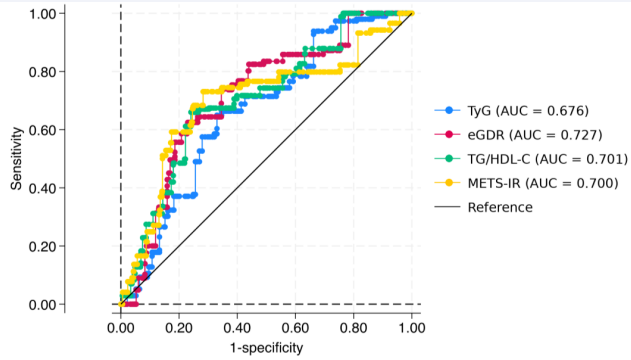


**Figure 4** ROC curves for four insulin-resistance surrogates and prevalent CKD.

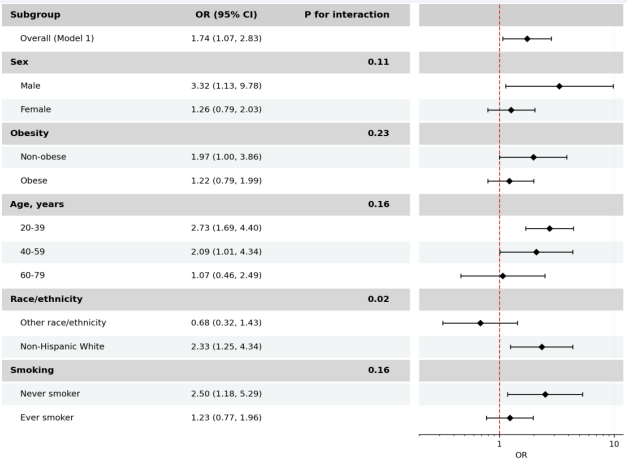


**Figure 5** Subgroup analyses of the association between TyG and prevalent CKD. ORs and 95% CIs were estimated using survey-weighted logistic regression with Model 1 adjustment as applicable. Interactions were evaluated using Wald tests.

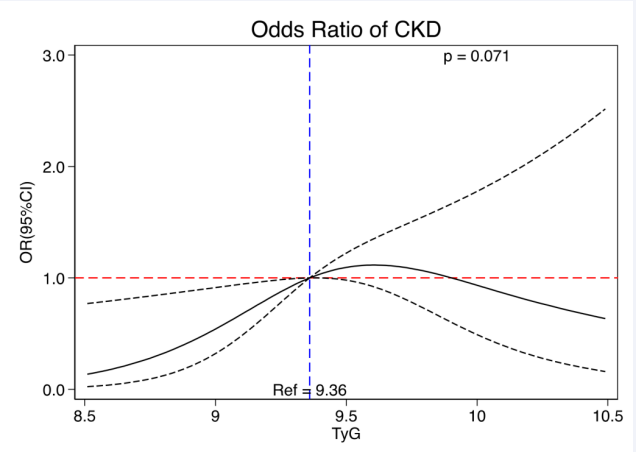


**Figure 6** Restricted cubic spline for the association between TyG and prevalent CKD. The solid line represents the OR and the dashed lines the 95% CI. The horizontal reference is OR = 1; the vertical reference is TyG = 9.36. The displayed P value is for nonlinearity.

1.55 (95% CI, 1.15-2.08) and a fully adjusted HR of 1.45 (95% CI, 1.04-2.03) (Figure 7). The unadjusted higher-versus-lower TyG HR was 2.35, but the association was attenuated and was no longer statistically significant after adjustment. eGDR and METS-IR were associated with all-cause mortality before adjustment, whereas TG/HDL-C was not. In Model 2, eGDR remained associated with lower all-cause mortality; TG/HDL-C and METS-IR did not (Figure 8). In ROC analysis of observed mortality status, the descriptive TyG AUC was 0.689 and the eGDR AUC was 0.662. The TyG cutoff was 9.263, with sensitivity of 0.675 and specificity of 0.636 (Table 4; Figure 9). Overall survival was lower in the higher-TyG group (log-rank P = 0.0100), whereas the difference between eGDR groups was not statistically significant (P = 0.0676) (Figure 10). The TyG association was stronger among participants without obesity (P for interaction = 0.01) (Figure 11). The spline analysis did not detect nonlinearity (P for nonlinearity = 0.360) (Figure 12).

For cardiovascular mortality, each 1-unit increase in TyG was associated with an unadjusted HR of 1.62 (95% CI, 1.14-2.29) and a fully adjusted HR of 1.76 (95% CI, 1.17-2.66). The fully adjusted higher-versus-lower TyG HR was 3.67 (95% CI, 1.13-11.94) (Figure 13). On their original measurement scales, TyG was associated with cardiovascular mortality in all three models, whereas eGDR was statistically significant only in Model 2; TG/HDL-C and METS-IR were not significant (Figure 14). TyG showed greater discrimination than eGDR (AUC 0.664 vs 0.583; P<0.001) and other indices, with a cutoff of 9.264 (Table 5; Figure 15). Cardiovascular survival was lower in the higher-TyG group (log-rank P = 0.0124) but did not differ significantly between eGDR groups (P = 0.2956) (Figure 16). No statistically significant subgroup interaction or spline nonlinearity was identified (Figures 17 and 18).

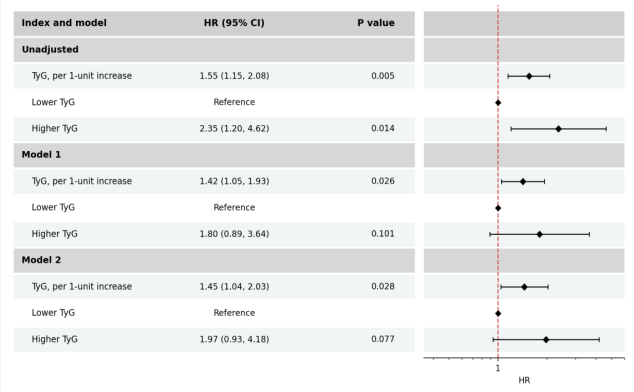


**Figure 7** Association of TyG with all-cause mortality. HRs and 95% CIs were estimated using survey-weighted Cox proportional hazards models. Model 1 adjusted for age, sex, and race/ethnicity; Model 2 additionally adjusted for BMI, smoking, and diabetes duration.

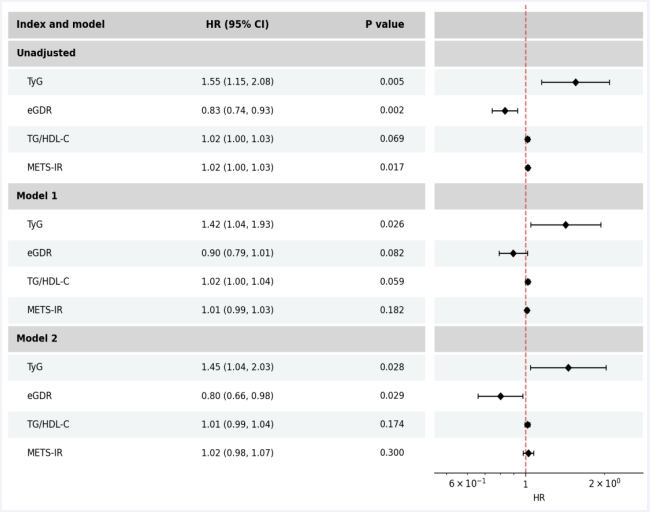


**Figure 8** Original-scale associations of four insulin-resistance surrogates with all-cause mortality. HRs and 95% CIs are reported per 1-unit increase in each index. Model 1 adjusted for age, sex, and race/ethnicity; Model 2 additionally adjusted for BMI, smoking, and diabetes duration.

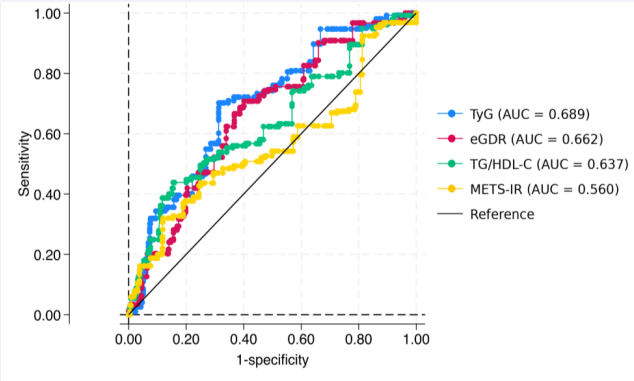


**Figure 9** ROC curves for four insulin-resistance surrogates and all-cause mortality status.

**Table 4:** ROC analysis of TyG and eGDR for all-cause mortality

| Metric | TyG | eGDR |
|---|---|---|
| AUC | 0.689 | 0.662 |
| 95% CI | 0.688-0.690 | 0.660-0.663 |
| *P* value for AUC comparison | <0.001 | |
| Youden cutoff | 9.263 | 5.414 |
| Sensitivity | 0.675 | 0.717 |
| Specificity | 0.636 | 0.594 |

Abbreviation: AUC: Area Under the Curve; eGDR: Estimated Glucose Disposal Rate; ROC: Receiver Operating Characteristic; TyG: triglyceride-glucose index.

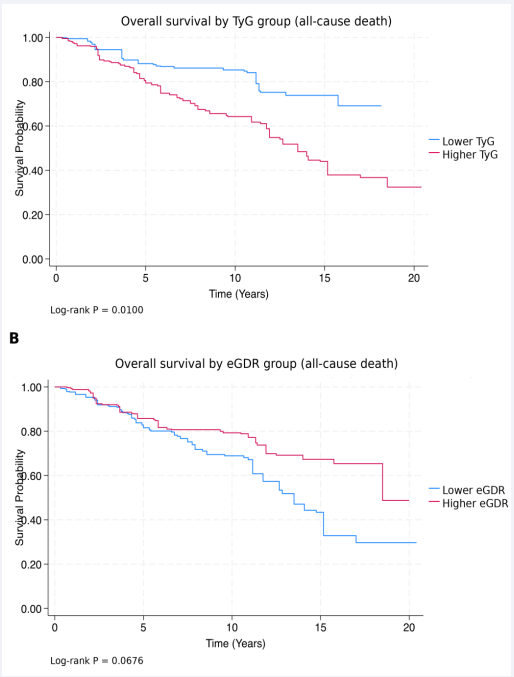


**Figure 10** Kaplan-Meier curves for all-cause mortality stratified by TyG index and eGDR. Participants were classified into lower and higher groups using the survey-weighted median of each index: (A) TyG index and (B) eGDR. P values were calculated using log-rank tests.

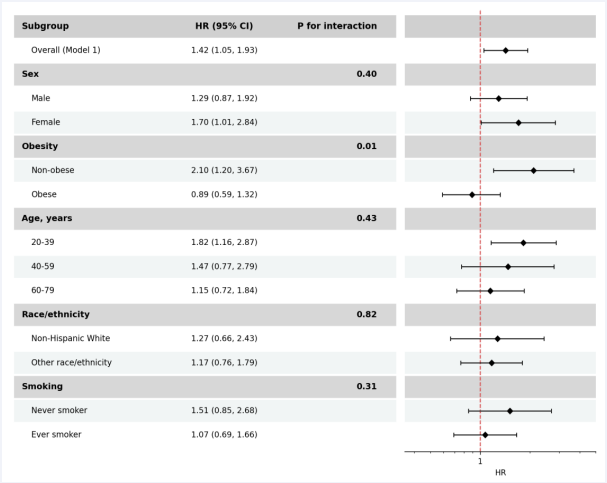


**Figure 11** Subgroup analyses of the association between TyG and all-cause mortality. HRs and 95% CIs were estimated using Model 1 Cox regression with covariate adjustment as applicable. Interactions were evaluated using Wald tests.

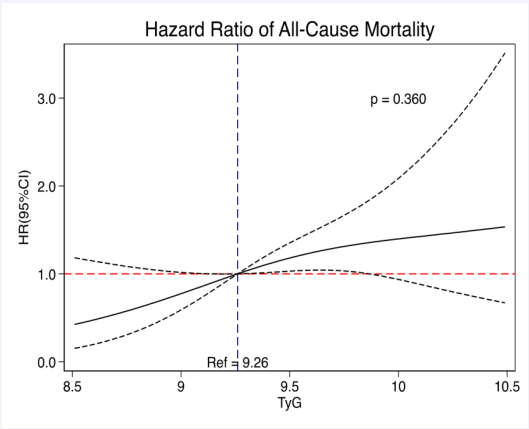


**Figure 12** Restricted cubic spline for the association between TyG and all-cause mortality. The solid line represents the HR and the dashed lines the 95% CI. The horizontal reference is HR = 1; the vertical reference is TyG = 9.26. The displayed P value is for nonlinearity.

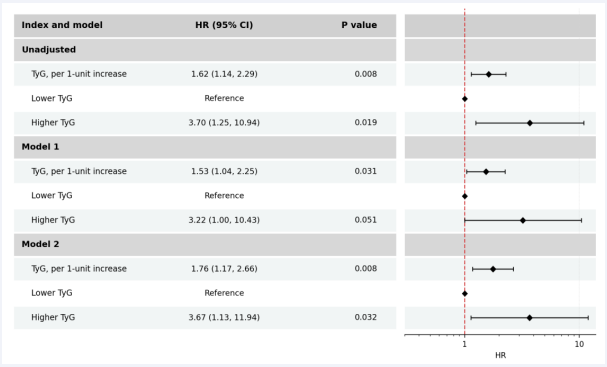


**Figure 13** Association of TyG with cardiovascular mortality. HRs and 95% CIs were estimated using survey-weighted cause-specific Cox proportional hazards models. Model 1 adjusted for age, sex, and race/ethnicity; Model 2 additionally adjusted for BMI, smoking, and diabetes duration.

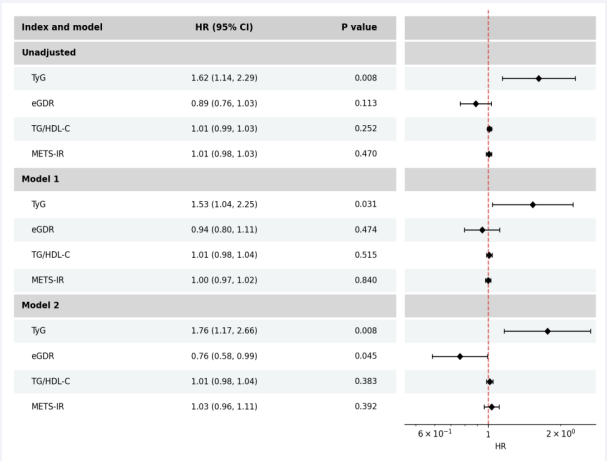


**Figure 14** Original-scale associations of four insulin-resistance surrogates with cardiovascular mortality. HRs and 95% CIs are reported per 1-unit increase in each index. Model 1 adjusted for age, sex, and race/ethnicity; Model 2 additionally adjusted for BMI, smoking, and diabetes duration.

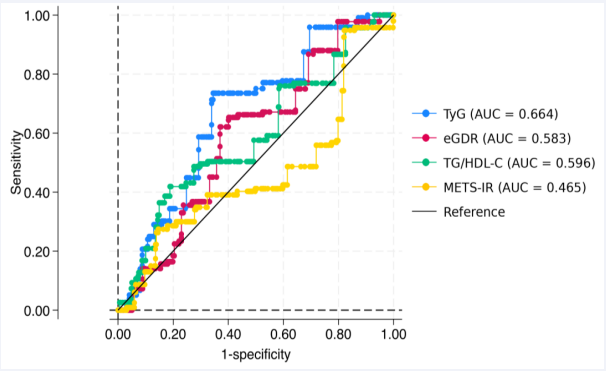


**Figure 15** ROC curves for four insulin-resistance surrogates and cardiovascular mortality status

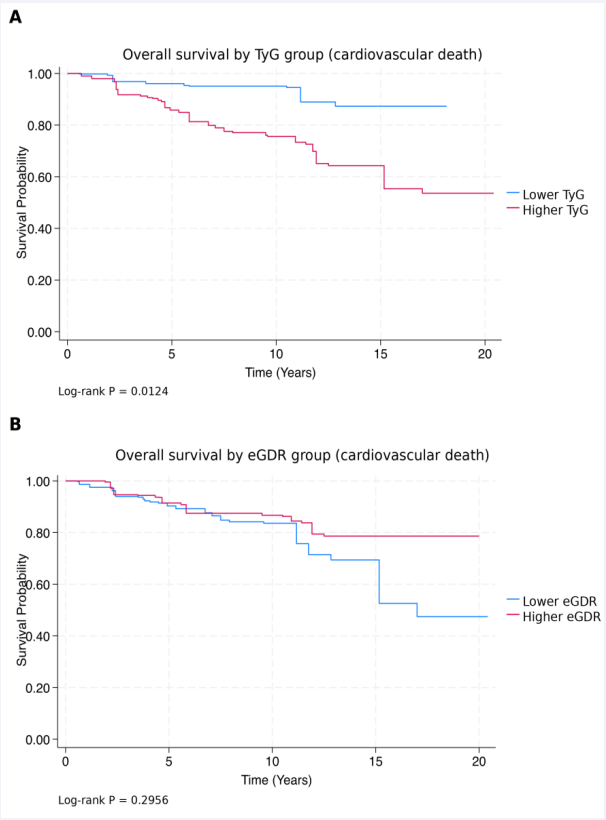


**Figure 16** Kaplan-Meier curves for cardiovascular mortality stratified by TyG index and eGDR. Participants were classified into lower and higher groups using the survey-weighted median of each index: (A) TyG index and (B) eGDR. P values were calculated using log-rank tests.

**Table 5:** ROC analysis of TyG and eGDR for cardiovascular mortality

| Metric | TyG | eGDR |
|---|---|---|
| AUC | 0.664 | 0.583 |
| 95% CI | 0.662-0.665 | 0.582-0.585 |
| *P* value for AUC comparison | <0.001 | |
| Youden cutoff | 9.264 | 5.083 |
| Sensitivity | 0.778 | 0.653 |
| Specificity | 0.613 | 0.589 |

Abbreviation: AUC: Area Under the Curve; eGDR: Estimated Glucose Disposal Rate; ROC: Receiver Operating Characteristic; TyG: triglyceride-glucose index.

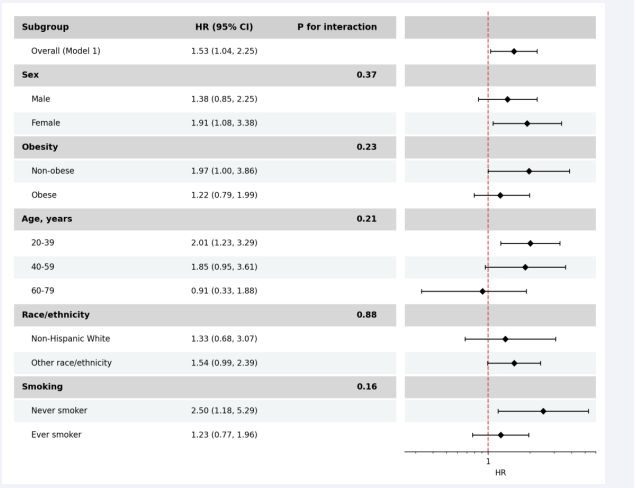


**Figure 17** Subgroup analyses of the association between TyG and cardiovascular mortality. HRs and 95% CIs were estimated using Model 1 cause-specific Cox regression with covariate adjustment as applicable. Interactions were evaluated using Wald tests.

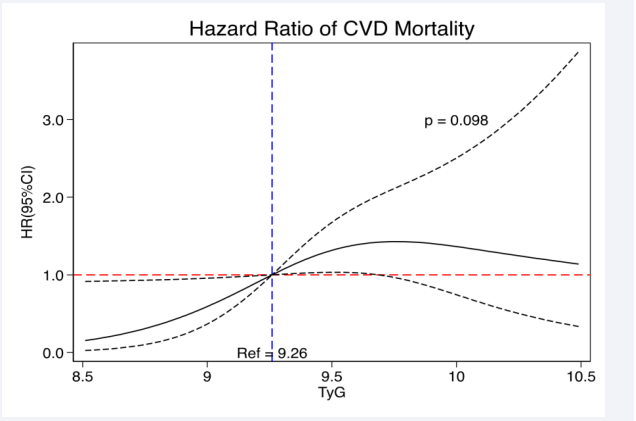


**Figure 18** Restricted cubic spline for the association between TyG and cardiovascular mortality. The solid line represents the HR and the dashed lines the 95% CI. The horizontal reference is HR = 1; the vertical reference is TyG = 9.26. The displayed P value is for nonlinearity.

## DISCUSSION

This study evaluated associations of the modified TyG index with prevalent CKD and subsequent mortality in adults classified as having T1DM in a nationally representative US sample. Higher TyG was independently associated with higher odds of prevalent CKD and with all-cause and cardiovascular mortality after adjustment for age, sex, race/ethnicity, BMI, smoking, and diabetes duration. To our knowledge, this is the first study to examine TyG in relation to mortality among adults with T1DM.

Our study showed that the TyG index was an independent risk factor of both all-cause and cardiovascular mortality in adults with T1DM. In this population, even with strict glycemic control (HbA1c≤6.9%), all-cause and cardiovascular mortality may remain approximately twice that of age- and BMI-matched individuals without diabetes [41]. This residual risk has been associated with IR-related factors [42]. Previously, a meta-analysis by Sun et al. found that each one-unit increase in eGDR was associated with 16% lower all-cause mortality and 17% lower cardiovascular mortality in T1DM [43]. The univariate findings in our study were similar: each one-unit increase in eGDR was associated with 16.7% lower all-cause mortality and 11.3% lower cardiovascular mortality (Table S3,S4). More importantly, our study found TyG to be a superior predictor, supported by larger AUCs than eGDR for both all-cause (AUC, 0.689 vs 0.662; P<0.001) and cardiovascular mortality (AUC, 0.664 vs 0.583; P<0.001). In Kaplan-Meier analyses, the higher-TyG group exhibited significantly poorer survival, while the differences between the two eGDR groups were not statistically significant. These results suggest that TyG may be a more effective mortality predictor in T1DM.

Our findings also validated the TyG index as a valuable clinical indicator for CKD in adults with CKD. Each one-unit increase in TyG was associated with 96% higher odds before and 70% higher odds after adjustment for age, sex, race/ethnicity, BMI, diabetes duration, and smoking. Calculated from HbA1c and TG levels, the TyG index may reflect both the effects of glucotoxicity and lipotoxicity in renal dysfunction, which are well-known factors for the development of diabetic kidney disease (DKD) [44,45]. In Asian populations, Lei et al. and Oh et al. similarly found the TyG index to be an independent risk factor for incident DKD or CKD with longitudinal cohorts [28,46].

In our study, the association between TyG and all-cause mortality was stronger among non-obese participants. Despite carrying an increased risk of metabolic disease and death, IR in people with normal weight or mild overweight may be missed by BMI based risk assessments [47]. Among individuals with obesity, mortality may be affected by multiple comorbidities and by more frequent treatment, which could reduce the relative contribution of the risk represented by TyG.

Our study also suggested stronger TyG–mortality associations in women and younger participants, although the statistical significance of these interactions potentially limited by our sample size. A large Korean cohort similarly found a stronger association among younger women than men, supporting further evaluation of TyG in this subgroup [48]. In our study, participants in the higher-TyG group were older at interview and at diagnosis, despite a similar duration of disease. This is consistent with the observation

of Merger et al. that later-onset T1DM may have a different metabolic phenotype and a greater tendency toward IR [16].

Studies in general and type 2 diabetes populations have reported nonlinear or U-shaped TyG-mortality relationships [49,50]. Reported mortality inflection points have generally been close to 9.0, including 8.95-9.0 in older adults with type 2 diabetes and 9.16-9.18 in younger adults with diabetes [51,52]. The present sample provided insufficient evidence to establish a nonlinear relationship for any outcome. The survey-weighted median of 9.14 was therefore used only for exploratory survival stratification. Median- or quantile-based classification may be reasonable for descriptive analyses until a reproducible threshold is externally validated.

Several limitations should be considered. First, diabetes type was determined from self-reported diagnosis and treatment because NHANES lacked C-peptide and islet-autoantibody measurements [29]. Some insulin-treated participants with type 2 diabetes may have been misclassified, while people with T1DM using adjunctive oral medication may have been excluded. Second, the T1DM sample was small, and the number of cardiovascular deaths was particularly limited, reducing statistical power after adjustment and within subgroups. Third, CKD was assessed cross-sectionally using a single eGFR or UACR measurement, which cannot confirm chronicity or establish that TyG preceded kidney disease. Fourth, both TyG and METS-IR substituted HbA1c-derived MBG for fasting glucose, which have not been extensively validated, and MBG may be affected by anemia, hemoglobinopathies, and CKD. Finally, future studies in large prospective cohorts with clinically classified T1DM are still needed to validate the prognostic value of TyG before it can be used for risk-guided care.

## CONCLUSION

In US adults with T1DM, a higher TyG index was independently associated with a more adverse metabolic profile, higher prevalence of CKD and subsequent all-cause and cardiovascular mortality. TyG may present as a more discriminative marker for mortality than other IR indices. Prospective studies in a confirmed T1DM population maybe needed to confirm clinical benefits of reducing TyG.

### Acknowledgements

The authors acknowledge the participants and staff of the National Health and Nutrition Examination Survey.

### Funding

This work was supported by the grants from National High Level Hospital Clinical Research Funding (2025-PUMCH-C-021, 2022-PUMCH-C-019).

## REFERENCES

1. Magliano DJ, Boyko EJ. IDF Diabetes Atlas 11th Edition Scientific Committee. IDF Diabetes Atlas. 2025.
2. Green A, Hede SM, Patterson CC, Wild SH, Imperatore G, Roglic G, et al. Type 1 diabetes in 2017: global estimates of incident and prevalent cases in children and adults. Diabetologia. 2021; 64: 2741-2750.
3. Gregory GA, Robinson TIG, Linklater SE, Wang F, Colagiuri S, de Beaufort C, et al. Global incidence, prevalence, and mortality of type 1 diabetes in 2021 with projection to 2040: a modelling study. Lancet Diabetes Endocrinol. 2022; 10: 741-760.
4. Yang K, Yang X, Jin C, Ding S, Liu T, Ma B, et al. Global burden of type 1 diabetes in adults aged 65 years and older, 1990-2019: population based study. BMJ. 2024; 385: e078432.
5. Yki-Järvinen H, Koivisto VA. Natural course of insulin resistance in type I diabetes. N Engl J Med. 1986; 315: 224-230.
6. Donga E, Dekkers OM, Corssmit EP, Romijn JA. Insulin resistance in patients with type 1 diabetes assessed by glucose clamp studies: systematic review and meta-analysis. Eur J Endocrinol. 2015; 173: 101-109.
7. Kacerovsky M, Brehm A, Chmelik M, Schmid AI, Szendroedi J, Kacerovsky-Bielesz G, et al. Impaired insulin stimulation of muscular ATP production in patients with type 1 diabetes. J Intern Med. 2011; 269: 189-199.
8. Szendroedi J, Saxena A, Weber KS, Strassburger K, Herder C, Burkart V, et al. Cohort profile: the German Diabetes Study (GDS). Cardiovasc Diabetol. 2016; 15: 59.
9. Schön M, Zaharia OP, Strassburger K, Kupriyanova Y, Bódis K, Heilmann G, et al. Intramyocellular Triglyceride Content During the Early Course of Type 1 and Type 2 Diabetes. Diabetes. 2023; 72: 1483-1492.
10. Burkart V, Strassburger K, Zivehe F, Markgraf D, Herder C, Müssig K, et al. Inverse association of insulin antibody levels with insulin sensitivity in adults with type 1 diabetes. Diabet Med. 2018; 35: 595-601.
11. Teupe B, Bergis K. Epidemiological evidence for "double diabetes". Lancet. 1991; 337: 361-362.
12. Kietsiriroje N, Pearson S, Campbell M, Ariëns RAS, Ajjan RA. Double diabetes: a distinct high-risk group? Diabetes Obes Metab. 2019; 21: 2609-2618.
13. Bielka W, Przezak A, Molęda P, Pius-Sadowska E, Machaliński B. Double diabetes-when type 1 diabetes meets type 2 diabetes: definition, pathogenesis and recognition. Cardiovasc Diabetol. 2024; 23: 62.
14. Kilpatrick ES, Rigby AS, Atkin SL. Insulin resistance, the metabolic syndrome, and complication risk in type 1 diabetes: "double diabetes" in the Diabetes Control and Complications Trial. Diabetes Care. 2007; 30: 707-712.
15. Nyström T, Holzmann MJ, Eliasson B, Svensson AM, Sartipy U. Estimated glucose disposal rate predicts mortality in adults with type 1 diabetes. Diabetes Obes Metab. 2018; 20: 556-563.
16. Merger SR, Kerner W, Stadler M, Zeyfang A, Jehle P, Müller-Korbsch M, et al. Prevalence and comorbidities of double diabetes. Diabetes Res Clin Pract. 2016; 119: 48-56.
17. Lachin JM, Orchard TJ, Nathan DM; DCCT/EDIC Research Group.

Update on cardiovascular outcomes at 30 years of the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study. Diabetes Care. 2014; 37: 39-43.

18. DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol. 1979; 237: E214-E223.

19. Apostolopoulou M, Lambadiari V, Roden M, Dimitriadis GD. Insulin resistance in type 1 diabetes: pathophysiological, clinical, and therapeutic relevance. Endocr Rev. 2025; 46: 317-348.

20. Williams KV, Erbey JR, Becker D, Arslanian S, Orchard TJ. Can clinical factors estimate insulin resistance in type 1 diabetes? Diabetes. 2000; 49: 626-632.

21. Mertens J, Roosens L, Braspenning R, Vandebeeck J, Francque S, De Block C. The 13C glucose breath test accurately identifies insulin resistance in people with type 1 diabetes. J Clin Endocrinol Metab. 2025; 110: e432-e442.

22. Chen W, Wang X, Jiang Q, Wu J, Shi W, Wang X, et al. Association between triglyceride glucose index and severity of diabetic foot ulcers in type 2 diabetes mellitus. J Foot Ankle Res. 2023; 16: 68.

23. Zhou Y, Lu Q, Zhang M, Yang L, Shen X. The U-shape relationship between triglyceride-glucose index and the risk of diabetic retinopathy among the US population. J Pers Med. 2023; 13: 495.

24. Zhang Q, Xiao S, Jiao X, Shen Y. The triglyceride-glucose index is a predictor for cardiovascular and all-cause mortality in CVD patients with diabetes or pre-diabetes: evidence from NHANES 2001-2018. Cardiovasc Diabetol. 2023; 22: 279.

25. 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: 168.

26. Gao YM, Chen WJ, Deng ZL, Shang Z, Wang Y. Association between triglyceride-glucose index and risk of end-stage renal disease in patients with type 2 diabetes mellitus and chronic kidney disease. Front Endocrinol (Lausanne). 2023; 14: 1150980.

27. Angelino S, Monda A, Di Martino N, Caruso P, Longo M, Maio A, et al. Exploring insulin resistance in adults with type 1 diabetes: the role of the estimated glucose disposal rate and the triglyceride-glucose index. Diabetes Metab Res Rev. 2025; 41: e70100.

28. Lei M, Ling P, Zhou Y, Lv J, Ni Y, Deng H, et al. Correlation between triglyceride-glucose index and diabetic kidney disease risk in adults with type 1 diabetes mellitus. Diabetol Metab Syndr. 2024; 16: 239.

29. Mosslemi M, Park HL, McLaren CE, Wong ND. A treatment-based algorithm for identification of diabetes type in the National Health and Nutrition Examination Survey. Cardiovasc Endocrinol Metab. 2020; 9: 9-16.

30. Wang Y, Zhu Y, Chen Z, Chen S, Fu G, Fu J. Association between electronic cigarettes use and whole blood cell among adults in the USA-a cross-sectional study of National Health and Nutrition Examination Survey analysis. Environ Sci Pollut Res Int. 2022; 29: 88531-88539.

31. National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002; 106: 3143-3421.

32. Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y, et al. New creatinine- and cystatin C-based equations to estimate GFR without race. N Engl J Med. 2021; 385: 1737-1749.

33. de Boer IH, Khunti K, Sadusky T, Tuttle KR, Neumiller JJ, Rhee CM, et al. Diabetes management in chronic kidney disease: a consensus report by the American Diabetes Association and Kidney Disease: Improving Global Outcomes (KDIGO). Diabetes Care. 2022; 45: 3075-3090.

34. Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine RJ; A1c-Derived Average Glucose Study Group. Translating the A1C assay into estimated average glucose values. Diabetes Care. 2008; 31: 1473-1478.

35. Guerrero-Romero F, Simental-Mendía LE, González-Ortiz M, Martínez-Abundis E, Ramos-Zavala MG, Hernández-González SO, et al. The product of triglycerides and glucose, a simple measure of insulin sensitivity: comparison with the euglycemic-hyperinsulinemic clamp. J Clin Endocrinol Metab. 2010; 95: 3347-3351.

36. Epstein EJ, Osman JL, Cohen HW, Rajpathak SN, Lewis O, Crandall JP. Use of the estimated glucose disposal rate as a measure of insulin resistance in an urban multiethnic population with type 1 diabetes. Diabetes Care. 2013; 36: 2280-2285.

37. Bittner V, Johnson BD, Zineh I, Rogers WJ, Vido D, Marroquin OC, et al. The TG/HDL-C cholesterol ratio predicts all-cause mortality in women with suspected myocardial ischemia: a report from the Women's Ischemia Syndrome Evaluation (WISE). Am Heart J. 2009; 157: 548-555.

38. Bello-Chavolla OY, Almeda-Valdes P, Gomez-Velasco D, Viveros-Ruiz T, Cruz-Bautista I, Romo-Romo A, et al. METS-IR, a novel score to evaluate insulin sensitivity, is predictive of visceral adiposity and incident type 2 diabetes. Eur J Endocrinol. 2018; 178: 533-544.

39. National Center for Health Statistics. NCHS data linkage-mortality data-public-use files. 2025.

40. National Center for Health Statistics. NHANES tutorials: weighting module. 2025.

41. Lind M, Svensson AM, Kosiborod M, Gudbjörnsdottir S, Pivodic A, Wedel H, et al. Glycemic control and excess mortality in type 1 diabetes. N Engl J Med. 2014; 371: 1972-1982.

42. Orchard TJ, Olson JC, Erbey JR, Williams K, Forrest KY, Smithline Kinder L, et al. Insulin resistance-related factors, but not glycemia, predict coronary artery disease in type 1 diabetes: 10-year follow-up data from the Pittsburgh Epidemiology of Diabetes Complications Study. Diabetes Care. 2003; 26: 1374-1379.

43. Sun R, Wang J, Li M, Li J, Pan Y, Liu B, et al. Association of insulin resistance with cardiovascular disease and all-cause mortality in type 1 diabetes: systematic review and meta-analysis. Diabetes Care. 2024; 47: 2266-2274.

44. Samsu N. Diabetic nephropathy: challenges in pathogenesis, diagnosis, and treatment. Biomed Res Int. 2021; 2021: 1497449.

45. Bjornstad P, Cherney D, Maahs DM. Early diabetic nephropathy in type 1 diabetes: new insights. Curr Opin Endocrinol Diabetes Obes. 2014; 21: 279-286.

46. Oh R, Kim S, Cho SH, Kim JY, Jang M, Park SH, et al. Elevated triglyceride-glucose index is associated with increased risk of chronic kidney disease and end-stage renal disease in type 1 diabetes: nationwide cohort study. Diabetes Obes Metab. 2026; 28: 2784-2794.

47. Ruderman N, Chisholm D, Pi-Sunyer X, Schneider S. The metabolically obese, normal-weight individual revisited. Diabetes. 1998; 47: 699-713.

48. Kim KS, Hong S, Hwang YC, Ahn HY, Park CY. Evaluating triglyceride and glucose index as a simple and easy-to-calculate marker for all-cause and cardiovascular mortality. J Gen Intern Med. 2022; 37: 4153-4159.

49. Liu XC, He GD, Lo K, Huang YQ, Feng YQ. The triglyceride-glucose index, an insulin resistance marker, was non-linearly associated with all-cause and cardiovascular mortality in the general population. Front Cardiovasc Med. 2020; 7: 628109.

50. Yu Y, Wang J, Ding L, Huang H, Cheng S, Deng Y, et al. Sex differences in the nonlinear association of triglyceride glucose index with all-cause and cardiovascular mortality in the general population. Diabetol Metab Syndr. 2023; 15: 136.

51. Zhao M, Xiao M, Tan Q, Lu F. Triglyceride glucose index as a predictor of mortality in middle-aged and elderly patients with type 2 diabetes in the US. Sci Rep. 2023; 13: 16478.

52. Liu C, Liang D, Xiao K, Xie L. Association between the triglyceride-glucose index and all-cause and CVD mortality in the young population with diabetes. Cardiovasc Diabetol. 2024; 23: 171.