

Relationship Between Triglyceride-Glucose Index and Erectile Dysfunction in Subjects Without Cardiovascular Disease

Kardiyovasküler Hastalığı Olmayan Kişilerde Trigliserid-Glukoz İndeksi ve Erektile Disfonksiyon Arasındaki İlişki

Ersan Oflar¹, Cennet Yildiz¹, Atilla Koyuncu¹, Dilay Karabulut¹, Fatma Nihan Turhan Caglar¹, Mehmet Pisirici¹, Hakan Polat²

¹Department of Cardiology, University of Health Sciences, Dr. Sadi Konuk Training and Research Hospital, Istanbul, Türkiye

²Department of Urology, University of Health Sciences, Dr. Sadi Konuk Training and Research Hospital, Istanbul, Türkiye

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Corresponding Author: Cennet Yildiz / University of Health Sciences, Dr. Sadi Konuk Training and Research Hospital, Department of Cardiology, Istanbul, Türkiye
cennet_yildiz@live.com / ORCID ID: 0000-0003-2456-3206

Abstract

Objective: Studies have shown that insulin resistance (IR) plays a role in the pathogenesis of erectile dysfunction (ED). Triglyceride-glucose (TyG) index has been found as a reliable marker of IR. In this study, our aim was to investigate the role of TyG index in patients with ED.

Materials and Methods: One hundred six patients with ED (study group) and 54 subjects with normal sexual function (control group) constituted our study population. Erectile function was assessed by using International Index of Erectile Function-5 (IIEF-5) questionnaire. TyG index was calculated for each participant.

Results: ED patient were older, had higher total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), glucose and triglyceride concentrations and TyG indexes ($p < 0.001$, $p < 0.001$, $p < 0.001$, $p = 0.036$, $p = 0.026$ and $p = 0.003$, respectively). IIEF-5 scores showed a negative correlation with TyG indexes ($r = -0.273$, $p = 0.001$). Receiver operating characteristic (ROC) curve analysis showed that TyG index cut-off value of 9.03 had 70.3% sensitivity and 65% specificity in predicting mild-to-moderate, moderate, and severe ED. Univariate logistic regression analysis showed that age, TC, LDL-C, and TyG index had predictive values for the identification of the patients who had mild-to-moderate, moderate, and severe ED.

Conclusion: TyG index might be a valuable diagnostic tool for ED, and it might be used in clinical practice for the evaluation of patients.

Keywords: erectile dysfunction, triglyceride, glucose

Öz

Amaç: Çalışmalar insülin direncinin (İD) erektil disfonksiyon (ED) patogenezinde rol oynadığını göstermiştir. Trigliserid-glukoz (TG) indeksi İD için güvenilir bir belirteçdir. Bu çalışmada amacımız ED'li hastalarda TG indeksinin rolünü araştırmaktır.

Gereçler ve Yöntemler: Yüz altı ED hastası (çalışma grubu) ile normal cinsel fonksiyonlu 54 kişi (kontrol grubu) çalışma popülasyonumuzu oluşturdu. Erektile Fonksiyon, Uluslararası Erektile İşlev Formu-5 (IIEF-5) ile değerlendirildi. Her katılımcı için TG indeksi hesaplandı.

Bulgular: ED olan hastalar daha yaşlı, daha yüksek total kolesterol (TK), düşük yoğunluklu lipoprotein-kolesterol (LDL-K), glukoz ve trigliserid konsantrasyonları ile TG indeks değerlerine sahip idi (sırası ile ($p < 0.001$, $p < 0.001$, $p < 0.001$, $p = 0.036$, $p = 0.026$ and $p = 0.003$). IIEF-5 skoru, TG indeks değerleri ile negatif bir korelasyon gösterdi ($r = -0.273$, $p = 0.001$). ROC eğrisi analizi; 9.03 TG indeksi değerinin hafif-orta, orta ve ciddi ED'yi öngörmede %70.3 duyarlılık ve %65 özgüllüğe sahip olduğunu gösterdi. Univaryant lojistik regresyon analizi; yaş, TK, LDL-K ve TG indeksinin hafif-orta, orta ve ciddi ED'ye sahip hastaların belirlenmesinde prediktif değere sahip olduğunu gösterdi.

Sonuç: TG indeksi, ED tanısında yararlı bir araç olabilir. Hastaların klinik değerlendirmesinde kullanılabilir.

Anahtar kelimeler: erektil disfonksiyon, trigliserid, glukoz

ORCID ID:	E. Oflar 0000-0002-0757-2496	D. Karabulut 0000-0003-1896-0096	M. Pisirici 0000-0001-8729-0474
	A. Koyuncu 0000-0002-1523-1034	F. N. Turhan Caglar 0000-0001-7925-2398	H. Polat 0000-0003-1525-1243

Introduction

Erectile dysfunction (ED) has a negative influence on the quality of life of patients. Its prevalence shows an association with age, surpassing over 80% in men who are older than 80 years [1]. Although this disorder might have organic or psychological causes, the most common underlying pathology is abnormalities of the penile blood vessels. ED shares the same risk factors for cardiovascular disease (CVD) with similar underlying pathophysiological mechanisms [2]. The relationship between ED and CVD is bidirectional. Studies have shown ED as a predictor of CVD and the presence of CVD has been found to be associated with more severe forms of ED [3]. As such, current guidelines have recommended a detailed examination of ED patients in terms of CVD and risk factors [2]. This approach gives physicians a chance for risk mitigation, early diagnosis, and management of CVD.

Insulin resistance (IR) coexists with the proatherogenic milieu and is a part of the atherogenic process [4]. By affecting systemic factors as well as intimal cells that are involved in atherosclerosis, IR seems to have an important role in plaque formation and progression of ED [5]. IR has been related to decreased nitric oxide production and vasodilatation both of which play a role in the pathogenesis of ED [6]. Men with ED have been shown to have higher levels of homeostatic model assessment insulin resistance (HOMA-IR) index which is the most popular method for the assessment of IR [7]. However, this test is relatively expensive and requires measurement of both serum insulin and glucose levels, which has led researchers to search for alternative methods. Triglyceride-glucose index (TyG index), the calculation of which is based on the measurements of serum triglyceride (TG) and glucose levels, is an easily obtainable and reliable marker for IR. The prognostic utility of the TyG index has been shown in acute coronary syndrome, lower extremity peripheral artery disease, heart failure, fatty liver disease, and stable coronary artery disease [8-12]. In the present study, we aimed to evaluate the TyG indexes of the ED patients and to find whether the TyG index has any predictive value in diagnosing ED.

Material and Methods

We retrospectively screened data files of the patients who were referred from the urology clinic to the cardiology outpatient clinic of a tertiary hospital between January 2022 and January 2023. One hundred sixty patients constituted our study population. Patients who had a history of percutaneous coronary artery intervention, coronary artery bypass graft operation, diabetes mellitus, peripheral arterial disease, liver failure, renal failure, malignancy, thyroid abnormalities, and hypertension were excluded. Patients were referred from the urology department for the purpose of cardiovascular evaluation. All patients gave informed consent for study participation. The study was approved by the local ethics committee (date: 06.03.2023, decision #: 2023-05-15) and conducted in compliance with The World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects.

Diagnosis of ED was made by using the International Index

of Erectile Function-5 (IIEF-5) questionnaire. The questionnaire consists of five Likert-type questions which are scored from one to five, while one point represents severe disease whereas five points indicate normal sexual function. According to the scores obtained by the patients in this questionnaire, the severity of ED was classified into groups of severe (5-7 pts), moderate (8-11 pts), mild-to-moderate (11-16 pts), and mild ED (17-21 pts), while scores ≥ 22 points indicated normal erectile function. Turkish validation of this questionnaire was made by Turunç et al [13]. Patients who had IIEF-5 scores between 1 and 21 constituted the study group (n=106) and the participants who had IIEF-5 scores between 22 and 25 constituted the control group (n=54).

For fasting blood tests blood samples were taken from the antecubital vein in a sitting position. Collected samples were analyzed for biochemical (AU 2700, Beckman Coulter Inc., California, USA) and complete blood count parameters (Sysmex XE 5000, Sysmex Medical Int., Kobe, Japan). TyG index of each patient was calculated as the natural logarithm of the product of plasma glucose and TG using the following formula: $\text{fasting glucose value (mg/dL)} \times \text{fasting triglyceride value (mg/dL)} / 2$. Cardiovascular status of the patients was evaluated based on the results of physical examinations, electrocardiograms, and treadmill exercise tests. Medications that influenced heart rate were stopped two days before the exercise test which was performed by using Schiller CS-200, Switzerland device.

Statistical Analysis

Normality of the data was assessed by examining skewness, kurtosis of the data and by use of Kolmogorov-Smirnov test. Since all data showed nonparametric distribution, comparison of two groups was done using Mann-Whitney U test. Categorical data were compared by chi-square test. Quade ANCOVA test was used to compare TyG values of the two groups where age was used as a covariate. Correlations between TyG indexes and IIEF-5 scores were performed using Spearman correlation analysis. ROC curve analysis was conducted to find the cut-off value of TyG index in predicting patients who had mild-to-moderate, moderate, and severe ED. Univariate logistic regression analysis was conducted to determine the variables that have a predictive value in diagnosing ED. A p value of less than 0.05 was considered statistically significant. All statistical analyses were conducted by using SPSS Statistics for Windows, Version 25.0 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM, USA).

Results

The mean age of the study population was 44.24 ± 7.29 years including 70 (43.8%) smokers, and 41 (25.6%) alcohol users. There were no differences between the two groups in terms of the prevalence of smoking, alcohol consumption, high-density lipoprotein-cholesterol (HDL-C), hemoglobin, creatinine concentrations, leukocyte, and platelet counts. ED patients were older and had higher total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), glucose and triglyceride concentrations, and TyG indexes. According to Quade ANCOVA

results, the TyG indexes were higher in ED patients when age was used as a covariate ($t=-1.876$, $p=0.045$). The clinical characteristics of the two groups are shown in **Table 1**. IIEF-5 scores showed a negative correlation with TyG indexes ($r=-0.273$, $p=0.001$).

A total of 37 patients had IIEF-5 scores under 17 points indicating the presence of mild-to-moderate, moderate, and severe ED. ROC curve analysis showed that cut-off value of 9.03 for TyG index had 70.3% sensitivity and 65% specificity in predicting mild-to-moderate, moderate, and severe ED (AUC: 0.729, $p<0.001$, 95% CI: 0.634-0.856) (**Figure 1**). Univariate logistic regression analysis showed that age, TC, LDL-C, and TyG index were the variables that had predictive values for the identification of patients who had mild-to-moderate, moderate, and severe ED (**Table 2**).

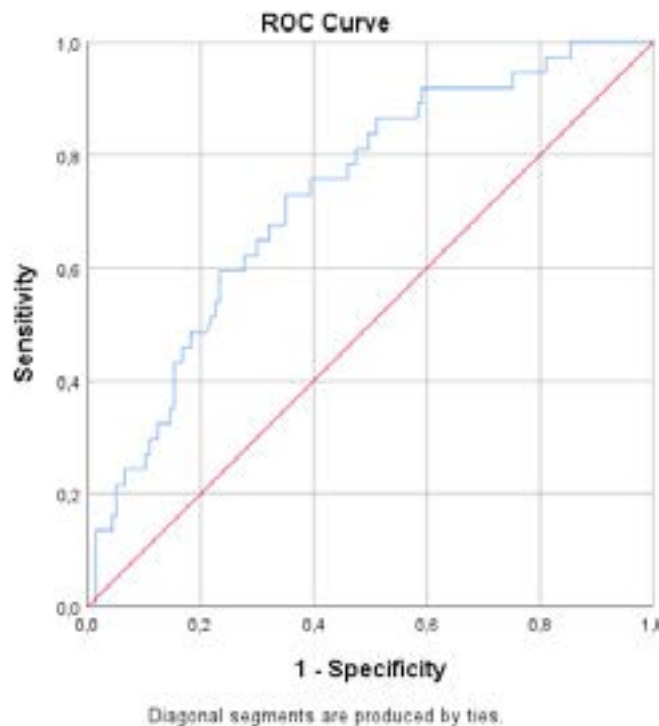


Figure 1. ROC curve analysis of TyG index for predicting mild-moderate, moderate and severe ED

Table 1. Clinical and demographic characteristics of the study and control groups

	Study group (n=106) (IIEF-5 score ≤ 21)	Control group (n=54) (IIEF-5 score ≥ 22)	P value
Age (years)	46.35 \pm 6.95 46 (42-51.25)	40.11 \pm 6.12 39 (35.75-44)	<0.001
Smoking (n, %)	44 (41.5)	26 (48.1)	0.423
Alcohol (n, %)	24 (22.6)	17 (31.5)	0.231
Total cholesterol (mg/dL)	206.92 \pm 92 207 (177-234)	173.19 \pm 36.28 162 (148-198.25)	<0.001
HDL-C (mg/dL)	47.26 \pm 19.45 44 (38-49)	50.04 \pm 23.09 42 (37-54)	0.937
LDL-C (mg/dL)	130.11 \pm 37.24 131.9 (101.25-154.25)	102.74 \pm 33.07 96 (80.25-119.3)	<0.001
Triglyceride (mg/dL)	163.85 \pm 87.95 143 (99.5-200.25)	137.12 \pm 77.79 101 (78.5-189.25)	0.026
Glucose (mg/dL)	109.39 \pm 12.35 111.5 (104-117)	103.41 \pm 5.93 103 (99.75-105)	0.036
Hemoglobin (g/dL)	14.73 \pm 1.26 15 (14-15)	14.40 \pm 2.20 15.4 (12.2-16)	0.956
Leukocyte count ($10^9/L$)	9.99 \pm 4.83 8.5 (6-14.25)	8.27 \pm 3.67 9 (4-11)	0.244
Platelet count ($10^9/L$)	247.49 \pm 71.16 235 (197-294)	234.61 \pm 71.20 241 (210.75-276)	0.973
Creatinine (mg/dL)	1.13 \pm 0.4 1.0 (0.72-0.99)	1.02 \pm 0.5 1.0 (0.8-1.00)	0.769
TyG index	8.95 \pm 0.56 9.00 (8.55-9.30)	8.52 \pm 0.53 8.61 (8.25-9.16)	0.003

HDL-C: high density lipoprotein-cholesterol; LDL-C: low density lipoprotein-cholesterol; TyG index: triglyceride-glucose index

Table 2. Univariate logistic regression for prediction of mild-to-moderate, moderate and severe disease

	P value	OR	95% CI
Age	<0.001	1.168	1.098-1.231
Total cholesterol	<0.001	1.027	1.013-1.043
LDL-C	<0.001	1.045	1.014-1.039
TyG index	<0.001	1.829	1.012-3.281

LDL-C: low density lipoprotein-cholesterol; TyG index; triglyceride-glucose index

Discussion

Our study has shown that the TyG index is an independent predictor for the presence of ED. Moreover, it had a negative correlation with IIEF-5 scores, with higher values indicating lower IIEF-5 scores. Besides TyG index, parameters of age, TC, and LDL-C were predictors for ED.

Although the HOMA-IR index is widely used in clinical practice, its calculation is based on the measurement of glucose and insulin concentrations. In contrast, the TyG index is calculated as the natural logarithm of the product of fasting plasma glucose and TG concentrations, both of which can be easily measured and evaluated [14]. Studies have shown that the TyG index is a valuable tool for measuring IR, making it a good alternative to the HOMA-IR index [15,16].

Previous studies evaluated the role of IR in ED and found that IR was associated with ED. Chen et al. demonstrated that insulin resistance correlated with the severity of ED. In that study, patients who had IR had decreased testosterone concentrations and deteriorated endothelial functions emphasizing the pathophysiological link between IR and ED [17]. Similarly, Rey-Valzacchi et al. showed that the addition of metformin treatment to sildenafil decreased the IR and ameliorated the ED in patients with IR [18]. Yilmaz et al. investigated the value of the TyG index in ED patients and found that the cut-off value of 8.88 for the TyG index predicted ED with sensitivity and specificity of 67% and 68.8%, respectively [19]. Li et al. evaluated National Health and Nutrition Examination Survey database to expose the link between the TyG index and ED in general population. They found that the prevalence of ED was increased in subjects who had higher TyG indexes [20]. IR is considered a predictor of prediabetes, and progression to diabetes is associated with the atherosclerotic process [17]. It has been shown that patients with IR had increased levels of sympathetic activity, endothelin-1 concentration, oxidative stress, inflammatory activity, and impaired endothelial function; all of which are thought to play a role in ED [21,22]. Our study was in line with the aforementioned studies in that we also detected higher TyG indexes in ED patients supporting the role of IR in the pathogenesis of ED. In our study, cut-off value of 9.03 for TyG index had 70.3% sensitivity and 65% specificity in predicting the presence of ED. In our study, no patient had a history of ischemic heart disease and all of them had negative treadmill exercise tests.

Although no patient in the current study had a history of ischemic heart disease and cardiovascular risk factors, patients

with ED had unfavorable metabolic profiles including increased levels of LDL-C, TC, glucose, triglyceride concentrations, and TyG index values, all of which have been shown to be related to endothelial dysfunction [23]. Patients with ED were older, however, age-adjusted TyG indexes have remained at a higher level in ED patients.

As the limitations of the study; our study was a single-center, retrospective study and the sample size was relatively small.

Long-term follow-up of the patients was not done and the effect of lifestyle and medical interventions on TyG index and ED was not assessed.

Conclusion

TyG index, an easily calculable and effective method for assessing IR, had a predictive role in patients with ED. It could be used in clinical practice to evaluate the cardiovascular status of ED patients.

Ethics Committee Approval: The protocol of the present study was reviewed and approved by the Institutional Review Board of University of Health Sciences Dr. Sadi Konuk Training and Research Hospital (date: 06.03.2023, decision #: 2023-05-15).

Informed Consent: An informed consent was obtained from all the patients.

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