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ORIGINAL RESEARCH

Association Between the Triglyceride-Glucose Index and All-Cause Mortality Among Patients with Diabetes and Chronic Kidney Disease: A Retrospective Cohort Study

Mengjiang Liu[1], Zhaodan Yan[1], Yi Zhang[1], Shengli Zhang[2]

[1]Department of Endocrinology, Hubei NO.3 People's Hospital of Jianghan University, Wuhan, 430032, People's Republic of China; [2]Department of Cardiology, Hubei NO.3 People's Hospital of Jianghan University, Wuhan, 430032, People's Republic of China

Correspondence: Shengli Zhang, Department of Cardiology, Hubei NO.3 People's Hospital of Jianghan University, Wuhan, 430032, People's Republic of China, Email 13971408346@163.com

Aim: This study aimed to explore the relationship between the triglyceride-glucose index (TyG) and all-cause mortality among patients with diabetes and chronic kidney disease (CKD).

Methods: This was a retrospective cohort study that included 512 patients with diabetes and CKD. The TyG index was considered the exposure factor, and patients were divided into three groups based on the tertiles of the TyG index. The association between the TyG index and all-cause mortality was evaluated using multivariate Cox regression analysis, subgroup analysis, sensitivity analysis, restricted cubic spline (RCS) plot, and receiver operating characteristic (ROC) curves.

Results: Significant differences in clinical and metabolic parameters were observed across TyG tertiles, and all-cause mortality was markedly higher in the T3 group ($P < 0.001$). Multivariate Cox regression analysis showed that in the fully adjusted model (Model 3), the TyG index remained an independent risk factor, both as a continuous variable (HR = 1.582, 95% CI: 1.089–2.298, $P = 0.016$) and as a categorical variable (T3 vs T1, HR = 3.300, 95% CI: 1.820–5.984, $P < 0.001$). Subgroup analysis further confirmed consistent associations across various populations, including different age, sex, and comorbidity strata. Sensitivity analysis excluding patients with estimated glomerular filtration rate < 15 mL/min/1.73m^2 showed robust associations in both continuous and categorical forms ($P < 0.05$). RCS analysis revealed a significant nonlinear relationship between Log_{10}-transformed TyG index and all-cause mortality (P-nonlinear < 0.001). ROC curve analysis demonstrated that the TyG index alone had better predictive ability for all-cause mortality (AUC = 0.690) than age, hemoglobin A1c, or total cholesterol. The baseline model had an AUC of 0.809, which increased significantly to 0.878 (95% CI: 0.846–0.911) when the TyG index was added.

Conclusion: The TyG index was independently and nonlinearly associated with all-cause mortality in patients with diabetes and CKD. These findings suggest that the TyG index may serve as a useful, non-invasive biomarker for risk stratification and mortality prediction in this high-risk population, with potential clinical implications for improving long-term management and prognosis.

Keywords: diabetes, chronic kidney disease, triglyceride-glucose index, all-cause mortality, receiver operating characteristic

Introduction

Diabetes and chronic kidney disease (CKD) are major public health issues globally, imposing a significant disease burden on patients.[1,2] Due to the chronic hyperglycemic state in diabetes, patients are prone to develop various complications such as cardiovascular diseases (CVD), renal disorders, and retinopathy, which significantly increase their risk of mortality.[3–5] Mortality rates among patients with CKD are primarily associated with CVD, with diabetes being one of the leading causes of CKD.[6,7] The coexistence of diabetes and CKD not only accelerates disease progression in both conditions but also markedly increases the risk of all-cause mortality. This is largely attributed to the high prevalence of

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insulin resistance (IR), systemic inflammation, and cardiovascular comorbidities in this population. Therefore, identifying reliable predictors of mortality in patients with both diabetes and CKD is of great clinical importance.

The triglyceride-glucose (TyG) index, which measures fasting blood glucose and triglyceride levels, indirectly reflects an individual's state of IR and has been proven to correlate with various cardiovascular and metabolic risk factors.[8–10] Notably, the TyG index may particularly reflect IR related to hepatic steatosis, rather than systemic IR alone. Recent evidence suggests that the liver, through increased secretion of glucose and triglycerides and dysregulation of hepatokines (eg, fetuin-A), plays a central role in promoting oxidative stress, systemic inflammation, and multi-organ metabolic disruption.[11] These processes may contribute to cardiovascular damage, renal impairment, and ultimately increased mortality risk. Since IR is a common pathophysiological basis for diabetes and CVD, the TyG index may therefore have predictive value for the prognosis of patients with diabetes and CKD.[12] Multiple studies have shown that the TyG index is not only closely associated with atherosclerosis and CVD but also linked to multi-organ dysfunction, including liver dysfunction (such as fatty liver disease and liver fibrosis), heart failure, and decline in renal function.[13–16] These associations suggest that the TyG index may also reflect broader systemic metabolic dysfunction and might be useful in mortality risk stratification. However, there is a lack of focused research examining the association between the TyG index and all-cause mortality specifically in patients with both diabetes and CKD. Most existing studies either address these populations separately or focus on surrogate cardiovascular outcomes. Moreover, evidence in Asian populations remains limited. Given the high mortality burden and the potential mechanistic relevance of the TyG index in this dual-diagnosis group, such investigation is both timely and clinically important.

Therefore, we hypothesize that the TyG index is independently and nonlinearly associated with all-cause mortality in patients with diabetes and CKD. To test this, we conducted a retrospective cohort study in a Chinese hospitalized population, aiming to evaluate the association between TyG index levels and long-term mortality risk. By employing multivariate Cox regression, subgroup and sensitivity analyses, restricted cubic spline (RCS) modeling, and receiver operating characteristic (ROC) curves, we sought to comprehensively assess the predictive utility of the TyG index and offer new insights into risk stratification and clinical management for this vulnerable population.

Methods

Study Design and Participants

This retrospective cohort study initially screened 689 patients with both diabetes and CKD who were hospitalized due to diabetes and its chronic complications at Hubei NO.3 People's Hospital of Jianghan University between July 2013 and July 2020. Patients were selected based on the following inclusion criteria: (1) aged 18 years or older; (2) diagnosed with diabetes according to the American Diabetes Association (ADA) criteria;[17] (3) diagnosed with CKD based on the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines.[18] Exclusion criteria included: (1) patients with acute kidney injury; (2) patients with malignant diseases or severe infections; (3) patients with incomplete medical records. After applying the inclusion and exclusion criteria, 177 patients were excluded. Finally, 512 eligible patients were included in the analysis. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Hubei NO.3 People's Hospital of Jianghan University, and written informed consent was obtained from all participants.

Data Collection and Definition

Baseline data were collected from the medical records, including demographic information (age, sex), lifestyle factor (smoking status), medical history (hypertension, hyperlipidemia, stroke, coronary heart disease [CHD], cancer), and biochemical measurements (body mass index [BMI], systolic blood pressure [SBP], diastolic blood pressure [DBP], fasting glucose, hemoglobin A1c [HbA1c], triglycerides, total cholesterol, low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C], estimated glomerular filtration rate [eGFR], uric acid, C-reactive protein [CRP], and albumin). The TyG index was calculated using the formula: $\mathrm{TyGindex} = \ln(\mathrm{triglycerides[mg/dL]} \times \mathrm{fasting\,glucose[mg/dL]}/2)$.[19]

Smoking status was defined based on self-reported smoking behavior, categorizing individuals as current or former smokers, and non-smokers. Hypertension was defined as a self-reported history of hypertension, use of antihypertensive medications, or having a measured SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg.[20] Hyperlipidemia was defined as a self-reported history of hyperlipidemia, or use of lipid-lowering medications. Stroke was defined as a self-reported history of a cerebrovascular accident diagnosed by a physician. CHD was defined as a self-reported history of myocardial infarction, angina, or any other physician-diagnosed coronary artery disease. Cancer was defined as a self-reported history of any type of cancer diagnosed by a physician. The eGFR was calculated using a modified Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation adapted for the Chinese population, which estimates eGFR based on serum creatinine levels, age, and gender.[21] Obesity was defined as a BMI ≥ 28 kg/m^2, in accordance with the criteria for the Chinese adult population.[22]

Follow-Up and Outcomes

Patients were followed up from the date of their initial admission until July 2024 or until death, whichever came first. The median follow-up duration was 51.0 months. The primary outcome was all-cause mortality, defined as death from any cause during the follow-up period, which was verified through hospital records and follow-up telephone calls.

Statistical Analysis

All statistical analyses were conducted using SPSS 26.0 and R version 4.1.3. Regarding missing data, only patients with complete core clinical variables were included. For a small number of auxiliary variables with missing values, mean imputation was applied to reduce bias and retain statistical power. For continuous variables, differences between the two groups were compared using either independent sample *t*-tests or non-parametric tests, depending on the normality of the data. Differences among three groups were compared using one-way ANOVA or non-parametric tests. For categorical variables, differences between groups were compared using chi-square tests. Subsequently, multivariate Cox regression analysis was performed to assess the association between the TyG index and all-cause mortality based on three multivariable-adjusted models. A subgroup analysis based on age, sex, hypertension, hyperlipidemia, stroke, CHD, cancer, and obesity was then conducted to further evaluate the stratified association between the TyG index and all-cause mortality. The robustness of the association between the TyG index and all-cause mortality in the three models was reassessed after excluding patients with eGFR < 15 mL/min/1.73m^2. RCS plot was used to assess the nonlinear association between the TyG index and all-cause mortality. ROC curve analysis was performed to evaluate the discriminatory ability of the TyG index for predicting all-cause mortality. The area under the curve (AUC) was calculated for predictors including TyG, age, HbA1c, total cholesterol, baseline model, and baseline model + TyG. A baseline prediction model was constructed using traditional risk factors (including age, hypertension, hyperlipidemia, stroke, CHD, cancer, obesity, antidiabetic drugs, DBP, HbA1c, total cholesterol, CRP, albumin, uric acid, and eGFR). Two-sided P values < 0.05 were considered statistically significant.

Results

Baseline Characteristics

As shown in Table 1, this study included 512 patients with an average age of 71.23 ± 10.18 years, among whom 359 were male (70.1%). Based on the tertiles of the TyG index, all patients were divided into three groups: T1: TyG ≤ 9.05, T2: 9.05 < TyG ≤ 9.51, T3: TyG > 9.51. Significant statistical differences were observed among the three TyG groups in age, CHD, fasting glucose, HbA1c, triglycerides, total cholesterol, LDL-C, and HDL-C levels (P < 0.05). Additionally, the all-cause mortality rate in the T3 group was significantly higher than those in the T2 and T1 groups (P < 0.001).

The Association Between TyG and All-Cause Mortality

As shown in Table 2, in the overall population, multivariate Cox regression analysis demonstrated that in Model 1 (adjusted for age only) and Model 2 (further adjusted for hypertension, hyperlipidemia, stroke, CHD, cancer, obesity, and use of antidiabetic drugs), higher TyG index values—whether treated as a continuous or categorical variable—were

Table 1 Baseline Characteristics of Diabetic Patients with CKD Grouped by TyG Index

Variables	Total Population	T1	T2	T3	P value
N	512	170	171	171	
Age, years	71.23 ± 10.18	71.64 ± 10.20	72.55 ± 8.75	69.50 ± 11.25	0.017
Sex, n (%)					0.493
Male	359 (70.1)	125 (73.5)	117 (68.4)	117 (68.4)	
Female	153 (29.9)	45 (26.5)	54 (31.6)	54 (31.6)	
Smoking, n (%)	157 (30.7)	51 (30.0)	50 (29.2)	56 (32.7)	0.760
Hypertension, n (%)	440 (85.9)	141 (82.9)	147 (86.0)	152 (88.9)	0.287
Hyperlipidemia, n (%)	315 (61.5)	102 (60.0)	101 (59.1)	112 (65.5)	0.418
Stroke, n (%)	84 (16.4)	30 (17.6)	30 (17.5)	24 (14.0)	0.591
CHD, n (%)	290 (56.6)	89 (52.4)	85 (49.7)	116 (67.8)	0.001
Cancer, n (%)	109 (21.3)	40 (23.5)	32 (18.7)	37 (21.6)	0.549
Obesity, n (%)	319 (62.3)	106 (62.4)	96 (56.1)	117 (68.4)	0.064
Antihypertensive drugs, n (%)	373 (72.9)	122 (71.8)	120 (70.2)	131 (76.6)	0.379
Lipid-lowering drugs, n (%)	215 (42.0)	80 (47.1)	69 (40.4)	66 (38.6)	0.248
Antidiabetic drugs, n (%)	353 (68.9)	121 (71.2)	109 (63.7)	123 (71.9)	0.195
BMI, kg/m^2	30.78 ± 6.78	30.89 ± 7.85	30.16 ± 6.23	31.28 ± 6.12	0.305
SBP, mmHg	138.05 ± 23.98	134.98 ± 24.81	139.00 ± 23.87	140.16 ± 23.08	0.112
DBP, mmHg	64.60 ± 14.13	63.52 ± 14.11	64.89 ± 13.39	65.40 ± 14.86	0.447
Fasting glucose, mmol/L	7.77 (7.22, 8.65)	7.32 (6.70, 7.88)	7.71 (7.38, 8.27)	8.60 (7.66, 10.77)	< 0.001
HbA1c, %	6.84 ± 1.37	6.62 ± 1.12	6.58 ± 0.99	7.32 ± 1.76	< 0.001
Triglycerides, mmol/L	1.67 (1.23, 2.32)	1.12 (0.91, 1.30)	1.72 (1.50, 1.91)	2.66 (2.30, 3.22)	< 0.001
Total cholesterol, mmol/L	4.70 ± 1.14	4.34 ± 0.91	4.64 ± 1.05	5.12 ± 1.28	< 0.001
LDL-C, mmol/L	2.63 ± 0.91	2.49 ± 0.81	2.65 ± 0.94	2.74 ± 0.97	0.037
HDL-C, mmol/L	1.23 ± 0.35	1.31 ± 0.36	1.26 ± 0.34	1.11 ± 0.32	< 0.001
eGFR, $mL/min/1.73m^2$	44.87 ± 12.92	44.31 ± 12.80	45.52 ± 13.54	44.77 ± 12.44	0.681
Uric acid, μmol/L	425.53 ± 103.92	417.90 ± 97.76	420.47 ± 102.93	438.17 ± 110.10	0.146
CRP, mg/dL	0.62 (0.18, 0.62)	0.62 (0.18, 0.62)	0.52 (0.15, 0.62)	0.62 (0.25, 0.62)	0.097
Albumin, g/L	40.15 ± 3.90	40.06 ± 3.76	40.60 ± 3.29	39.78 ± 4.54	0.144
All-cause mortality, n (%)	87 (17.0)	14 (8.2)	17 (9.9)	56 (32.7)	< 0.001

Notes: T1: TyG ≤ 9.05, T2: 9.05 < TyG ≤ 9.51, T3: TyG > 9.51.

Abbreviations: CKD, chronic kidney disease; TyG, triglyceride-glucose index; CHD, coronary heart disease; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HbA1c, hemoglobin A1c; eGFR, estimated glomerular filtration rate; CRP, C-reactive protein; HR, hazard ratio; CI, confidence interval.

significantly associated with an increased risk of all-cause mortality (P < 0.05). In Model 3, which was additionally adjusted for DBP, HbA1c, total cholesterol, CRP, albumin, uric acid, and eGFR, the TyG index remained independently associated with the risk of all-cause mortality (as a continuous variable, HR: 1.582, 95% CI: 1.089–2.298, P = 0.016; as a categorical variable, T3 vs T1, HR: 3.300, 95% CI: 1.820–5.984, P < 0.001).

Furthermore, after excluding patients with eGFR < 15 $mL/min/1.73m^2$, multivariate Cox regression analysis indicated that the TyG index was significantly associated with all-cause mortality in both Model 1 and Model 2 (P < 0.05). In Model 3, which was further adjusted for DBP, HbA1c, total cholesterol, CRP, albumin, uric acid, and eGFR based on Model 2, the TyG index remained significantly associated with all-cause mortality as a continuous variable (HR = 1.781, 95% CI: 1.269–2.501, P = 0.001). When treated as a categorical variable, individuals in the T3 group had a significantly higher risk of all-cause mortality compared to those in the T1 group (HR = 3.339, 95% CI: 1.774–6.283, P < 0.001).

Subgroup Analysis

As shown in Table 3, the TyG index was significantly associated with all-cause mortality across multiple subgroups. Among individuals aged < 75 years, the risk of all-cause mortality in the T3 group was significantly higher than in the T1 group (HR = 4.389, P = 0.009). In those aged ≥ 75 years, both the TyG index as a continuous variable (HR = 2.029, P = 0.024) and the T3 group (HR = 2.647, P = 0.019) were significantly associated with increased mortality risk. In males,

Table 2 Multivariate Cox Regression Analysis of TyG Index for All-Cause Mortality

Variable	Model 1		Model 2		Model 3	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Total population						
TyG index (continuous)	1.951 (1.420, 2.679)	< 0.001	1.909 (1.337, 2.725)	< 0.001	1.582 (1.089, 2.298)	0.016
TyG index (categorical)						
T1	Ref		Ref		Ref	
T2	1.013 (0.499, 2.058)	0.971	1.081 (0.528, 2.212)	0.831	1.101 (0.536, 2.264)	0.793
T3	4.119 (2.288, 7.412)	< 0.001	3.402 (1.885, 6.142)	< 0.001	3.300 (1.820, 5.984)	< 0.001
Excluding patients with eGFR < 15 mL/min/1.73m^2						
TyG index (continuous)	2.068 (1.506, 2.838)	< 0.001	2.088 (1.461, 2.985)	< 0.001	1.781 (1.269, 2.501)	0.001
TyG index (categorical)						
T1	Ref		Ref		Ref	
T2	1.115 (0.527, 2.360)	0.776	1.167 (0.547, 2.490)	0.689	0.955 (0.443, 2.058)	0.907
T3	4.848 (2.595, 9.058)	< 0.001	4.023 (2.147, 7.539)	< 0.001	3.339 (1.774, 6.283)	< 0.001

Notes: Model 1: adjusted for age; Model 2: adjusted for age, hypertension, hyperlipemia, stroke, coronary heart disease, cancer, obesity, and antidiabetic drugs; Model 3: adjusted for Model 2 plus diastolic blood pressure, hemoglobin A1c, total cholesterol, C-reactive protein, albumin, uric acid and eGFR.
Abbreviations: TyG, triglyceride-glucose index; eGFR, estimated glomerular filtration rate; HR, hazard ratio; CI, confidence interval.

Table 3 Stratified Association Between TyG and All-Cause Mortality

Subgroups	TyG		T2 vs T1		T3 vs T1		
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	P for Trend
Age							
< 75 years	1.109 (0.546, 2.251)	0.774	0.826 (0.228, 2.992)	0.771	4.389 (1.447, 13.314)	0.009	0.004
≥ 75 years	2.029 (1.100, 3.745)	0.024	0.663 (0.259, 1.698)	0.392	2.647 (1.175, 5.960)	0.019	< 0.001
Sex							
Male	1.688 (1.110, 2.567)	0.014	1.200 (0.506, 2.848)	0.679	2.887 (1.372, 6.073)	0.005	0.002
Female	1.469 (0.658, 3.278)	0.348	0.437 (0.110, 1.737)	0.240	3.892 (1.305, 11.604)	0.015	< 0.001
Hypertension							
Yes	1.328 (0.809, 2.181)	0.263	0.956 (0.455, 2.009)	0.906	3.299 (1.812, 6.005)	< 0.001	< 0.001
No	–	–	–	–	–	–	–
Hyperlipidemia							
Yes	1.208 (0.701, 2.080)	0.496	0.803 (0.366, 1.762)	0.584	2.219 (1.163, 4.233)	0.016	0.003
No	3.601 (1.902, 6.815)	< 0.001	3.105 (0.322, 29.947)	0.327	19.526 (2.609, 146.115)	0.004	< 0.001
Stroke							
Yes	0.342 (0.061, 1.917)	0.222	0.379 (0.085, 1.686)	0.203	1.332 (0.173, 10.254)	0.783	0.209
No	1.913 (1.176, 3.109)	0.009	1.084 (0.421, 2.789)	0.868	4.676 (2.188, 9.994)	< 0.001	< 0.001
CHD							
Yes	1.290 (0.807, 2.063)	0.288	1.000 (0.487, 2.050)	0.999	2.915 (1.610, 5.280)	< 0.001	< 0.001
No	–	–	–	–	–	–	–
Cancer							
Yes	0.806 (0.268, 2.421)	0.700	0.962 (0.219, 4.214)	0.958	3.998 (0.895, 17.859)	0.070	0.107
No	2.271 (1.378, 3.742)	0.001	0.971 (0.413, 2.284)	0.947	3.309 (1.633, 6.703)	0.001	< 0.001
Obesity							
Yes	2.310 (1.442, 3.700)	< 0.001	1.217 (0.522, 2.836)	0.650	4.026 (2.007, 8.078)	< 0.001	< 0.001
No	0.800 (0.265, 2.418)	0.692	0.202 (0.039, 1.061)	0.059	1.375 (0.327, 5.786)	0.664	0.032

Abbreviations: TyG, triglyceride-glucose index; CHD, coronary heart disease; HR, hazard ratio; CI, confidence interval.

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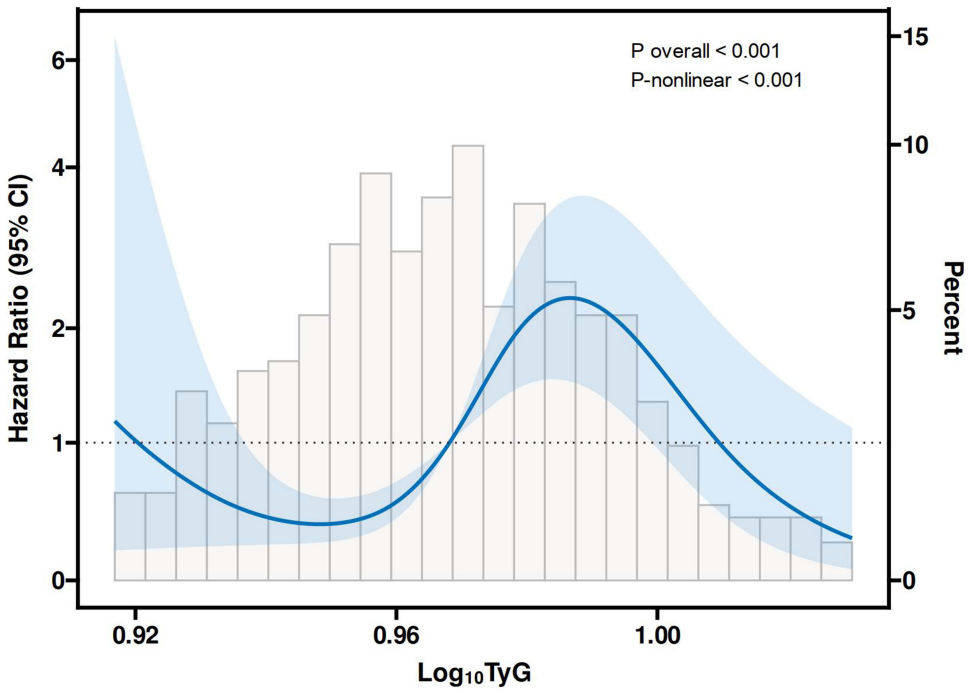

Figure 1 Restricted cubic spline plot for the nonlinear association between TyG and all-cause mortality.
Abbreviations: TyG, triglyceride-glucose index; CI, confidence interval.

the TyG index as a continuous variable (HR = 1.688, P = 0.014) and the T3 group (HR = 2.887, P = 0.005) were both significantly linked to higher mortality risk. Among females, the T3 group also showed a significantly elevated risk (HR = 3.892, P = 0.015). Significantly increased mortality risk in the T3 group was also observed among individuals with hypertension (HR = 3.299), hyperlipidemia (HR = 2.219), CHD (HR = 2.915), and obesity (HR = 4.026), all with P-values < 0.05. In participants without hyperlipidemia, the TyG index as a continuous variable (HR = 3.601, P < 0.001) and the T3 group (HR = 19.526, P = 0.004) had particularly strong associations with mortality risk. Among individuals without a history of stroke, the TyG index (HR = 1.913, P = 0.009) and the T3 group (HR = 4.676, P < 0.001) were both significantly associated with all-cause mortality. In participants without cancer, the TyG index was also consistently and significantly associated with mortality, whether treated as a continuous or categorical variable (all P < 0.01).

RCS Analysis

As shown in Figure 1, since the TyG index is not normally distributed, a base-10 logarithmic transformation (Log_{10}TyG) was applied to improve its normality and more accurately characterize the relationship between the TyG index and all-cause mortality. In the RCS regression model, the red curve represents the trend of risk variation between Log_{10}TyG and all-cause mortality, while the red shaded area indicates the 95% CI. The results demonstrated a clear nonlinear relationship between increasing Log_{10}TyG levels and all-cause mortality risk (P-overall < 0.001, P-nonlinear < 0.001).

Predictive Value of TyG Index for All-Cause Mortality

As shown in Table 4 and Figure 2, the ROC curve analysis demonstrated that among individual predictors, the TyG index had the strongest ability to predict all-cause mortality, with an area under the curve (AUC) of 0.690 (95% CI: 0.633–0.747, P < 0.001), outperforming age (AUC = 0.608), HbA1c (AUC = 0.619), and total cholesterol (AUC = 0.595). The baseline model, which included age, hypertension, hyperlipidemia, stroke, CHD, cancer, obesity, antidiabetic drugs, DBP, HbA1c, total cholesterol, CRP, albumin, uric acid, and eGFR, achieved an AUC of 0.809 (95% CI: 0.768–0.850, P < 0.001). Notably, when the TyG index was added to the baseline model, the AUC significantly increased to 0.878 (95% CI: 0.846–0.911, P < 0.001).

Table 4 ROC Curves Evaluating Predictive Indicators for All-Cause Mortality Risk

Variables	AUC	95% CI	P value
Age	0.608	0.542–0.674	0.001
HbA1c	0.619	0.559–0.679	< 0.001
TC	0.595	0.530–0.660	0.005
TyG	0.690	0.633–0.747	< 0.001
Baseline model	0.809	0.768–0.850	< 0.001
Baseline model + TyG	0.878	0.846–0.911	< 0.001

Notes: The baseline model consisted of the following variables: age, hypertension, hyperlipidemia, stroke, coronary heart disease, cancer, obesity, antidiabetic drugs, diastolic blood pressure, hemoglobin A1c, total cholesterol, C-reactive protein, albumin, uric acid, and estimated glomerular filtration rate.
Abbreviations: ROC, receiver operating characteristic; TyG, triglyceride-glucose index; TC, total cholesterol; HbA1c, hemoglobin A1c; AUC, area under the curve; CI, confidence interval.

Discussion

This study explored the association between the TyG index and all-cause mortality among patients with diabetes and CKD. By analyzing retrospective cohort data from 512 patients with diabetes and CKD, the study found that a high TyG

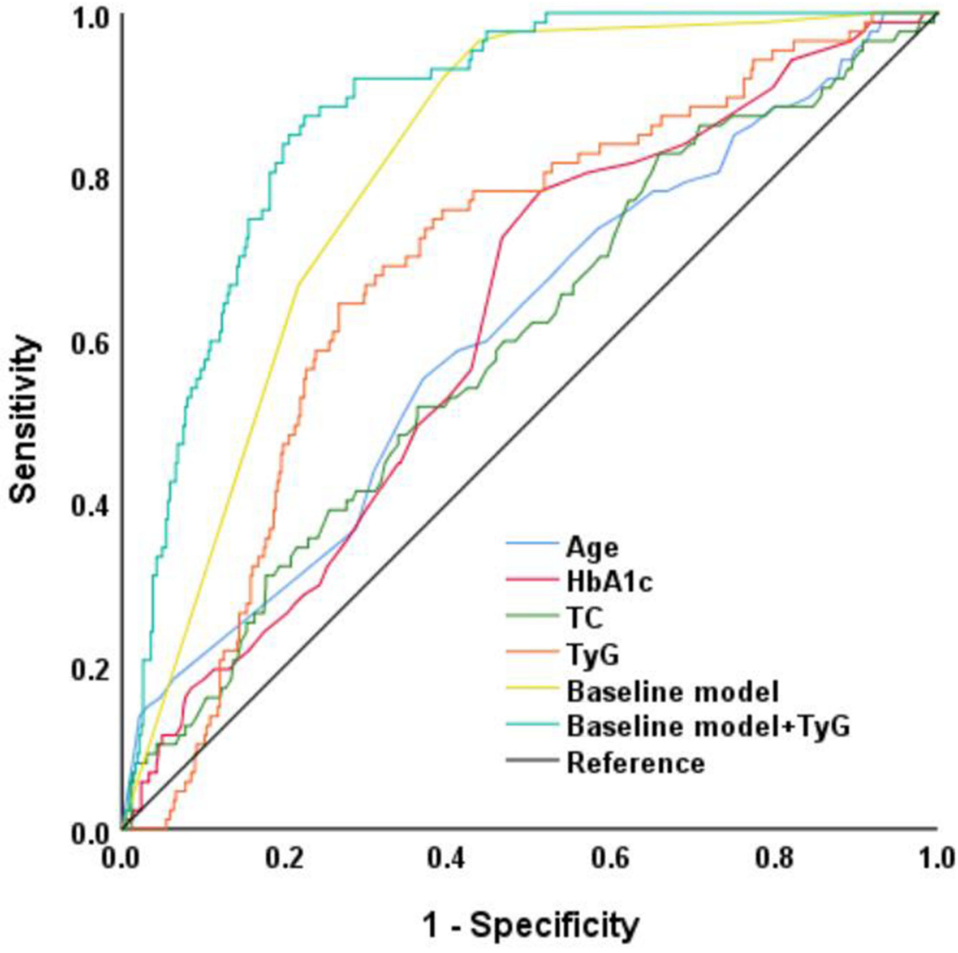

Figure 2 ROC curves evaluating predictive indicators for all-cause mortality risk. The baseline model consisted of the following variables: age, hypertension, hyperlipidemia, stroke, coronary heart disease, cancer, obesity, antidiabetic drugs, diastolic blood pressure, HbA1c, TC, C-reactive protein, albumin, uric acid, and estimated glomerular filtration rate.
Abbreviations: ROC, receiver operating characteristic; TyG, triglyceride-glucose index; TC, total cholesterol; HbA1c, hemoglobin A1c.

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index was significantly associated with all-cause mortality and demonstrated consistent independent predictive value in multivariate Cox regression models. Additionally, subgroup analyses revealed that the relationship between the TyG index and all-cause mortality varied among different subgroups, such as age, gender, and comorbidities. Further, the study employed RCS analysis to verify the potential nonlinear association between the TyG index and all-cause mortality. To further evaluate its predictive performance, we performed ROC curve analysis and found that the TyG index outperformed traditional indicators such as age, HbA1c, and total cholesterol. When added to a baseline prediction model containing conventional risk factors, the TyG index significantly improved the model's discriminatory ability, as reflected by an increase in the AUC from 0.809 to 0.878. These findings further strengthen the potential of the TyG index as a predictive tool for all-cause mortality risk in patients with diabetes and CKD, suggesting that personalized risk assessment and management strategies may be needed in clinical practice for patient groups with different characteristics. Notably, the TyG index tertile cut-off values in our study were relatively higher than those reported in studies involving other populations or disease groups. This difference is likely attributable to the specific characteristics of our study population, which included hospitalized patients with both diabetes and CKD—a group that tends to exhibit more severe metabolic derangements such as hyperglycemia, elevated triglyceride levels, and heightened IR. These factors contribute to a generally higher baseline TyG index, thereby shifting the tertile thresholds upward. Recognizing these population-specific characteristics is important for accurate interpretation and comparison of TyG-related findings across different clinical contexts.

The results showed that the all-cause mortality rate was significantly higher in the high TyG group compared to the low TyG group. This finding aligns with existing literature that indicates a positive association between the TyG index and the risk of cardiovascular events and all-cause mortality. For example, Shen et al evaluated the effectiveness of the TyG index in predicting all-cause mortality risk in diabetic patients over 80 years old with acute coronary syndrome, and they found a significant positive correlation between the TyG index and all-cause mortality.[23] The study results support using the TyG index as an important tool for assessing mortality risk in this patient population. Another study explored the relationship between the TyG index and prognosis under different renal function states, finding that all-cause mortality was significantly reduced in the high TyG index group with impaired renal function.[24] Additionally, there was a significant interaction between the TyG index and renal function status. After adjusting for all covariates, the group with a low TyG index combined with low renal function had a higher risk of mortality. Besides, a large prospective cohort study explored the role of the non-insulin-dependent IR index and metabolic syndrome in predicting all-cause mortality and renal outcomes in Asian patients with CKD stages 1–4.[25] The results showed that metabolic syndrome and high TyG index were significantly associated with adverse renal outcomes, while the obesity paradox affected the predictive power of these indicators. Furthermore, multiple studies have shown that surrogate markers of IR are not only closely associated with CVD but are also independently related to mortality in diabetic populations.[26–29] In our study, even after adjusting for key risk factors such as age, comorbidities, blood pressure, and blood biomarkers, the high TyG index remained an independent predictor of all-cause mortality. This suggests that the TyG index may influence long-term prognosis by reflecting the degree of IR in patients.

The association between the TyG index and all-cause mortality can be mediated through multiple mechanisms. First, high levels of IR are associated with enhanced oxidative stress in the body, which can lead to cell damage and increased inflammatory responses, thereby increasing the risk of mortality.[30] Second, patients with a high TyG index often present with metabolic syndrome, including hypertension, hyperglycemia, abdominal obesity, and dyslipidemia, which collectively increase the risk of CVD and mortality.[31] Third, IR is closely related to diabetic microvascular complications such as retinopathy, nephropathy, and neuropathy, which further increase the overall mortality rate in patients.[32–34] Fourth, emerging evidence suggests that the TyG index may particularly reflect a subtype of IR associated with non-alcoholic fatty liver disease (NAFLD).[11] NAFLD is not only a result of IR but also an important contributor to systemic IR and cardiometabolic diseases. In patients with NAFLD, dysregulated hepatokines—liver-derived signaling proteins such as fetuin-A—play a key role in metabolic disturbances by mediating organ crosstalk and promoting inflammation and lipid accumulation.[11] The liver's overproduction of glucose and triglycerides in the context of hepatic steatosis may explain why an elevated TyG index strongly correlates with increased mortality.[11] This hepatokine-mediated pathway might represent a specific mechanism by which liver-driven metabolic stress contributes to worse outcomes in patients with

diabetes and CKD. These mechanisms together support the TyG index as not merely a surrogate marker of IR, but also a proxy for complex metabolic dysregulation that underlies increased all-cause mortality.

Given the significant association between the TyG index and all-cause mortality, it has the potential to serve as an independent risk assessment tool in clinical practice. Due to its simplicity and non-invasive nature, the TyG index can be used as a routine monitoring indicator for patients with diabetes and CKD. In our subgroup analysis, we found that the association between the TyG index and all-cause mortality was more pronounced in individuals without hyperlipidemia, whereas this association was attenuated in those with hyperlipidemia. This suggests that lipid-lowering interventions may influence the prognostic value of the TyG index in certain populations. Furthermore, ROC curve modeling confirmed that TyG index could be incorporated into clinical prediction models to improve prognostic accuracy. Recent studies also emphasize the importance of identifying metabolic risk clusters to better stratify cardiometabolic risk and tailor treatment approaches. For example, Stefan and Schulze highlighted that subphenotyping based on metabolic profiles—including indices like the TyG index—may help refine risk prediction in individuals with diabetes, especially when traditional models lack sufficient discrimination in specific subgroups.[35] The integration of such indices into precision risk models could improve prediction, prevention, and communication of cardiometabolic risk in clinical settings. However, there are challenges to its widespread clinical application. First, while this study shows an association between the TyG index and all-cause mortality, further research is needed to integrate this indicator into existing risk assessment models to optimize treatment strategies for patients with diabetes and CKD. Second, more research is needed to clarify the applicability and interpretability of the TyG index across different races, ages, and genders.

Additionally, the limitations of this study include the following points: (1) Retrospective design: This study employed a retrospective design, which may be subject to selection bias and information bias, potentially affecting the generalizability and accuracy of the results. (2) Single-center and limited sample size: The study was conducted at a single center with a relatively small sample size, which might limit the statistical power of the analysis and the external validity of the findings. This limitation is particularly relevant in subgroup analyses, where some subgroups had relatively few participants, potentially affecting the robustness of stratified results. Future studies should incorporate data from larger, multicenter cohorts or public databases such as the National Health and Nutrition Examination Survey (NHANES) or the UK Biobank to further validate the results across broader populations. (3) Lack of data on other potential confounding factors: Factors such as lifestyle (eg, diet, exercise habits), genetic factors, and detailed medication use could influence the relationship between the TyG index and all-cause mortality. (4) Incomplete information on antidiabetic, lipid-lowering and CKD-specific medications: Although the use of antidiabetic drugs was included as a variable in the multivariate analysis, due to the retrospective nature of the study, detailed information regarding specific drug classes (eg, glucagon-like peptide-1 receptor agonists, sodium-glucose cotransporter 2 inhibitors), dosage, and duration was unavailable, which limits our ability to assess their potential confounding or modifying effects on the association between the TyG index and mortality. Furthermore, we found no statistically significant association between lipid-lowering drug use and all-cause mortality. Additionally, due to incomplete documentation in electronic medical records and the fact that many patients were treated in multiple institutions, information on CKD-specific therapies was not systematically collected and therefore not included in the analysis. (5) Focus on all-cause mortality: This study focused solely on all-cause mortality, without considering other important endpoints such as cardiovascular events and cancer. Future research should explore the relationship between the TyG index and multiple endpoint events. To further validate the clinical application value of the TyG index, future research should consider the following directions: (1) Large-scale prospective studies: Conduct larger prospective cohort studies to validate the relationship between the TyG index and all-cause mortality as well as other important clinical endpoints. (2) Mechanism studies: Delve into the specific links between the TyG index and mechanisms such as IR, inflammatory responses, oxidative stress, and metabolic syndrome to uncover its potential role in patients with diabetes and CKD. (3) Multicenter studies: Conduct multicenter studies to evaluate the applicability of the TyG index across different races, ages, and genders, ensuring its broad applicability and reliability in diverse populations. (4) Integration into risk assessment models: Incorporate the TyG index into existing risk assessment models to evaluate its clinical application effect and optimize the management and treatment strategies for patients with diabetes and CKD.

Conclusions

Overall, this study highlights the importance of the TyG index as a predictor of all-cause mortality in patients with diabetes and CKD, providing new perspectives for future risk management and patient interventions. Our findings demonstrated that a higher TyG index was independently and significantly associated with increased all-cause mortality, especially in subgroups such as obese individuals, suggesting its potential as a valuable clinical marker for risk stratification. With further research and clinical trials, we hope to better utilize the TyG index to optimize prognosis evaluation and treatment decision-making for chronic disease patients, ultimately improving their quality of life and survival rates.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Human Ethics and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Hubei NO.3 People's Hospital of Jianghan University. Written informed consent was obtained from all participants prior to their inclusion in the study.

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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