RESEARCH

The association between triglyceride-glucose atherogenic predictor index and central retinal artery occlusion

Trigliserit-glukoz aterojenik prediktör indeksi ile santral retinal arter oklüzyonu arasındaki ilişki

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Abstract

Purpose: Central retinal artery occlusion (CRAO) is an acute ischemic event causing severe visual loss and is a precursor to further cerebrovascular and cardiovascular events. The triglyceride-glucose index (TyG) indicates insulin resistance in healthy individuals. Numerous research links the TyG index to metabolic syndrome, hypertension, and new-onset diabetes. Recent research also suggests its role as a sign of atherosclerosis in cardiovascular diseases, with potential clinical significance in assessing vascular damage. In this study, the relationship between CRAO and TyG index was evaluated.

Materials and Methods: This case-control study involved 116 adults (50 CRAO patients and 66 control subjects without chronic eye diseases) at our hospital from January 2018 to March 2023. The TyG index was formulated as ln[fasting TG (mg/dL) × fasting plasma glucose (mg/dL)/2].

Results: The CRAO group had a mean age of 65.0±14.7 years, with 27 (55.1 % 54) females. The control group had a mean age of 61.2±12.1 years, with 32 (48.5) females. The mean TyG index was 9.05±0.7 in the CRAO group and 8.7±0.7 in controls, a statistically significant difference. Univariate regression analysis showed an association between the TyG index and CRAO (OR=2.04; CI: 1.11-3.73). This association remained significant in multivariate logistic regression analysis (OR=1.88; CI: 1.01-3.50).

Conclusion: This study found a significantly higher mean TyG index, an atherogenic indicator, in CRAO patients compared to controls.

Keywords:. Atherosclerosis, central retinal artery occlusion, retina, triglyceride-glucose index, vascular disease

Öz

Amaç: Santral retinal arter tıkanıklığı (CRAO), ciddi görme kaybına neden olan akut bir iskemik olaydır ve daha ileri serebrovasküler ve kardiyovasküler olayların habercisidir. Trigliserid-glikoz indeksi (TyG), sağlıklı bireylerde insülin direncini gösterir. Çok sayıda araştırma, TyG indeksini metabolik sendrom, hipertansiyon ve yeni başlayan diyabetle ilişkilendirir. Son araştırmalar ayrıca, kardiyovasküler hastalıklarda ateroskleroz belirtisi olarak rolünü ve vasküler hasarı değerlendirmede potansiyel klinik önemi olduğunu ileri sürmektedir. Bu çalışmada, CRAO ve TyG indeksi arasındaki ilişki değerlendirilmiştir.

Gereç ve Yöntem: Bu vaka kontrol çalışmasına Ocak 2018'den Mart 2023'e kadar hastanemizde 116 yetişkin (50 CRAO hastası ve kronik göz hastalığı olmayan 66 kontrol deneği) katılmıştır. TyG indeksi ln[açlık TG (mg/dL) × açlık plazma glikozu (mg/dL)/2] olarak formüle edilmiştir.

Bulgular: CRAO grubunun ortalama yaşı 65,0±14,7 yıldı ve 27 (%55,1 54) kadın vardı. Kontrol grubunun ortalama yaşı 61,2±12,1 yıldı ve 32 (%48,5) kadın vardı. Ortalama TyG indeksi CRAO grubunda 9,05±0,7 ve kontrollerde 8,7±0,7 idi ve istatistiksel olarak anlamlı bir farktı. Tek değişkenli regresyon analizi, TyG indeksi ve CRAO arasında bir ilişki olduğunu gösterdi (OR=2,04; CI: 1,11-3,73). Bu ilişki, çok değişkenli lojistik regresyon analizinde anlamlılığını korudu (OR=1,88; CI: 1,01-3,50).

Sonuç: Bu çalışma, aterojenik bir gösterge olan TyG indeksinin CRAO hastalarında kontrollerle karşılaştırıldığında anlamlı derecede daha yüksek olduğunu saptadık.

Anahtar kelimeler: Santral retinal arter tıkanıklığı, retina, trigliserid-glukoz indeksi, vasküler hastalık

INTRODUCTION

Central retinal artery occlusion (CRAO) is a critical eye condition that can lead to severe and permanent vision loss. It typically presents painless vision loss in one eye, along with specific eye abnormalities like a "cherry red spot" on the macula and a decrease in retinal vessel visibility[1,2].

 CRAO occurs when the central retinal artery becomes suddenly blocked. If left untreated, it can cause injury to the inner retinal layer, resulting in irreversible harm to the optic nerve and surrounding structures. The main cause of CRAO is often an embolism that blocks the artery, with these emboli usually originating from the internal carotid artery or other sources like the heart or aortic arch[3]. Identifying and addressing the source of the embolism is crucial in managing CRAO, as it is closely linked to cardiovascular risk factors[4,5].

The triglyceride-glucose index (TyG) serves as an indicator of insulin resistance in healthy individuals and has been associated with conditions like metabolic syndrome, hypertension, and new-onset diabetes. Recent studies provide further evidence supporting the use of the TyG index as an indicator of cardiovascular health and suggest its potential clinical value in identifying individuals at risk for heart-related conditions[6-8].

The TyG index, a highly valuable tool, allows for the comprehensive assessment of vascular damage and plays a crucial role in accurately predicting outcomes in the context of cardiovascular diseases[9]. Previous research has highlighted its role as a reliable marker for insulin resistance, aiding in risk assessment and outcome prediction for cardiovascular issues[9]. Given the influence of atherosclerotic risk factors on CRAO, we hypothesized a potential link between the TyG index and this eye condition. To explore this further, we conducted a study investigating the relationship between the TyG index and CRAO, as no prior studies have delved into this connection.

MATERIALS AND METHODS

Study design and sample

In this retrospective study, 50 patients aged 40 to 90 years diagnosed with CRAO and 66 control subjects aged 40 to 90 years without chronic eye diseases were examined who applied to the Ophthalmology Outpatient Clinic of Balıkesir Atatürk City Hospital from January 2018 to March 2023. Although 103 patients with CRAT diagnosis were reached for the study, 63 patients were not included due to incomplete blood data. Patients with BRAO were excluded. Control and patient groups have similar comorbidities such as diabetes, hypertension, and coronary artery disease. Computer-recorded results of patients' complete blood counts and biochemistry tests (glucose, total cholesterol, HDL, LDL, triglycerides, and glycosylated hemoglobin) from routine outpatient clinic follow-ups in the last month were retrospectively accessed.

Exclusion criteria included previous diagnosis of eye disease other than CRAO, age under 40, advanced organ failure, active infection history, smoking or alcohol use, impaired cognitive function, and absence of recent blood test results in the hospital system.

Ethical approval was obtained from the Ethics Committee of Balıkesir Atatürk City Hospital (Karar No: 2023/3/28 Tarih: 01.06.2023) before the research, which was conducted following the Declaration of Helsinki.

Covariates for all participants

Ocular examination findings, demographic data, and laboratory and clinical parameters were retrieved from the tertiary hospital's information system and archives. The modified Charlson comorbidity index (CCI) score was used to assess comorbid disease burden[10-12]. The index assigns weights to specific diseases, with different weights for various conditions[13-16].

Assessment of Atherosclerosis (TyG Index)

The TyG index was calculated using the formula: ln[fasting TG (mg/dL) × fasting plasma glucose (mg/dL)/2][17].

Statistical analysis

Due to its retrospective design, this study only enrolled patients admitted to our hospital within the specified date range. Therefore, we performed post-hoc computational power analysis using G*Power 3.1.9.6 and calculated the power (1-d err probe) as 0.95 and the effect size as 0.572 with the above-mentioned sample size (n=116).

IBM SPSS Statistics 22 was utilized for statistical analyses. Student's t-test and chi-square test were used for continuous and categorical data. Data

normality was assessed with the Kolmogorov-Smirnov test. Normally distributed values were presented as mean ± standard deviation, and non-normally distributed values as median (min-max). Univariate and multivariate regression analyses (adjusted covariates including age ,gender and CCI score) were performed to identify independent predictors of CRAO. ROC curve analysis and the Youden index method were employed to determine cut-off values for the TyG index in predicting CRAO. A significance level of $p<0.05$ was used for all statistical analyses.

RESULTS

A total of 116 participants were enrolled in the research (mean age: 60.7±13.1 years, male: 41.0%). The CRAO group comprised 50 patients (23 men and 27 women) and the control group included 66 patients (34 men and 32 women). CRAO group had a mean age of 65.0±14.7 years, with 27 (55.1 % 54) females. The control group had a mean age of 61.2±12.1 years, with 32 (48.5) females. Table 1 displays the demographic and laboratory parameters of all participants.

Table 1. Characteristics of the sample

Variables	Total (N=116)	Central retinal artery occlusion (N=50)	Normal (N=66)	*p-value*
Demographics				
Age (years), mean ± SD				
Gender (Female), n (%)				
CCI, median (min-max)	1 (0-3)	1 (0-3)	1 (0-3)	0.15
Diabetes mellitus, n (%)	21 (18.1)	11 (22)	10 (15.2)	0.34
Hypertension, n (%)	38 (32.8)	22 (44)	16 (24.2)	0.03
Coronary heart disease, n (%)	25 (21.6)	11 (22)	14 (21.2)	0.92
Laboratory parameters				
Glucose (mg/dl)	118.3±55.5	128.6±69.9	110.7±40.8	0.06
Triglyceride (mg/dl)	147.6±81.4	160.8±81.3	137.9±80.7	0.35
Total cholestrol (mg/dl)	204.5±44.1	208.6±46.8	200.1±41.1	0.35
HDL-cholestrol (mg/dl)	54.3±21.0	50.6±16.8	58.5±24.9	0.07
LDL-Cholestrol (mg/dl)	122.3±52.8	131.3±62.5	112.3±37.6	0.08
HbA1c (%)	6.5±1.6	6.5±1.5	6.4±1.8	0.86
TyG index	8.8±0.7	9.05±0.7	8.7±0.7	0.02

Abbreviations: CCI, Charlson comorbidity index; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG index, Triglyceride-glucose index.
Normally distributed values were expressed as mean ± standard deviation and non-normally distributed values as median (min-max).
Student's t-test was used to evaluate continuous variables. The chi-square test was used to compare categorical data.

There were no remarkable differences between the CRAO group and the control group in terms of the use of cholesterol medications (p=0.54), modified Charlson comorbidity index (CCI) scores (p=0.15), and triglyceride values (p=0.35). However, the mean TyG index was 9.05±0.7 in the CRAO group and 8.7±0.7 in the control group, with a statistically remarkable difference (p=0.02) as shown in Figure 1.
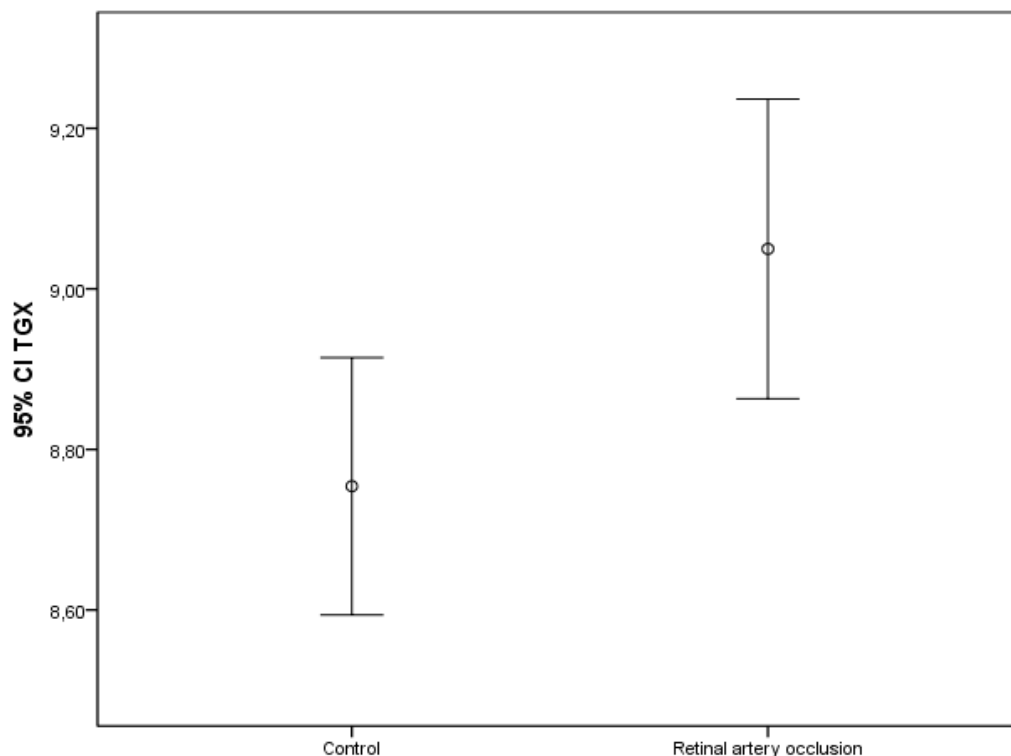
Figure 1. Comparison of Triglyceride-glucose index between CRAO and control group.

The mean TyG index value was 9.05±0.7 in the CRAO group and 8.7±0.7 in the control group (p=0.02).

Univariate regression analysis revealed an association between the TyG index and CRAO (OR=2.04; CI: 1.11-3.73; p=0.02). This association remained significant even after adjusting for age, sex, and CCI in multivariate logistic regression analysis (Model) (OR=1.88; CI: 1.01-3.50; p=0.04) detailed in Table 2.

Table 2. Association of TyGx with CRAO.

	Unadjusted		Model	
	OR (95% CI)	*p*	OR (95% CI)	*p*
TyG index	2.04 (1.11-3.73)	**0.02**	1.88 (1.01-3.50)	**0.04**
Age	1.02 (0.99-1.05)	0.13	1.04 (1.01-1.08)	**0.03**
Gender (Female)	0.77 (0.36-1.61)	0.48	0.58 (0.25-1.30)	0.18
CCI	1.39 (0.88-2.17)	0.15	1.17 (0.72-1.89)	0.53

The predictive ability of the TyG index for detecting CRAO was assessed through receiver operating characteristic (ROC) curve analysis, with the AUC value presented in Figure 2. The TyG index effectively predicted the presence of CRAO, with a cut-off value of 8.79 based on the Youden index (AUC=0.62, sensitivity: 67%, specificity: 61%) (p=0.03) shown in Figure 2.
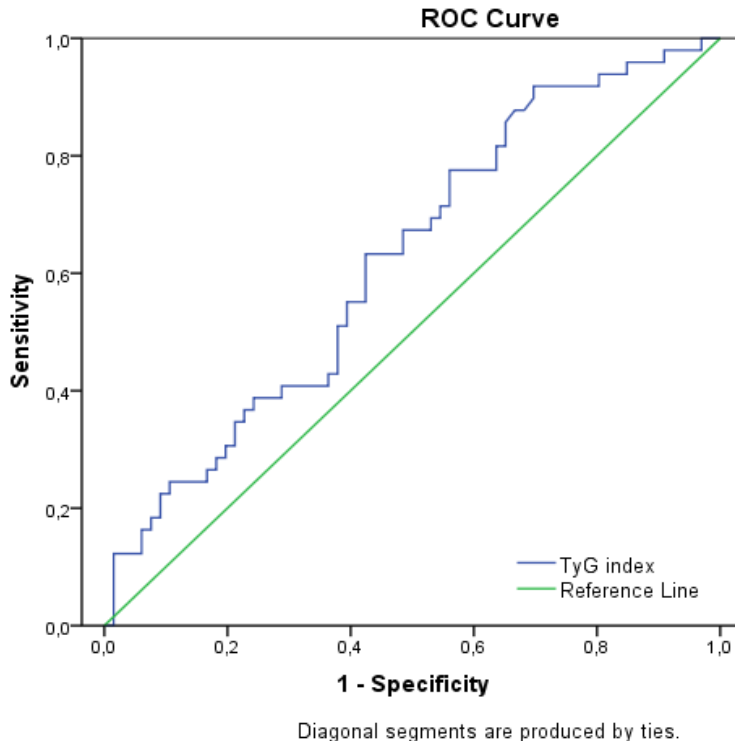
Figure 2. ROC curve analysis of Triglyceride-glucose index.

The TyG index cut-off value for CRAO was 8.79 (AUC=0.62, sensitivity: 67%, specificity: 61%) (p=0.03).

A sensitivity analysis conducted on cases where no cholesterol medication was used yielded results consistent with the main analysis, indicating a statistically remarkable association between the presence of CRAO and the TyG index (OR=1.98; CI: 1.02-3.85; p=0.042).

DISCUSSION

In this research, it was found that patients with CRAO had remarkably higher TyG index values compared to the control group. This finding persisted notable even after modifying for potential factors. These results suggest that the TyG index may be linked to CRAO. A higher TyG index value doubles the risk of CRAO. The uniqueness of these data in the research field was noted when reviewing the literature.

The TyG index is used to assess insulin resistance in patients and healthy individuals[18,19]. Recent studies have established a strong connection between the TyG index and cardiovascular diseases, such as calcification, coronary artery stenosis, and carotid artery atherosclerosis[20-22]. This indicates that the TyG index is a dependable sign of insulin resistance and aids in predicting cardiovascular disease risks[23,24]. A large-scale study in China revealed that raised TyG index values were independently related to a higher risk of myocardial infarction (MI), underscoring the importance of monitoring the TyG index to identify cardiovascular risk[25].

Apart from systemic diseases, researchers have explored the association of the TyG index with eye diseases. A recent study examined the TyG index values in patients with pseudoexfoliation syndrome (PSX), revealing a remarkable correlation between the TyG index and PSX[26]. In this study, which we conducted in the patient group with SRAT, similar to the patient group with PSX, we can say that the TyG index is associated with the presence of SRAT.

Patients with CRAO typically present with sudden vision loss, often leading to severe and permanent monocular vision loss[27,28]. Non-arteritic cases, which account for 95% of cases, are commonly caused by embolic or prothrombotic disorders[28,29]. The most frequent cause is proximal embolism from the carotid artery, aortic arch, or heart[30,31]. The study's finding of elevated TyG index values in CRAO patients, influenced by atherosclerotic risk factors, aligns with existing literature.

Multiple studies have identified male gender, advanced age, hypertension, diabetes, and cardiovascular diseases as significant CRAO risk factors[32,33]. While our study confirmed the association between CRAO and advanced age, the link with gender was not significant, it may be the research's small sample size. Larger multicenter studies may provide more insights into this aspect. This marker, which indicates atherosclerotic risk, can be easily used in the clinic. It can provide awareness for clinicians in terms of coronary artery diseases and cerebrovascular diseases in patients who have had CRAO.

The power of this research was its population-based design, the addition of a control group, and comprehensive clinical and ophthalmological assessments. The limitations of our study are that it was a cross-sectional observational study design and was conducted in a single center. Despite adjusting for confusing factors like sex, age, and comorbidities, the study has limitations such as its observational design and single-center nature. Even after adjustment for certain demographic values and clinical characteristics, there may be additional confounding factors (hematological diseases, arrhythmia, etc.). Future randomized controlled studies are necessary to fully comprehend the impact of the triglyceride glucose index on central retinal artery occlusion.

In conclusion, this study highlights the higher TyG index values in CRAO patients compared to controls. This underscores the importance of considering the increased risk of systemic atherosclerotic events in such patients. Furthermore, individuals had cardiovascular diseases are at higher risk for CRAO, emphasizing the need for early preventive measures to safeguard public health.

Author Contributions: Concept/Design : ZT, MT; Data acquisition: ZK; Data analysis and interpretation: MT, ZK; Drafting manuscript: ZK; Critical revision of manuscript: MT, ZK; Final approval and accountability: ZK, MT; Technical or material support: -; Supervision: ZK, MT; Securing funding (if available): n/a.

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