



Could Triglyceride-Glucose Index, a Predictor of Atherosclerosis, Be Associated with Retinal Vein Occlusion?

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Abstract

Objectives: The triglyceride-glucose (TyG) index is a sign of atherosclerosis in cardiovascular diseases. The TyG index is thought to have clinical significance for the assessment of vascular damage. In this study we aimed to demonstrate the connection between the TyG index and retinal vein occlusion (RVO).

Materials and Methods: This case-control observational study involved 492 participants aged 40-90, admitted to the ophthalmology outpatient clinic of our hospital. TyG index was calculated using the formula: $\ln(\text{fasting TG [mg/dL]} \times \text{fasting plasma glucose [mg/dL]}/2)$.

Results: The RVO group included 387 patients (181 women and 206 men) and the control group included 115 patients (61 women and 54 men). The average patient age was 62.9 ± 11.1 years in the RVO group and 56.7 ± 8.7 years in the control group. The TyG index was higher in the RVO group (8.9 ± 0.7) than in the control group (8.8 ± 0.6). This difference was statistically significant ($p=0.04$). The correlation was statistically significant when evaluated according to age and sex by multivariate logistic regression analysis (odds ratio: 1.45, confidence interval: 1.03-2.02, $p=0.03$).

Conclusion: The TyG index is a novel atherogenicity index that is derived from routine blood tests and can be used to determine the risk of RVO in at-risk individuals with a simple calculation. Therefore, the TyG index could help as a reliable guide to identify individuals at RVO with high risk and initiate early intervention.

Keywords: Atherogenic index, retinal vein occlusion, triglyceride-glucose index, vascular disease

Introduction

Retinal vein occlusion (RVO) is the occlusion of the retinal venous system by thrombi and can occur in three different forms: central, hemicentral, or branch RVO. The most common etiologic factor for the disease is the compression of atherosclerotic retinal arteries at the arterial-venous junction.¹ Risk factors for RVO include advanced age, diabetes mellitus (DM), hypertension, atherosclerotic disease, and glaucoma. Studies show mixed results regarding the involvement of hypercoagulability and inflammatory factors in its development.^{2,3} Moreover, hypertension and diabetes may accelerate the progression of atherosclerosis, contributing to the development of RVO.⁴ While the cause of RVO in younger people is not well understood, some case reports suggest inflammation, physical exercise, dehydration, and congenital anomalies as possible factors.⁵

The triglyceride-glucose (TyG) index is a marker of insulin resistance in healthy populations. Various studies have demonstrated that the TyG index is linked to the development of diabetes, high blood pressure, and metabolic syndrome. Recent research has also used this index as a marker for atherosclerosis in cardiovascular disease (CVD). The TyG index is considered clinically significant for evaluating vascular damage.⁶ However, the normal range of the TyG index has not been determined in the literature, as varying results from different studies hinder a consensus. Thai et al.⁷ reported that a higher TyG index value was related to a greater number of narrowed coronary arteries and more severe coronary stenosis. This suggests that the TyG index might be an effective parameter in assessing risk of atherosclerosis in patients with type 2 DM.

Clinicians need different non-invasive and simple tools to predict the presence of atherosclerosis.⁸ A recent study with a small sample size (57 RVO patients) and age- and gender-matched controls examined the connection between the TyG index and RVO.⁹ However, this study did not assess the burden of comorbidities in multivariate analysis. We hypothesized that a high TyG index may be linked to RVO independent of age, gender, and multiple comorbidities. Thus, this study aimed

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to investigate the relationship between TyG index and other measurements in patients with RVO.

Materials and Methods

Study Population, Design, and Setting

This retrospective, observational, case-control study involved 492 participants aged 40-90 years who presented to the ophthalmology clinic of a tertiary center from January 2018 to March 2023. Patients with eye diseases other than RVO that were previously diagnosed by an ophthalmologist, patients under 40 years old, patients with advanced liver and kidney failure, patients who had active infections or uncontrolled chronic diseases, smokers and alcohol users, patients with impaired cognitive function, and patients who did not have blood test results recorded in the hospital system within the last month were excluded from the study.

Informed consent was not obtained because the study was retrospective. The study was approved by the Atatürk City Hospital Ethics Committee (no: 2023/2/15, date: 04.05.2023) and adhered to the Declaration of Helsinki.

Assessment of Atherosclerosis (TyG Index)

The TyG index is calculated as $\ln(\text{fasting TG [mg/dL]} \times \text{fasting plasma glucose [mg/dL]}/2)$.¹⁰

Covariates for All Participants

Demographic (age, gender, chronic disease) and laboratory data of all patients, including hemograms and biochemical tests (glucose, triglycerides, total cholesterol, high-density lipoprotein, low-density lipoprotein) performed in the last month during routine outpatient follow-up visits were retrieved from the hospital's electronic records system.

We used the Deyo-Charlson comorbidity index to score the total comorbidity burden of multiple comorbid conditions.^{11,12,13}

Statistical Analysis

The statistical analysis was performed using IBM SPSS Statistics version 22.0 (IBM Corp., Armonk, NY, USA). Kolmogorov-Smirnov test was used to assess whether the data showed normal distribution. Normally distributed values were expressed as mean ± standard deviation, while non-normally distributed values were expressed as median (min-max). Student's t-test or the Mann-Whitney U test was used to compare continuous variables. Chi-square test was used to compare categorical data. Multivariate and univariate logistic regression analyses were used to identify independent factors associated with RVO. A p value <0.05 was noted as statistically significant.

Results

The study included 492 participants (61.0% men) with an average age of 68.2±1.2 years. The RVO group consisted of 387 patients (181 women and 206 men) with a mean age of 62.9±11.1 years, while the control group consisted of 115 patients (61 women and 54 men) with a mean age of 56.7±8.7 years. Statistically significant age and sex differences were found between the two groups (p=0.01 and p=0.04, respectively).

There was no significant difference between the groups in Deyo-Charlson comorbidity index values (p=0.46) or triglyceride levels (p=0.35). However, a statistically significant difference was found between the RVO and control groups in terms of glucose (p=0.01) and mean TyG index value (p=0.04). The RVO group had a mean TyG index value of 8.9±0.7, while the control group had a mean TyG index value of 8.8±0.6 (Figure 1).

Associations of TyG Index with RVO

In the univariate logistic regression analysis, we observed an association between RVO and TyG index (odds ratio [OR]: 1.39, 95% confidence interval [CI]: 1.01-1.93, p=0.04), age (OR: 1.05, 95% CI: 1.03-1.08, p=0.01), and female sex (OR: 1.57, 95% CI: 1.02-2.44, p=0.04).

In the multivariate logistic regression analysis (Model), RVO was significantly associated with TyG index (OR: 1.45, 95% CI: 1.03-2.02, p=0.03) and age (OR: 1.06, 95% CI: 1.03-1.08, p=0.01). A 1.45-fold increased risk of RVO was observed among subjects with higher TyG index when compared to healthy individuals (Table 1).

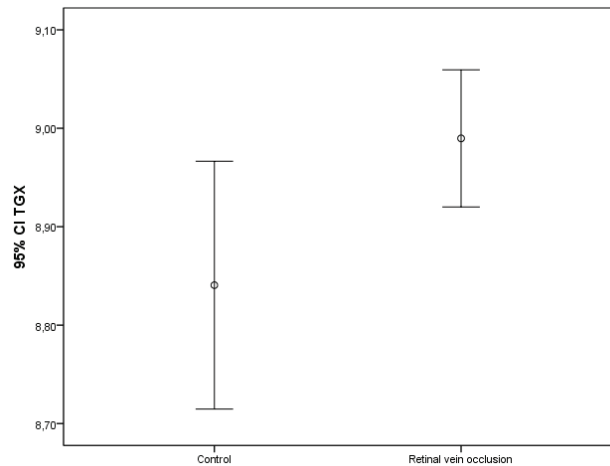


Figure 1. Comparison of triglyceride-glucose index between the retinal vein occlusion and control group
CI: Confidence interval, TGX: Triglyceride-glucose index

Table 1. Association between triglyceride-glucose index and retinal vein occlusion

	Unadjusted		Model	
	OR (95% CI)	p	OR (95% CI)	p
TyG index	1.39 (1.01-1.93)	0.04	1.45 (1.03-2.02)	0.03
Age	1.05 (1.03-1.08)	0.01	1.06 (1.03-1.08)	0.01
Gender (female)	1.57 (1.02-2.44)	0.04	1.55 (0.96-2.43)	0.06

Model: Adjusted for age and sex, OR: Odds ratio, CI: Confidence interval, TyG: Triglyceride-glucose

Discussion

The results of our research show that the TyG index was higher in the RVO group compared to the control group. This difference remained significant even when age and sex were taken into account. Our findings also suggest that a high TyG index score is a predictive factor for RVO. In fact, a high TyG index increased the risk of RVO by almost 50%. This is one of the first studies to demonstrate the association of TyG index with RVO, regardless of covariates such as age, sex, and comorbidity burden.

Insulin resistance is a crucial factor in the development of CVD.¹⁴ Therefore, it is important to identify reliable markers for its assessment to stratify and predict risk. Recently, researchers have demonstrated that the TyG index, a cost-effective measure calculated from triglyceride levels and fasting glucose, is a dependable indicator of insulin resistance. This finding suggests that the TyG index may be a valuable tool for identifying individuals at higher risk of CVD and for tailoring interventions. Its simple measurement and strong predictive power make it a promising marker for clinical use.^{10,15} In a cohort study of 49,579 participants, Li et al.¹⁶ found that a high TyG index value was an independent predictor of an increased risk of CVD. In a recent study, we examined the TyG index values of patients with pseudoexfoliation syndrome, which is potentially caused by atherosclerotic changes. The study revealed a significant association between TyG index and pseudoexfoliation syndrome.¹⁷ Consistent with prior research, we showed in this study that the TyG index, strongly linked to atherosclerotic vascular disease, was also associated with RVO. However, additional research and validation of the TyG index in diverse populations will be crucial for its widespread adoption in clinical practice.^{18,19,20,21,22,23,24,25}

RVO is a widespread and long-lasting condition that poses a significant risk to vision and is closely associated with CVD. The disease is usually associated with typical atherosclerotic risk factors that are known to be related to various forms of RVO.²⁶ The retinal vein and artery share a common sheath, and the thin-walled vein traverses the thick and rigid arterial wall and extends posteriorly.^{27,28,29} This mechanical constriction at the transition zones between artery and vein leads to hemodynamic changes, potentially causing chronic venous endothelial damage.^{27,28,30} As a result, endothelial cell proliferation and vein wall remodeling contribute significantly to occlusion at these sites. The age-related increased stiffness of the retinal artery may increase the risk of compression and vascular occlusion at these junctions. Therefore, atherosclerosis and other cardiovascular risk factors that favor arteriolar sclerosis, such as systemic hypertension or diabetes, are prevalent in RVO patients.^{31,32} The results of the present study are a valuable addition to the literature on this topic.

However, it is unclear whether the high TyG index observed in patients with potential sequelae of atherosclerosis is due to underlying neuropathologic changes that occur in diseases. To clarify this, we minimized the likelihood of changes due to uncontrolled diseases (e.g., DM, hypertension, CVD) through

the exclusion criteria. The notable association between RVO and high TyG index values discovered in our study may provide further insight into the relationship between cardiovascular risk factors and the development of RVO. On the other hand, there may be other factors, including insulin level, glycosylated hemoglobin (HbA1c) and body mass index (BMI), that affect the TyG index and should be considered in future research.

Study Limitations

Strengths of this study are its community-based design, considerable sample size, and comprehensive clinical and ophthalmologic evaluations. The significance of the results persisted even after adjustment for several major confounding factors (age, sex, concomitant diseases). However, the study is limited by its retrospective, single-centered, case-control design without age and sex matching. Finally, even after adjusting for certain potential demographic and clinical variables, there may still be residual confounding factors (e.g., HbA1c, BMI). Therefore, prospective studies on this issue are needed to better characterize the relationship between TyG index and RVO.

Conclusion

The TyG index, a novel atherogenicity index derived from routine blood tests, has shown promise as a potential marker for RVO. This simple calculation may serve as a reliable indicator to identify individuals at high risk of RVO and initiate early intervention. Further prospective, randomized, controlled, large-scale research is needed to validate the TyG index in various populations and to fully understand its potential impact on RVO risk assessment and management.

Ethics

Ethics Committee Approval: Atatürk City Hospital Ethics Committee (no: 2023/2/15, date: 04.05.2023) and adhered to the Declaration of Helsinki.

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: Z.K., M.T., Concept: Z.K., M.T., Design: Z.K., Data Collection or Processing: Z.K., Analysis or Interpretation: Z.K., M.T., Literature Search: Z.K., Writing: Z.K., M.T.

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