

# Evaluation of the Relationship Between Five Different Insulin Resistance Indices and Glycemic Control in Patients with Prediabetes and Type 2 Diabetes

Sinem Aydın, Levent Deniz, Özlem Demirelce

University of Health Sciences Türkiye, İstanbul Training and Research Hospital, Clinic of Medical Biochemistry, İstanbul, Türkiye

## ABSTRACT

**Introduction:** This study was designed for comparing the performance of insulin resistance (IR) indices in individuals with prediabetes and type 2 diabetes mellitus (T2DM).

**Methods:** Participants were classified into four categories according to HbA1c using the American Diabetes Association criteria: control group (<5.7%) (n=192), prediabetes (5.7%-6.4%) (n=147), regulated T2DM (6.5%-7.0%) (n=28), and non-regulated T2DM (>7.0%) (n=61). Patient records and laboratory information system data were reviewed to determine serum glucose, triglyceride, high-density lipoprotein cholesterol (HDL-C), insulin, and to determine homeostatic model assessment of IR (HOMA-IR), insulin sensitivity index (ISI/McAuley index), quantitative insulin sensitivity check index (QUICKI), triglyceride to HDL-C ratio (TG/HDL-C), and triglyceride-glucose (TyG) index.

**Results:** The non-regulated T2DM group had higher HOMA-IR and TyG levels and lower QUICKI values than the prediabetic and regulated T2DM groups. TyG and HOMA-IR indices have a positive correlation with HbA1c ( $r=0.547$  and  $r=0.456$ , respectively). According to the receiver operating characteristic analysis, TyG had the highest area under the curve (AUC) of 0.749 (0.705-0.789) to identify patients with HbA1c  $\geq 5.70\%$ , and the Turkish population-specific cut-off value was set at 8.55. Findings from the binary logistic regression highlighted that TyG, HOMA-IR, TG/HDL-C, QUICKI, and ISI indices were associated with patients with HbA1c  $\geq 5.70\%$ , independent of age and sex.

**Conclusion:** Among the evaluated IR indices, the TyG index demonstrated the highest correlation coefficient with HbA1c. In addition, it yielded the largest AUC, indicating superior diagnostic performance compared to the other indices. These findings suggest that the TyG index may serve as a useful marker of IR in individuals with prediabetes and T2DM.

**Keywords:** HbA1c, type 2 diabetes mellitus, TyG index, QUICKI, HOMA-IR

## Introduction

A rising health concern, type 2 diabetes mellitus (T2DM) increases the risk of macrovascular and microvascular complications due to hyperglycemia and insulin resistance (IR) (1). The prognosis of patients with T2DM is largely determined by the level of disease control; chronic hyperglycemia is associated with a higher risk of microvascular complications, as evidenced by studies (2). Therefore, achieving effective glycemic control and improving insulin sensitivity are crucial for minimizing the likelihood of T2DM-associated complications. Recognizing the individuals who are at an elevated risk of DM and determining the course of the disease are key strategies for preventing and managing diabetes.

Over the last few decades, many different methods have been used to measure IR and determine glycemic control. The hyperinsulinemic-

euglycemic clamp is commonly used as the gold standard method for assessing IR, although it is complicated and requires specialized expertise (3). The most commonly used method of measurement is the homeostatic model assessment of IR (HOMA-IR), which is an easier, although less accurate, method (4). It requires fasting insulin levels, which is relatively expensive and not available in many laboratories. Therefore, an easy-to-use, reliable, and affordable index for evaluating glycemic control and IR is crucial. Recently, several novel and readily accessible tools have been developed to predict IR.

This study aimed to evaluate and compare the performance of IR indices, including HOMA-IR, triglyceride to high-density lipoprotein cholesterol ratio (TG/HDL-C), triglyceride-glucose (TyG) index, insulin sensitivity index (ISI/McAuley index), and quantitative insulin



**Address for Correspondence:** Sinem Aydın MD, University of Health Sciences Türkiye, İstanbul Training and Research Hospital, Clinic of Medical Biochemistry, İstanbul, Türkiye  
E-mail: sinem00aydin@gmail.com ORCID ID: orcid.org/0009-0007-2945-4945

**Cite this article as:** Aydın S, Deniz L, Demirelce Ö. Evaluation of the relationship between five different insulin resistance indices and glycemic control in patients with prediabetes and type 2 diabetes. İstanbul Med J. 2025; 26(4): 300-6

**Received:** 16.04.2025

**Accepted:** 01.10.2025

**Publication Date:** 12.11.2025



©Copyright 2025 by the University of Health Sciences Türkiye, İstanbul Training and Research Hospital/İstanbul Medical Journal published by Galenos Publishing House.  
Licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 (CC BY-NC-ND) International License

sensitivity check index (QUICKI), in predicting patients diagnosed with prediabetes and T2DM.

## Methods

Ethics approval for this study was approved by the University of Health Sciences Türkiye, İstanbul Training and Research Hospital, Clinical Research Ethics Committee (approval number: 16, date: 25.01.2025). All stages of this study were designed in accordance with the rules of the Declaration of Helsinki. Medical records of 428 patients who attended the Family Medicine outpatient clinic at University of Health Sciences Türkiye, İstanbul Training and Research Hospital between January and December 2018 were retrospectively reviewed. We included participants aged 18-65 years who were tested for HbA1c, fasting glucose, fasting insulin, fasting TG, and HDL-C levels by reviewing their patient folders and laboratory information system records. Patients with type 1 diabetes mellitus, those who are pregnant, have cardiovascular diseases, malignancy, hematological disorders, liver or kidney diseases, or autoimmune disorders were excluded from this study.

We categorized patients with HbA1c concentrations higher than 5.7% into three groups: prediabetic (5.7%-6.4%) (n=147), regulated T2DM (6.5%-7.0%) (n=28), and non-regulated T2DM (>7.0%) (n=61), using criteria set by the American Diabetes Association (5,6). Patients with HbA1c levels below 5.7% were taken as the control group (n=192).

## Laboratory Parameters

All measurements were performed using venous blood samples after an overnight fast of at least 8 hours. Fasting glucose, total cholesterol (TC), HDL-C, and TG levels were analyzed using the analytical chemistry system AU5800 (Beckman Coulter Inc., Brea, California, US). Insulin levels were quantified via the DxI800 (Beckman Coulter Inc., Brea, California, US). Measurement of HbA1c was performed with the ADAMS A1c HA8180V (Arkray, Kyoto, Japan). HOMA-IR values were derived by the following formula: fasting insulin (mIU/L)  $\times$  fasting glucose (mg/dL) / 405 (7). TyG index calculated as  $\ln$  [fasting Triglyceride (mg/dL)  $\times$  fasting glucose (mg/dL)/2] (8). Triglyceride/HDL-C was calculated as TG (mg/dL)/HDL-C (mg/dL). QUICKI figured out as  $1/[\log(\text{fasting insulin, mIU/L}) + \log(\text{fasting glucose, mg/dL})]$  (9). ISI (McAuley Index) calculated as  $e(2.63 - 0.28 \times \ln FI - 0.31 \times \ln TG)$  (TG refers to triglyceride levels in mmol/L and FI refers to fasting insulin levels in mIU/L) (10).

## Statistical Analysis

The Shapiro-Wilk test was conducted to evaluate the distribution of the data. Continuous data are presented as mean  $\pm$  standard deviation or median (25<sup>th</sup> and 75<sup>th</sup> percentiles), and discrete data as numbers (percentages). Discrete data were analyzed using the Pearson chi-square test. Comparative studies among the groups were conducted by employing one-way ANOVA and the Kruskal-Wallis analysis according to the distribution characteristics of the data. Bonferroni-adjusted p-values were used to control for type 1 errors in multiple pairwise comparisons (n=6), with the threshold for statistical significance set at p<0.008. The association between each index and both HbA1c and HOMA-IR was evaluated using Spearman correlation analysis. To assess the discriminative power of the indices in identifying individuals with

elevated HbA1c levels ( $\geq 5.70\%$ ), receiver operating characteristic (ROC) analysis was applied. Binary logistic regression was conducted, both univariate, and multivariate, for patients with HbA1c levels higher than 5.70%. Considering the multicollinearity among the IR indices, separate logistic regression analyses were performed for each index to assess their individual predictive relationships with the outcome variable. Statistical evaluation and graphical representation were applied using SPSS 26 (IBM C.A., US) and GraphPad Prism v. 8.3.0 (GraphPad Software, US). Although a general threshold value of p<0.05 was applied for statistical significance, a criterion of p<0.008 was employed for multiple pairwise comparisons (n=6) due to the Bonferroni correction.

## Results

Of all the groups included in the study, 165 (38.6%) were men and 263 (61.4%) were women. The mean age of the patients was  $50 \pm 11$  years. There was no difference in age between the prediabetic, regulated T2DM, and non-regulated T2DM groups. The non-regulated T2DM group had a higher proportion of males than the prediabetic and control groups. Age, glucose, insulin, TC, TG, HOMA-IR, TyG, and TG/HDL-C were higher in the prediabetic group than in the control group. QUICKI and ISI were lower in the prediabetic population than in the controls. Age, glucose, TG, TyG, HOMA-IR, and TG/HDL-C were higher in the regulated T2DM group than in the control group, whereas QUICKI and ISI indices were lower in the regulated T2DM group than in the control group. Age, glucose, insulin, TG, TyG, HOMA-IR, and TG/HDL-C levels were higher in the non-regulated T2DM group than in the controls, whereas QUICKI and ISI indices were lower in the non-regulated T2DM group than in controls. Glucose levels and TyG index were higher in the regulated T2DM group than in the prediabetic group. Glucose, TyG, HOMA-IR, and TG/HDL-C levels were higher in the non-regulated T2DM group than in the prediabetic group, whereas HDL-C, QUICKI were lower in the non-regulated T2DM group than in the prediabetic group. TyG and HOMA-IR levels were higher in the non-regulated T2DM group than in the regulated T2DM group, whereas the QUICKI was lower in the non-regulated T2DM group than in the regulated T2DM group (Table 1 and Figure 1).

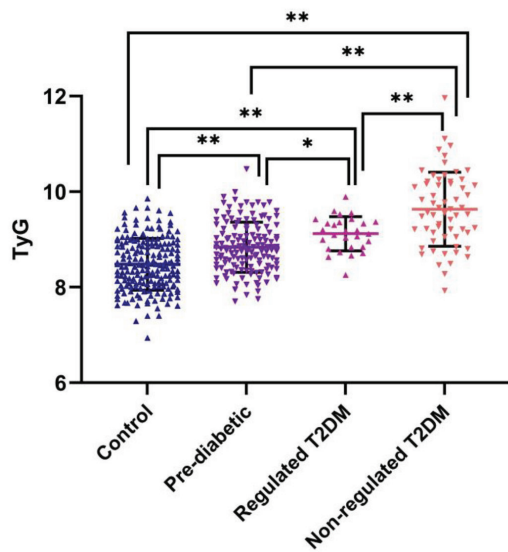
TyG level (r=0.547, p<0.001), TG/HDL-C (r=0.306, p<0.001), and HOMA-IR (r=0.456, p<0.001) have positive correlations with HbA1c level. QUICKI (r=-0.457, p<0.001) and ISI (r=-0.345, p<0.001) had a negative correlation with HbA1c levels. The correlation coefficient between TyG and HbA1c was higher than those between other indices. HOMA-IR levels were positively correlated with TyG (r=0.559, p<0.001) and TG/HDL-C ratio (r=0.485, p<0.001). Conversely, QUICKI (r=-1.000, p<0.001) and ISI (r=-0.821, p<0.001) were negatively correlated with HOMA-IR (Table 2 and Figure 2).

Among the indices assessed through ROC analysis for identifying individuals with HbA1c  $\geq 5.70\%$ , TyG had the largest area under the curve (AUC) of 0.749 [95% confidence interval (CI) =0.705-0.789]. The AUC value for HOMA-IR was 0.727 (95% CI =0.682-0.769). QUICKI had an AUC level of 0.724 (95% CI =0.679-0.766). The ISI had an AUC of 0.675 (95% CI =0.629-0.720). TG/HDL-C ratio had an AUC of 0.635 (95% CI =0.587-0.681) (Table 3 and Figure 3).

**Table 1. Comparison of demographic characteristics and laboratory findings between the groups**

| Parameter       | Control (n=192)  | Pre-diabetic (n=147)            | Regulated T2DM (n=28)                         | Non-regulated T2DM (n=61)                                         | p*     |
|-----------------|------------------|---------------------------------|-----------------------------------------------|-------------------------------------------------------------------|--------|
| Age (years)     | 46.0 (35.0-55.0) | 57.0 (50.3-62.0) a <sup>2</sup> | 55.5 (51.0-59.5) a <sup>2</sup>               | 57.0 (52.8-61.0) a <sup>2</sup>                                   | <0.001 |
| Gender n (%)    |                  |                                 |                                               |                                                                   |        |
| Female          | 120 (62.5%)      | 104 (70.7%)                     | 14 (50.0%)                                    | 25 (40.9%)                                                        | <0.001 |
| Male            | 72 (37.5%)       | 43 (29.3%)                      | 14 (50.0%)                                    | 36 (59.1%)                                                        |        |
| Glucose (mg/dL) | 89.5 (84.0-95.5) | 101 (94.3-109) a <sup>2</sup>   | 119 (108-127) a <sup>2</sup> , b <sup>1</sup> | 178 (136-227) a <sup>2</sup> , b <sup>2</sup>                     | <0.001 |
| Insulin (mU/L)  | 6.69 (4.64-10.1) | 8.61 (5.98-13.0) a <sup>2</sup> | 8.19 (5.94-11.9)                              | 10.4 (6.29-16.3) a <sup>2</sup>                                   | <0.001 |
| TC (mg/dL)      | 212 (175-240)    | 227 (193-258) a <sup>1</sup>    | 228 (186-282)                                 | 220 (187-260)                                                     | 0.012  |
| TG (mg/dL)      | 103 (72.5-155)   | 129 (95.3-191) a <sup>2</sup>   | 165 (129-194) a <sup>2</sup>                  | 157 (107-233) a <sup>2</sup>                                      | <0.001 |
| HDL-C (mg/dL)   | 49.0 (40.0-60.0) | 51.0 (43.0-58.8)                | 49.0 (40.0-57.0)                              | 45.0 (39.0-53.3) b <sup>1</sup>                                   | 0.044  |
| LDL-C (mg/dL)   | 138 (108-161)    | 145 (121-173)                   | 147 (111-185)                                 | 134 (109-159)                                                     | 0.077  |
| TyG index       | 8.48±0.54        | 8.84±0.53 a <sup>2</sup>        | 9.12±0.36 a <sup>2</sup> , b <sup>1</sup>     | 9.63±0.77 a <sup>2</sup> , b <sup>2</sup> , c <sup>2</sup>        | <0.001 |
| HOMA-IR         | 1.49 (1.01-2.38) | 2.16 (1.47-3.31) a <sup>2</sup> | 2.68 (1.80-3.46) a <sup>2</sup>               | 4.75 (3.05-7.07) a <sup>2</sup> , b <sup>2</sup> , c <sup>1</sup> | <0.001 |
| QUICKI          | 0.36 (0.34-0.38) | 0.34 (0.32-0.36) a <sup>2</sup> | 0.33 (0.32-0.35) a <sup>2</sup>               | 0.30 (0.29-0.32) a <sup>2</sup> , b <sup>2</sup> , c <sup>1</sup> | <0.001 |
| TG/HDL-C        | 2.17 (1.27-3.47) | 2.65 (1.77-4.04) a <sup>1</sup> | 3.18 (2.51-4.34) a <sup>1</sup>               | 3.58 (2.20-6.13) a <sup>2</sup> , b <sup>1</sup>                  | <0.001 |
| ISI             | 7.62 (6.28-9.33) | 6.64 (5.61-7.83) a <sup>2</sup> | 6.34 (5.67-7.11) a <sup>2</sup>               | 5.89 (4.92-7.40) a <sup>2</sup>                                   | <0.001 |

\*p<0.05, considered statistically significant. Bonferroni correction was used for pairwise comparisons of the four groups, with significance set at p<0.008. a<sup>1</sup>: p<0.008, a<sup>2</sup>: p<0.001, a: Comparison with controls, b<sup>1</sup>: p<0.008, b<sup>2</sup>: p<0.001, b: Comparison with prediabetics, c<sup>1</sup>: p<0.008, c<sup>2</sup>: p<0.001, c: Comparison with regulated type 2 DM group  
 DM: Diabetes mellitus, TyG: Triglyceride glucose, HOMA-IR: Homeostatic model assessment for insulin resistance, QUICKI: Quantitative insulin sensitivity check index, TG/HDL-C: Triglyceride-to-high-density lipoprotein cholesterol, ISI: Insulin sensitivity index, T2DM: Type 2 diabetes mellitus, LDL-C: Low-density lipoprotein cholesterol



**Figure 1.** Comparison of the TyG index among the control, prediabetic, regulated T2DM, and non-regulated T2DM groups.

\*p<0.008, \*\*p<0.001, TyG: Triglyceride glucose, T2DM: Type 2 diabetes mellitus

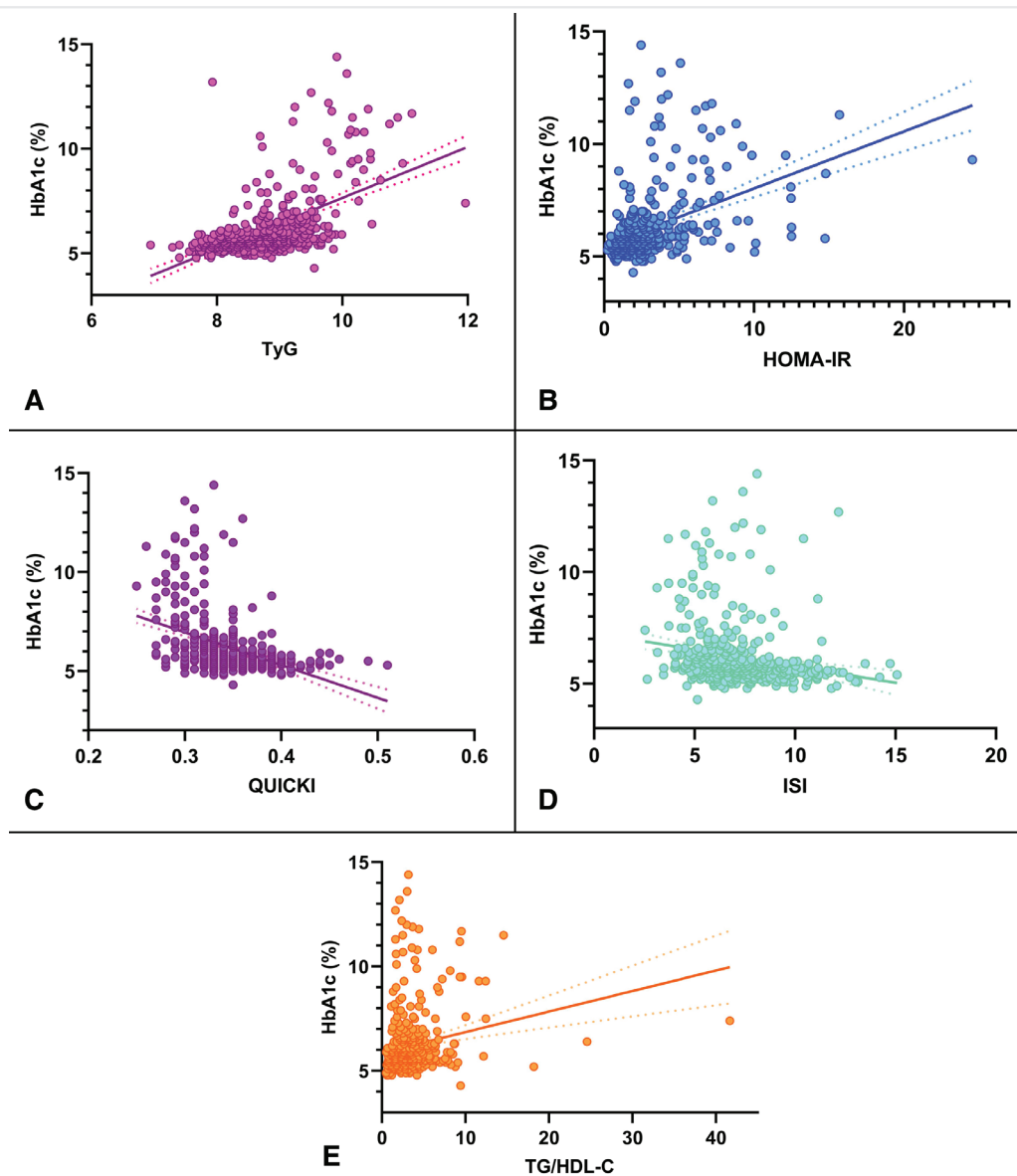
In the univariate logistic regression analysis applied to identify patients with HbA1c levels higher than 5.70%, TyG, HOMA-IR, and TG/HDL-C indices showed positive predictive values, whereas QUICKI and ISI indices demonstrated negative predictive values. Independent of age and sex, TyG, HOMA-IR, TG/HDL-C, QUICKI, and ISI indices were significantly associated with HbA1c levels higher than 5.70% (Table 4).

## Discussion

IR is an essential trigger in the development of microvascular and macrovascular complications. In addition according to the diabetes

complications and control trial study (11), glycemic control with HbA1c maintained under 7.0% significantly decreased the likelihood of microvascular and macrovascular complications. We aimed to identify the most specific, sensitive, and inexpensive biochemical predictor of IR in prediabetic and diabetic patients. Therefore, IR indices were investigated as potential indicators in patients with prediabetes and diabetes, who were divided into three categories based on HbA1c values. Ethnicity, socioeconomic characteristics, and dietary patterns of the population have been shown to cause differences in IR. Few studies have suggested cut-offs for TyG, TG/HDL-C, QUICKI, and ISI values in Turkish prediabetic and diabetic adult populations. The study by Aslan Çin et al. (12) on TyG and TG/HDL-C indices was conducted in an obese adolescent cohort, and found TG/HDL-C >2.16, TyG >8.50, and HOMA-IR >2.52. Dundar et al. (13) determined separate cut-offs for TyG in obese girls and boys. In adults, Kirtıl et al. (14) found the value for the TyG index in individuals with impaired glucose tolerance to be 4.44 using the  $[FG \text{ (mg/dL)} \times fTG \text{ (mg/dL)}] / 2$  formula. For QUICKI, Gokcel et al. (15) study on the Turkish adult hospital population also found a value of  $0.347 \pm 0.028$ . Fakı et al. (16) revealed that the TyG index is associated with diabetic nephropathy in patients with T2DM.

Although elevated TG and reduced HDL-C levels, when considered separately, are commonly detected in individuals with T2DM and IR, they are weaker risk indicators than TG/HDL-C. Performance of TG/HDL-C has been outlined as being almost the same as those for fasting insulin concentration in determining IR in overweight individuals (17). In a cohort study by Liu et al. (18), as in our study, an increased TG/HDL-C level was reported to be a significant indicator for T2DM risk, independent of gender and age. Similar to our findings, numerous earlier research have identified a positive relationship between TG/HDL-C and the occurrence of T2DM (19-21). According to Chauhan et al. (22), high TG/HDL-C levels may contribute to the early detection of



**Figure 2.** Correlations between HbA1c and (a) TyG, (b) HOMA-IR, (c) QUICKI, (d) ISI, and (e) TG/HDL-C ratio in all groups  
 TyG: Triglyceride glucose, HOMA-IR: Homeostatic model assessment for insulin resistance, QUICKI: Quantitative insulin sensitivity check index, TG/HDL-C: Triglyceride-to-high-density lipoprotein cholesterol, ISI: Insulin sensitivity index

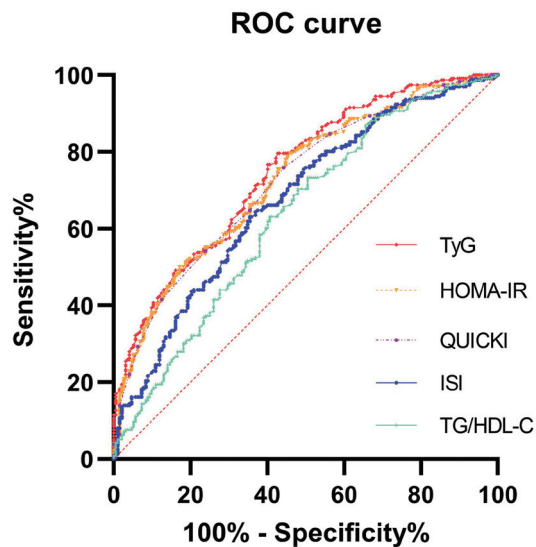
**Table 2.** Correlations between indices and HbA1c (%) and HOMA-IR in all groups

| Parameter | HbA1c (%) |        | HOMA-IR |        |
|-----------|-----------|--------|---------|--------|
|           | r         | p      | r       | p      |
| TyG index | 0.547     | <0.001 | 0.559   | <0.001 |
| HOMA-IR   | 0.456     | <0.001 | 1.000   | <0.001 |
| QUICKI    | -0.457    | <0.001 | -1.000  | <0.001 |
| ISI       | -0.345    | <0.001 | -0.821  | <0.001 |
| TG/HDL-C  | 0.306     | <0.001 | 0.485   | <0.001 |

TyG: Triglyceride glucose, HOMA-IR: Homeostatic model assessment for insulin resistance, QUICKI: Quantitative insulin sensitivity check index, TG/HDL-C: Triglyceride-to-high-density lipoprotein cholesterol, ISI: Insulin sensitivity index

atherosclerotic complications, even in prediabetes. In support of this, we found a significant difference ( $p<0.008$ ) in TG/HDL-C values between the prediabetic and control groups. Chen et al. (23) highlighted the association between higher baseline TG/HDL-C or TyG levels and an elevated risk of T2DM in prediabetic individuals. Similar to our findings, TyG showed superior predictive power for the risk of DM.

Several studies have reported that TyG is related to the risk of DM and may be a valuable biomarker (24-27). In our study, we found that among



**Figure 3.** Receiver operating curve analysis of IR indices in determining individuals with HbA1c levels  $\geq 5.7\%$   
 TyG: Triglyceride glucose, HOMA-IR: Homeostatic model assessment for insulin resistance, QUICKI: Quantitative insulin sensitivity check index, TG/HDL-C: Triglyceride-to-high-density lipoprotein cholesterol, ISI: Insulin sensitivity index, ROC: Receiver operating characteristic

the indices investigated, TyG best demonstrated the development and progression of diabetes in the Turkish adult population [AUC=0.749, (95% CI =0.705-0.789), with 79.7% sensitivity and 57.3% specificity]. When we examined the development of diabetes using the correlations of the indices with HbA1c and HOMA-IR, we found that TyG was their best indicator ( $r=0.547$ ,  $p<0.001$ ;  $r=0.559$ ,  $p<0.001$ , respectively). Navarro-González et al. (27) suggested a TyG index cutoff value of 8.8 for incident IR and T2DM. In our study, we determined the cut-off level for the TyG index to be 8.55 in the prediabetic and diabetic groups. Additionally, Lee et al. (25) identified a TyG index cut-off level of 8.86 in men and 8.52 in women for predicting T2DM in middle-aged Koreans. Our cut-off value may be slightly lower because of the inclusion of the prediabetes group in the evaluation, and ethnic differences. This value is predictive for future studies conducted in larger populations in our country.

Katz et al. (28) defined QUICKI as potentially useful in clinical research. In an investigation by Yokoyama et al. (29), QUICKI was highly correlated with Clamp-IR in T2DM patients with relatively wide fasting plasma glucose ranges. In a study conducted by Sarafidis et al. (30), QUICKI was confirmed as a valid tool for assessing T2DM patients; however, they stated that further studies should be conducted for McAuley's index. According to a study by Straczowski et al. (31), in individuals with normal glucose tolerance, fasting insulin levels in plasma may be sufficient as a crude indicator of insulin sensitivity because beta cell function is intact. However, in cases of prediabetes and diabetes, indices based on logarithmically transformed data, such as QUICKI and plasma glucose levels, are recommended. In our study, we found an important difference between the prediabetic, diabetic, and control groups for both tests (Table 1), and significant negative correlations between QUICKI-HbA1c, QUICKI-HOMA-IR, McAuley index-HbA1c and McAuley index-HOMA-IR in all groups (Table 2).

**Table 3.** Receiver operating curve analysis of the indices for patients with HbA1c levels higher than 5.70%

| Index     | AUC   | 95% CI      | Cut-off     | Sensitivity | Specificity | p        |
|-----------|-------|-------------|-------------|-------------|-------------|----------|
| TyG Index | 0.749 | 0.705-0.789 | $>8.55$     | 79.7%       | 57.3%       | $<0.001$ |
| HOMA-IR   | 0.727 | 0.682-0.769 | $>1.56$     | 79.7%       | 54.2%       | $<0.001$ |
| QUICKI    | 0.724 | 0.679-0.766 | $\leq 0.35$ | 75.9%       | 55.7%       | $<0.001$ |
| ISI       | 0.675 | 0.629-0.720 | $\leq 6.98$ | 63.1%       | 64.6%       | $<0.001$ |
| TG/HDL-C  | 0.635 | 0.587-0.681 | $>2.06$     | 73.3%       | 49.5%       | $<0.001$ |

TyG: Triglyceride glucose, HOMA-IR: Homeostatic model assessment for insulin resistance, QUICKI: Quantitative insulin sensitivity check index, TG/HDL-C: Triglyceride-to-high-density lipoprotein cholesterol, ISI: Insulin sensitivity index, AUC: Area under the curve, CI: Confidence interval

**Table 4.** Binary logistic regression analysis for patients with HbA1c levels higher than 5.70%

| Parameter | Unadjusted       |          | Adjusted*        |              |
|-----------|------------------|----------|------------------|--------------|
|           | OR (95% CI)      | p        | OR (95% CI)      | p            |
| TyG       | 5.40 (3.61-8.09) | $<0.001$ | 4.12 (2.65-6.41) | $<0.001$     |
| HOMA-IR   | 1.62 (1.39-1.89) | $<0.001$ | 1.65 (1.39-1.95) | $<0.001$     |
| QUICKI    | 0.00 (0.00-0.00) | $<0.001$ | 0.00 (0.00-0.00) | $<0.001$     |
| ISI       | 0.73 (0.66-0.81) | $<0.001$ | 0.76 (0.68-0.85) | $<0.001$     |
| TG/HDL-C  | 1.19 (1.08-1.31) | $<0.001$ | 1.12 (1.01-1.23) | <b>0.029</b> |

\*Adjusted for age and sex. Dependent variable: control (HbA1c  $<5.70\%$ ) vs. patient groups (HbA1c  $\geq 5.70\%$ )

TyG: Triglyceride glucose, HOMA-IR: Homeostatic model assessment for insulin resistance, QUICKI: Quantitative insulin sensitivity check index, TG/HDL-C: Triglyceride-to-high-density lipoprotein cholesterol, ISI: Insulin sensitivity index, CI: Confidence Interval, OR: Odds ratio

A study has shown that an elevated TyG index and HOMA-IR in T2DM patients are associated with a higher risk of diabetic kidney disease (DKD). Using HOMA-IR in combination with the TyG index provided higher sensitivity and specificity in predicting DKD than HOMA-IR alone (32). The correlation between the TyG index and albuminuria in T2DM patients was found to be higher than the correlations with other IR indices, such as HOMA-IR, visceral adiposity index, and lipid accumulation product (33). In some studies, an independent association between the TyG index and diabetic retinopathy was identified in patients with T2DM, even after controlling for confounding variables (34,35). Among patients with T2DM, those diagnosed with cardiac autonomic neuropathy (CAN) exhibited significantly elevated TyG index and elevated HbA1c levels, in comparison to their counterparts without CAN (36,37). In patients with T2DM, the TG/HDL-C ratio demonstrated the highest AUC (0.721) for predicting coronary artery disease, whereas TyG-waist circumference exhibited the highest specificity (78%) (38). In another study, ROC analyses showed that metabolic score for IR had a higher AUC and better predictive power than the TyG index in defining major adverse cardiovascular events (39). IR indices may play an important role in identifying and managing the risk of complications in patients with T2DM. Their use may enhance early detection, risk stratification, and personalized intervention, ultimately improving patient outcomes.

### Study Limitations

Because our study was cross-sectional and had a relatively small sample size, a study with more data points is necessary to clarify cause-and-effect relationships. In addition, instead of the hyperinsulinemic euglycemic clamp, HOMA-IR was used to determine IR in this study. Finally, some factors, such as body mass index, possible comorbidities, diet, characteristics of standard of living, and the use of statins or other drugs, could not be included in the study.

### Conclusion

Among the evaluated IR indices, the TyG index demonstrated the highest correlation coefficient with HbA1c. In addition, it yielded the largest AUC, indicating superior diagnostic performance to the other indices. These findings indicate that the TyG index may serve as a useful indicator of IR in individuals with prediabetes and T2DM.

### Ethics

**Ethics Committee Approval:** The study was approved by the University of Health Sciences Türkiye, İstanbul Training and Research Hospital, Clinical Research Ethics Committee (approval number: 16, date: 25.01.2025).

**Informed Consent:** Retrospective study.

### Footnotes

**Authorship Contributions:** Concept - S.A.; Design - S.A., L.D.; Data Collection or Processing - S.A., L.D., Ö.D.; Analysis or Interpretation - S.A., L.D., Ö.D.; Literature Search - S.A., L.D., Ö.D.; Writing - S.A., L.D., Ö.D.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

### References

1. International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels, Belgium: 2021. Available at: <https://www.diabetesatlas.org>
2. Bijelic R, Balaban J, Milicevic S, Sipka SU. The association of obesity and microvascular complications with glycemic control in patients with type 2 diabetes mellitus. *Med Arch.* 2020; 74: 14-8.
3. DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. *Am J Physiol.* 1979; 237: E214-E23.
4. Jog KS, Eagappan S, Santharam RK, Subbiah S. Comparison of novel biomarkers of insulin resistance with homeostasis model assessment of insulin resistance, its correlation to metabolic syndrome in south indian population and proposition of population specific cutoffs for these indices. *Cureus.* 2023; 15: e33653.
5. American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2025. *Diabetes Care.* 2025; 48(Suppl 1): S27-S49.
6. American Diabetes Association Professional Practice Committee. 6. Glycemic Targets: Standards of Medical Care in Diabetes-2022. *Diabetes Care.* 2022; 45(Suppl 1): S83-S96.
7. Masoodian SM, Omidifar A, Moradkhani S, Asiabanha M, Khoshmirsafa M. HOMA-IR mean values in healthy individuals: a population-based study in iranian subjects. *J Diabetes Metab Disord.* 2022; 22: 219-24.
8. Simental-Mendía LE, Guerrero-Romero F. The correct formula for the triglycerides and glucose index. *Eur J Pediatr.* 2020; 179: 1171.
9. Antuna-Puente B, Faraj M, Karelis AD, Garrel D, Prud'homme D, Rabasa-Lhoret R, et al. HOMA or QUICKI: is it useful to test the reproducibility of formulas? *Diabetes Metab.* 2008; 34: 294-6.
10. Patarrão RS, Wayne Lutt W, Macedo MP. Assessment of methods and indexes of insulin sensitivity. *Revista Portuguesa de Endocrinologia, Diabetes e Metabolismo.* 2014; 9: 65-73.
11. Rohlfing CL, Wiedmeyer HM, Little RR, England JD, Tennill A, Goldstein DE. Defining the relationship between plasma glucose and HbA(1c): analysis of glucose profiles and HbA(1c) in the Diabetes Control and Complications Trial. *Diabetes Care.* 2002; 25: 275-8.
12. Aslan Çin NN, Yardımcı H, Koç N, Uçaktürk SA, Akçıl Ok M. Triglycerides/high-density lipoprotein cholesterol is a predictor similar to the triglyceride-glucose index for the diagnosis of metabolic syndrome using International Diabetes Federation criteria of insulin resistance in obese adolescents: a cross-sectional study. *J Pediatr Endocrinol Metab.* 2020; 33: 777-84.
13. Dundar C, Terzi O, Arslan HN. Comparison of the ability of HOMA-IR, VAI, and TyG indexes to predict metabolic syndrome in children with obesity: a cross-sectional study. *BMC Pediatr.* 2023; 23: 74.
14. Kırtıl G, Alpdemir M, Alpdemir ME, Şeneş M. Evaluation of the triglyceride glucose index as a marker of insulin resistance in adults with isolated impaired glucose tolerance. *Ahi Evran Med J.* 2023; 7: 205-11.
15. Gokcel A, Baltali M, Tarim E, Bagis T, Gumurdulu Y, Karakose H, et al. Detection of insulin resistance in Turkish adults: a hospital-based study. *Diabetes Obes Metab.* 2003; 5: 126-30.
16. Faki S, Tam AA, Ince N, Altay FP, Karaahmetli G, Houssein M, et al. Relationship between triglyceride-glucose index and microvascular complications in hospitalized patients with type 2 diabetes mellitus. *Turk J Diab Obes.* 2024; 8: 13-8.
17. McLaughlin T, Abbasi F, Cheal K, Chu J, Lamendola C, Reaven G. Use of metabolic markers to identify overweight individuals who are insulin resistant. *Ann Intern Med.* 2003; 139: 802-9.
18. Liu H, Yan S, Chen G, Li B, Zhao L, Wang Y, et al. Association of the ratio of triglycerides to high-density lipoprotein cholesterol levels with the risk of type

- 2 diabetes: a retrospective cohort study in beijing. *J Diabetes Res.* 2021; 2021: 5524728.
19. Young KA, Maturu A, Lorenzo C, Langefeld CD, Wagenknecht LE, Chen YI, et al. The triglyceride to high-density lipoprotein cholesterol (TG/HDL-C) ratio as a predictor of insulin resistance,  $\beta$ -cell function, and diabetes in Hispanics and African Americans. *J Diabetes Complications.* 2019; 33: 118-22.
20. Qin H, Chen Z, Zhang Y, Wang L, Ouyang P, Cheng L, et al. Triglyceride to high-density lipoprotein cholesterol ratio is associated with incident diabetes in men: a retrospective study of Chinese individuals. *J Diabetes Investig.* 2020; 11: 192-8.
21. Qin Y, Qiao Y, Yan G, Wang D, Tang C. Relationship between indices of insulin resistance and incident type 2 diabetes mellitus in Chinese adults. *Endocrine.* 2024; 85: 1228-37.
22. Chauhan A, Singhal A, Goyal P. TG/HDL Ratio: A marker for insulin resistance and atherosclerosis in prediabetics or not? *J Family Med Prim Care.* 2021; 10: 3700-5.
23. Chen B, Zeng J, Fan M, You Q, Wang C, Wang K, et al. A longitudinal study on the impact of the TyG Index and TG/HDL-C ratio on the risk of type 2 diabetes in Chinese patients with prediabetes. *Lipids Health Dis.* 2024; 23: 262.
24. Chamroonkiadtikun P, Ananchaisarp T, Wanichanon W. The triglyceride-glucose index, a predictor of type 2 diabetes development: a retrospective cohort study. *Prim Care Diabetes.* 2020; 14: 161-7.
25. Lee JW, Lim NK, Park HY. The product of fasting plasma glucose and triglycerides improves risk prediction of type 2 diabetes in middle-aged Koreans. *BMC Endocr Disord.* 2018; 18: 33.
26. Janghorbani M, Almasi SZ, Amini M. The product of triglycerides and glucose in comparison with fasting plasma glucose did not improve diabetes prediction. *Acta Diabetol.* 2015; 52: 781-8.
27. Navarro-González D, Sánchez-Iñigo L, Pastrana-Delgado J, Fernández-Montero A, Martínez JA. Triglyceride-glucose index (TyG index) in comparison with fasting plasma glucose improved diabetes prediction in patients with normal fasting glucose: The Vascular-Metabolic CUN cohort. *Prev Med.* 2016; 86: 99-105.
28. Katz A, Nambi SS, Mather K, Baron AD, Follmann DA, Sullivan G, et al. Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. *J Clin Endocrinol Metab.* 2000; 85: 2402-10.
29. Yokoyama H, Emoto M, Fujiwara S, Motoyama K, Morioka T, Komatsu M, et al. Quantitative insulin sensitivity check index and the reciprocal index of homeostasis model assessment are useful indexes of insulin resistance in type 2 diabetic patients with wide range of fasting plasma glucose. *J Clin Endocrinol Metab.* 2004; 89: 1481-4.
30. Sarafidis PA, Lasaridis AN, Nilsson PM, Pikilidou MI, Stafilas PC, Kanaki A, et al. Validity and reproducibility of HOMA-IR, 1/HOMA-IR, QUICKI and McAuley's indices in patients with hypertension and type II diabetes. *J Hum Hypertens.* 2007; 21: 709-16.
31. Straczkowski M, Stepień A, Kowalska I, Kinalska I. Comparison of simple indices of insulin sensitivity using the euglycemic hyperinsulinemic clamp technique. *Med Sci Monit.* 2004; 10: CR480-CR4.
32. Yan H, Zhou Q, Wang Y, Tu Y, Zhao Y, Yu J, et al. Associations between cardiometabolic indices and the risk of diabetic kidney disease in patients with type 2 diabetes. *Cardiovasc Diabetol.* 2024; 23: 142.
33. Nabipoorashrafi SA, Adeli A, Seyedi SA, Rabizadeh S, Arabzadeh Bahri R, Mohammadi F, et al. Comparison of insulin resistance indices in predicting albuminuria among patients with type 2 diabetes. *Eur J Med Res.* 2023; 28: 166.
34. Neelam K, Aung KCY, Ang K, Tavintharan S, Sum CF, Lim SC. Association of triglyceride glucose index with prevalence and incidence of diabetic retinopathy in a Singaporean population. *Clin Ophthalmol.* 2023; 17: 445-54.
35. Srinivasan S, Singh P, Kulothungan V, Sharma T, Raman R. Relationship between triglyceride glucose index, retinopathy and nephropathy in type 2 diabetes. *Endocrinol Diabetes Metab.* 2020; 4: e00151.
36. Akbar M, Bhandari U, Habib A, Ahmad R. Potential association of triglyceride glucose index with cardiac autonomic neuropathy in type 2 diabetes mellitus patients. *J Korean Med Sci.* 2017; 32: 1131-8.
37. Jeyaseeli A, R G, Mathivanan D, Prabakaran A. Assessment of triglyceride glucose index in type 2 diabetes mellitus patients with and without cardiac autonomic neuropathy. *Cureus.* 2023; 15: e42541.
38. Yadegar A, Mohammadi F, Seifouri K, Mokhtarpour K, Yadegar S, Bahrani Hazaveh E, et al. Surrogate markers of insulin resistance and coronary artery disease in type 2 diabetes: U-shaped TyG association and insights from machine learning integration. *Lipids Health Dis.* 2025; 24: 96.
39. Pan L, Zou H, Meng X, Li D, Li W, Chen X, et al. Predictive values of metabolic score for insulin resistance on risk of major adverse cardiovascular events and comparison with other insulin resistance indices among Chinese with and without diabetes mellitus: Results from the 4C cohort study. *J Diabetes Investig.* 2023; 14: 961-72.