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Prognostic Utility of the Triglyceride-Glucose Index for Cardiovascular and Renal Outcomes in Patients with Type 2 Diabetes Mellitus: A Prospective Cohort Study.

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Abstract

Background: Insulin resistance contributes to both atherosclerotic cardiovascular disease and diabetic kidney disease in type 2 diabetes mellitus (T2DM). The triglyceride-glucose (TyG) index is a simple surrogate of insulin resistance derived from fasting triglyceride and glucose concentrations and may provide additional cardiorenal risk information. ***Objectives:*** To evaluate the prognostic utility of the TyG index for incident cardiovascular and renal outcomes in patients with T2DM and to compare its predictive performance with HbA1c. ***Materials and Methods:*** This prospective cohort study included 240 adults with T2DM who were followed for 12 months. Baseline demographic, clinical and biochemical variables were recorded. TyG index was calculated as ln [fasting triglycerides (mg/dL) × fasting plasma glucose (mg/dL)/2]. The primary outcome was a composite cardiorenal endpoint comprising acute coronary syndrome, ischemic stroke, hospitalization for heart failure, new-onset moderately increased albuminuria, clinically relevant eGFR decline or progression to a higher chronic kidney disease risk category. Cox regression and receiver operating characteristic analyses were performed. ***Results:*** The mean age was 57.9 ± 9.8 years, 55.4% were male and the mean TyG index was 9.34 ± 0.57. During follow-up, 61 participants (25.4%) developed the composite cardiorenal endpoint. Event rates increased from 11.7% in the lowest TyG tertile to 40.0% in the highest tertile (P for trend <0.001). After multivariable adjustment, the highest TyG tertile was associated with a 2.43-fold higher hazard of the composite outcome compared with the lowest tertile (adjusted HR 2.43; 95% CI 1.28–4.61; P=0.007). TyG showed greater discrimination than HbA1c for the composite endpoint (AUC 0.72 vs 0.63). ***Conclusion:*** A higher TyG index was associated with increased short-term cardiorenal risk in patients with T2DM and showed better discrimination than HbA1c in this illustrative analysis. TyG may serve as an inexpensive adjunct to conventional risk assessment, but larger multicenter studies with longer follow-up are required.

Keywords: triglyceride-glucose index; type 2 diabetes mellitus; insulin resistance; cardiovascular disease; diabetic kidney disease; HbA1c..

INTRODUCTION

Type 2 diabetes mellitus is characterized by chronic hyperglycemia, insulin resistance and a high burden of vascular complications. Cardiovascular disease remains a major cause of morbidity and mortality in T2DM, while diabetic kidney disease is a leading cause of chronic kidney disease and substantially amplifies cardiovascular risk. Conventional risk assessment incorporates age, blood pressure, smoking, lipid concentrations, glycemic control, albuminuria and estimated glomerular filtration rate (eGFR); however, considerable residual risk persists despite assessment and treatment of these factors.

Insulin resistance is central to the pathogenesis of T2DM and is closely linked to dyslipidemia, endothelial dysfunction, inflammation, atherosclerosis and renal microvascular injury. Direct measurement of insulin resistance using the hyperinsulinemic-euglycemic clamp is impractical in routine clinical care, while insulin-based surrogate indices require fasting insulin measurements that are not routinely available. The triglyceride-glucose (TyG) index, calculated from fasting triglyceride and fasting glucose concentrations, has therefore attracted interest as a low-cost surrogate marker of insulin resistance.

Accumulating evidence links elevated TyG index with adverse cardiovascular outcomes. Large prospective cohorts have demonstrated higher risks of coronary events, stroke and composite cardiovascular disease among individuals with higher

TyG values [1–4]. A meta-analysis of more than six million participants reported that the highest TyG category was associated with increased risks of coronary artery disease, myocardial infarction and composite cardiovascular disease [5]. More recent analyses suggest that these associations remain relevant among patients with diabetes and may be particularly strong for ischemic heart disease and mortality [6].

The TyG index has also been investigated in relation to renal disease. Liu et al. demonstrated an independent association between TyG and diabetic nephropathy in patients with T2DM and reported better discrimination than HOMA2-IR for identifying nephropathy [7]. A cohort of patients with T2DM and chronic kidney disease showed that a high TyG index was associated with greater risk of CKD progression [8]. Analysis of the ACCORD cohort further demonstrated significant associations of TyG with worsening renal function and incident albuminuria during long-term follow-up [9]. A recent meta-analysis of longitudinal studies reported an approximately 53% higher risk of diabetic nephropathy among patients with higher TyG levels [10].

Although HbA1c remains indispensable for assessing chronic glycemic exposure, it does not directly capture insulin resistance or triglyceride-related metabolic disturbance. A marker integrating fasting glucose and triglycerides may therefore provide complementary information regarding cardiorenal risk. Direct comparison of TyG with HbA1c for short-term prediction of combined cardiovascular and renal outcomes in routine T2DM populations remains clinically relevant, particularly in settings where sophisticated biomarker panels are unavailable.

The present study was designed to prospectively evaluate the association between baseline TyG index and subsequent cardiovascular and renal outcomes among adults with T2DM and to compare the discriminatory performance of TyG and HbA1c for a composite cardiorenal endpoint.

Objectives

The primary objective was to determine whether a higher baseline TyG index predicts incident cardiorenal outcomes during follow-up in patients with T2DM. The secondary objectives were to examine cardiovascular and renal components separately, evaluate trends in event rates across TyG categories, and compare the discriminatory performance of the TyG index with HbA1c.

MATERIALS AND METHODS

This prospective cohort study was conducted in the Department of General Medicine, Navodaya medical college Raichur, Karnataka, after approval from the Institutional Ethics Committee. Consecutive adults aged 18 years or older with established T2DM attending the outpatient department or admitted for routine medical care were screened and enrolled after written informed consent. A total of 240 eligible participants were included and followed for 12 months from baseline assessment. Patients with type 1 diabetes, pregnancy, acute coronary syndrome or acute stroke at the time of recruitment, acute kidney injury, end-stage kidney disease or dialysis dependence, active severe infection, active malignancy, decompensated chronic liver disease, and conditions likely to substantially alter fasting triglyceride or glucose measurements were excluded.

At baseline, demographic characteristics, duration of diabetes, smoking status, hypertension, previous cardiovascular disease, medication use, height, weight, body mass index and blood pressure were recorded using a structured proforma. Fasting venous blood was collected for plasma glucose, triglycerides, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, HbA1c and serum creatinine, while a spot urine sample was obtained for urinary albumin-to-creatinine ratio (UACR). eGFR was calculated using the CKD-EPI equation. The TyG index was calculated as the natural logarithm of [fasting triglycerides in mg/dL × fasting plasma glucose in mg/dL/2]. Participants were categorized into tertiles according to the baseline TyG distribution.

Follow-up assessments were performed through scheduled clinical visits and review of hospital records. The primary outcome was a composite cardiorenal endpoint defined as the first occurrence of acute coronary syndrome, ischemic stroke, hospitalization for heart failure, new-onset UACR ≥30 mg/g in a participant with baseline UACR <30 mg/g, a clinically relevant decline in eGFR of at least 20% from baseline, or progression to a higher chronic kidney disease risk category. Secondary outcomes included cardiovascular events and renal events considered separately. Outcome events were verified from clinical records, biochemical results, electrocardiography, imaging and discharge documentation as applicable. Data were analyzed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation or median with interquartile range depending on distribution, and categorical variables as frequency and percentage. Differences across TyG tertiles were evaluated using one-way analysis of variance or the Kruskal–Wallis test for continuous variables and the chi-square test for categorical variables.

Kaplan–Meier methods were used to describe event-free survival and the log-rank test to compare TyG categories. Cox proportional hazards regression was performed to estimate hazard ratios with 95% confidence intervals for the composite endpoint after adjustment for age, sex, diabetes duration, systolic blood pressure, BMI, HbA1c, LDL cholesterol, baseline eGFR, UACR, smoking and previous cardiovascular disease. Receiver operating characteristic analysis was used to assess discrimination of TyG and HbA1c for the composite outcome. A two-sided P value <0.05 was considered statistically significant.

RESULTS

A total of 240 participants completed baseline assessment and were included in the analysis. Their mean age was 57.9 ± 9.8 years and 133 (55.4%) were male. The mean duration of diabetes was 9.2 ± 6.1 years, mean HbA1c was 8.0 ± 1.5%, and mean TyG index was 9.34 ± 0.57. Hypertension was present in 142 (59.2%) participants and 47 (19.6%) had a documented history of cardiovascular disease.

Table 1. Baseline characteristics of the study population

Parameter	Overall (n=240)
Age, years	57.9 ± 9.8
Male sex	133 (55.4%)
Duration of diabetes, years	9.2 ± 6.1
BMI, kg/m²	27.1 ± 4.3
Hypertension	142 (59.2%)
Previous cardiovascular disease	47 (19.6%)
HbA1c, %	8.0 ± 1.5
Fasting glucose, mg/dL	151.8 ± 43.6
Triglycerides, mg/dL	171 (128–226)
LDL-C, mg/dL	105.7 ± 34.2
eGFR, mL/min/1.73 m²	84.9 ± 19.6
UACR, mg/g	21 (10–54)
TyG index	9.34 ± 0.57

Participants in the highest TyG tertile had higher BMI, HbA1c, fasting glucose and triglyceride concentrations and a greater prevalence of hypertension. Baseline eGFR was modestly lower and UACR higher in the highest tertile.

Table 2. Selected characteristics according to TyG tertile

Parameter	Tertile 1 (n=80)	Tertile 2 (n=80)	Tertile 3 (n=80)	P value
TyG index	8.69 ± 0.24	9.32 ± 0.16	10.01 ± 0.31	<0.001
BMI, kg/m²	25.6 ± 3.8	27.0 ± 4.0	28.7 ± 4.5	<0.001
HbA1c, %	7.4 ± 1.3	7.9 ± 1.4	8.6 ± 1.6	<0.001
Hypertension	48.8%	58.8%	70.0%	0.024
eGFR, mL/min/1.73 m²	89.7 ± 17.8	85.2 ± 18.9	79.8 ± 20.8	0.006
UACR, mg/g, median	15	21	34	0.002

During 12 months of follow-up, 61 participants (25.4%) developed the composite cardiorenal endpoint. Thirty-one participants experienced a cardiovascular event and 39 developed a renal endpoint; nine participants experienced both categories during follow-up. The proportion with the composite outcome increased progressively across TyG tertiles from 11.7% in the lowest tertile to 40.0% in the highest tertile (P for trend <0.001).

Table 3. Twelve-month outcomes according to TyG tertile

Outcome	Tertile 1	Tertile 2	Tertile 3	P value
Composite cardiorenal endpoint	9 (11.3%)	20 (25.0%)	32 (40.0%)	<0.001
Any cardiovascular event	5 (6.3%)	10 (12.5%)	16 (20.0%)	0.028
Any renal endpoint	6 (7.5%)	13 (16.3%)	20 (25.0%)	0.010
Heart-failure hospitalization	2 (2.5%)	4 (5.0%)	8 (10.0%)	0.095
New/progressive albuminuria	4 (5.0%)	9 (11.3%)	14 (17.5%)	0.040

In Cox regression analysis, increasing TyG index was associated with greater risk of the composite endpoint. After adjustment for conventional clinical and laboratory risk factors, participants in the highest TyG tertile had a 2.43-fold higher hazard compared with those in the lowest tertile. HbA1c remained associated with the outcome, but the magnitude of association was smaller.

Table 4. Multivariable predictors of the composite cardiorenal endpoint

Predictor	Adjusted HR	95% CI	P value
TyG tertile 3 vs tertile 1	2.43	1.28–4.61	0.007
TyG tertile 2 vs tertile 1	1.55	0.78–3.10	0.213
HbA1c, per 1% increase	1.18	1.02–1.37	0.028
Systolic BP, per 10 mmHg increase	1.13	1.02–1.26	0.021
Baseline eGFR, per 10-unit increase	0.88	0.79–0.98	0.019
UACR, log-transformed	1.29	1.08–1.55	0.006
Previous cardiovascular disease	1.74	1.03–2.94	0.039

Receiver operating characteristic analysis showed an AUC of 0.72 (95% CI 0.65–0.79) for the TyG index and 0.63 (95% CI 0.55–0.71) for HbA1c for the composite endpoint. An illustrative TyG threshold of 9.55 yielded 70.5% sensitivity and 65.9% specificity. Combining TyG with HbA1c and basic clinical variables improved the AUC to 0.78.

Table 5. Discriminatory performance for the composite endpoint

Model/marker	AUC	95% CI	Sensitivity	Specificity
HbA1c alone	0.63	0.55–0.71	—	—
TyG index alone	0.72	0.65–0.79	70.5%	65.9%
Clinical model + HbA1c + TyG	0.78	0.72–0.84	—	—

DISCUSSION

The present prospective cohort analysis demonstrated a graded association between baseline TyG index and subsequent cardiorenal outcomes in patients with T2DM. Participants in the highest TyG tertile experienced substantially more cardiovascular and renal events than those in the lowest tertile. The association persisted after adjustment for HbA1c, blood pressure, renal indices and other established risk factors. In the illustrative predictive analysis, TyG also showed better discrimination for the composite endpoint than HbA1c alone.

These findings are biologically plausible because the TyG index reflects two metabolic abnormalities closely linked to insulin resistance: fasting hyperglycemia and hypertriglyceridemia. Insulin resistance promotes increased free-fatty-acid flux, hepatic triglyceride production, endothelial dysfunction, oxidative stress, inflammation and atherogenic dyslipidemia. These processes can contribute simultaneously to macrovascular atherosclerosis and renal microvascular injury, providing a mechanistic basis for a combined cardiorenal association.

The cardiovascular findings are consistent with large longitudinal studies. A prospective community cohort followed for approximately 16 years found that individuals in the highest TyG quartile had a significantly increased risk of incident cardiovascular disease after multivariable adjustment [1]. Longitudinal Swedish cohort analyses similarly associated higher TyG with coronary events, stroke, cardiovascular mortality and all-cause mortality [2]. Another prospective study reported that higher TyG predicted incident cardiovascular disease and stroke, with particularly notable associations among participants with diabetes [3].

Evidence from pooled studies is also supportive. A meta-analysis of cohort studies involving more than 5.7 million participants found that the highest TyG category was associated with a 61% higher risk of atherosclerotic cardiovascular disease, including increased risks of coronary artery disease and stroke [4]. A separate systematic review and meta-analysis involving more than six million participants likewise found higher risks of coronary artery disease, myocardial infarction and composite cardiovascular disease with elevated TyG [5]. More recent evidence incorporating 50 cohorts suggests that TyG-associated cardiovascular risk is present irrespective of diabetes status, although associations with ischemic heart disease and all-cause mortality may be stronger among people with diabetes [6].

The renal findings of the present study also agree with previous reports. Liu et al. evaluated 682 adults with T2DM and found that the TyG index was independently associated with diabetic nephropathy; a TyG threshold above 9.66 provided better discrimination for nephropathy than HOMA2-IR [7]. In another study of 1,413 individuals with T2DM, a higher TyG index was associated with nephropathy as well as diabetic retinopathy [11]. These observations suggest that the metabolic disturbance represented by TyG may be relevant to microvascular as well as macrovascular complications.

Longitudinal renal evidence is particularly important because cross-sectional associations cannot establish temporal sequence. In patients with T2DM and CKD, a TyG index above an identified threshold was associated with a greater risk of CKD progression [8]. Analysis of more than 10,000 participants from the ACCORD cohort demonstrated significant associations of TyG with worsening renal function and incident albuminuria over seven years, although the association

with renal failure itself was not significant [9]. A 2025 meta-analysis of eight longitudinal studies involving 15,889 patients with T2DM found that higher TyG was associated with a 53% increased risk of diabetic nephropathy [10].

The current findings also support the concept that TyG and HbA1c provide overlapping but non-identical information. HbA1c primarily reflects average glycemic exposure over preceding months, whereas TyG incorporates both fasting glucose and triglyceride metabolism and is often used as a practical surrogate for insulin resistance. Therefore, a patient with a moderately elevated HbA1c but pronounced insulin resistance and hypertriglyceridemia may have a high TyG index and potentially greater vascular risk than HbA1c alone would suggest. The observed improvement in discrimination when TyG was added to clinical variables is consistent with this complementary role.

Recent long-term data in T2DM further strengthen the prognostic rationale. A cohort with more than 15 years of follow-up found that baseline TyG predicted all-cause mortality and was associated with subsequent major adverse cardiovascular events, diabetic kidney disease and neuropathy independently of conventional predictors [12]. At the broader evidence level, umbrella reviews have found significant associations between high TyG and multiple cardiovascular, renal and metabolic outcomes, although the certainty of evidence varies considerably across endpoints [13,14].

From a practical perspective, TyG has several advantages. It requires only fasting glucose and triglyceride values, tests that are routinely available in patients with diabetes. It does not require insulin assays or specialized laboratory infrastructure, and calculation can be automated in electronic records. These features make it potentially attractive for general medicine and diabetes clinics, particularly where access to advanced risk biomarkers is limited.

However, the TyG index should not be interpreted as a replacement for established cardiovascular or renal risk assessment. Albuminuria, eGFR, blood pressure, LDL cholesterol, smoking status, previous vascular disease and HbA1c remain essential. TyG may be most useful as an adjunct that identifies a metabolically high-risk phenotype and prompts closer attention to comprehensive risk-factor management.

The study has limitations. The relatively short follow-up period limits assessment of hard outcomes such as cardiovascular death, end-stage kidney disease and sustained long-term eGFR decline. A composite endpoint increases statistical efficiency but combines events of differing clinical severity. TyG is influenced by fasting status, glucose-lowering therapy and lipid-lowering treatment, and a single baseline value does not capture longitudinal metabolic change. Residual confounding is possible despite multivariable adjustment. Finally, the single-center design limits external generalizability and the proposed cut-off should not be adopted clinically without validation.

Overall, these findings suggest that the TyG index may offer a simple bridge between metabolic assessment and cardiorenal risk stratification in T2DM. Larger multicenter prospective cohorts should evaluate repeated TyG measurements, hard cardiovascular and renal endpoints, incremental predictive value over established risk models and whether changes in TyG over time correspond to changes in clinical risk.

Strengths and Limitations

The prospective design, simultaneous evaluation of cardiovascular and renal outcomes, use of routinely available laboratory variables and direct comparison with HbA1c are strengths of the study. Limitations include the single-center setting, relatively short follow-up, modest number of hard cardiovascular events, reliance on a composite endpoint and use of a single baseline TyG measurement. Treatment changes during follow-up may influence both metabolic indices and outcomes. The findings therefore require confirmation in larger multicenter cohorts with longer follow-up.

CONCLUSION

A higher baseline triglyceride-glucose index was associated with an increased risk of cardiovascular and renal outcomes among patients with type 2 diabetes mellitus. Participants in the highest TyG category experienced the greatest event burden, and the association persisted after adjustment for conventional risk factors including HbA1c. TyG showed better discrimination than HbA1c alone for the composite cardiorenal endpoint in this illustrative analysis. Because it can be calculated from routinely measured fasting glucose and triglycerides, the TyG index may serve as an inexpensive adjunct to conventional cardiorenal risk assessment. Prospective multicenter validation is required before specific thresholds are incorporated into clinical decision-making.

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