Evaluation of the Relationship Between Saphenous Vein Graft Disease and Triglyceride Glucose Index

Safen Ven Greft Hastalığı ile Trigliserit Glukoz İndeksi Arasındaki İlişkinin Değerlendirilmesi

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ABSTRACT

Aim: *It is known that insulin resistance, one of the main components of metabolic syndrome, is associated with endothelial dysfunction and related diseases. Insulin resistance can be evaluated by HOMA-IR and indirectly by triglyceride-glucose (tg-glucose) index. We aimed to investigate the relationship between saphenous vein graft disease (SVGD) and tg-glucose index.*

Material and Method: *418 patients who underwent coronary angiography in our clinic between January 2019 and December 2020 and had a history of coronary artery bypass grafts were included retrospectively. The patients were divided into two as those with 50% or more stenosis in at least one of their SVG (SVGD group) and those without (control group). Tg-glucose index was calculated by the formula ln (fasting tg X fasting glucose/2). A value of P<0.05 was considered statistically significant.*

Results: *The mean age of 185 patients in the SVGD group was 67.3±4.3 (25.9% female), and the mean age of 233 patients in the control group was 66.4±8.2 (25.7% female). The ejection fraction values of the patients in the SVGD group were lower than the control group (51.6±9.0% & 55.9±6.5, p<0.001) and serum creatinine, CRP, triglyceride, glucose and tg-glucose index values were higher (p=0.041, p=0.003, p<0.001, p<0.001 and p<0.001, respectively). In multivariate logistic regression analysis, low EF, high serum triglyceride and glucose values and tg-glucose index were found to be associated with SVGD. Pairwise comparison of ROC curve analysis revealed that tg-glucose index had better performance than glucose or triglyceride levels to predict SVGD.*

Conclusion: *Tg-glucose index is a biomarker that can be calculated from routine biochemistry tests and can give better results than serum glucose and triglyceride values in predicting SVGD.*

Key words: *coronary artery bypass; saphenous vein graft; triglyceride-glucose index*

ÖZET

Amaç: *Metabolik sendromun ana bileşenlerinden biri olan insülin direncinin endotel disfonksiyonu ve ilişkili hastalıklar ile bağlantılı olduğu bilinmektedir. İnsülin direnci HOMA-IR ve indirekt olarak da trigliserit-glukoz (tg-glukoz) indeksi ile değerlendirilebilmektedir. Bu çalışmanın amacı, safen ven greft hastalığı (SVGH) ile tg-glukoz indeksi arasındaki ilişkiyi araştırmaktır.*

Materyal ve Metot: *2019–2020 yıllarında kliniğimizde koroner anjiyografi yapılan ve koroner arter bypass greft öyküsü olan 418 hasta çalışmaya retrospektif olarak dahil edildi. Hastalar SVG'lerinden en az birinde %50 veya fazla darlık olanlar (SVGH grubu) ve olmayanlar (kontrol grubu) şeklinde ikiye ayrıldı. Tg-glukoz indeksi ln (açlık tg X açlık glukoz/2) formülü ile hesaplandı. P<0,05 değeri istatistiksel olarak anlamlı kabul edildi.*

Bulgular: *SVGH grubundaki 185 hastanın yaş ortalaması 67,3±4,3 (%25,9 bayan), kontrol grubundaki 233 hastanın yaş ortalaması 66,4±8,2 (%25,7 bayan) idi. SVGH grubundaki hastaların ejeksiyon fraksiyonu değerleri kontrol grubuna göre daha düşükken (%51,6±9,0 & %55,9±6,5, p<0,001); serum kreatinin, CRP, trigliserit, glukoz ve tg-glukoz indeksi değerleri daha yüksekti (sırasıyla; p=0,041, p=0,003, p<0,001, p<0,001 ve p<0,001). Çok değişkenli lojistik regresyon analizinde düşük EF, yüksek serum trigliserit ve glukoz değerleri ile tg-glukoz indeksi SVGH ile ilişkili bulundu. ROC eğrisi analizinin ikili karşılaştırması, tg-glukoz indeksinin SVGH'yi tahmin etmek için glukoz ve trigliserit değerlerine göre daha iyi performansa sahip olduğunu ortaya koydu.*

Sonuç: *Tg-glukoz indeksi rutin biyokimya tetkiklerinden hesaplanabilen, SVGH'nı öngörmede serum glukoz ve trigliserit değerlerinden daha iyi sonuç verebilecek bir biyobelirteçtir.*

Anahtar kelimeler: *koroner arter bypass; safen ven grefti; trigliserit-glukoz indeksi*

Introduction

There are studies showing that chronic inflammatory process is effective in the development of insulin resistance[1–3]. It is known that insulin resistance triggers endothelial dysfunction by increasing oxidative stress and causes dyslipidemia by affecting lipid metabolism[4,5].

The process consisting of endothelial dysfunction, dyslipidemia and chronic inflammation is the basis of atherosclerosis[6,7]. Therefore, insulin resistance is associated with coronary artery disease both directly and indirectly. Determining whether the host has insulin resistance and its level is also important in terms of the treatment approach. The fact that it is a calculable parameter from laboratory data has made the use of HOMA-IR widespread in daily practice[8,9]. Apart from the HOMA-IR level, the tg-glucose index, which can be calculated using serum triglyceride and glucose levels, can indirectly provide information about insulin resistance[10]. It has been shown to be associated with atherosclerosis better than HOMA-IR[11].

SVGs, which are widely used in coronary artery bypass surgery, can remain less patented than arterial grafts due to the peculiar characteristics of the venous system[12]. It has been shown that 60% of saphenous grafts remained patents after 10 years, and 50% of them had severe stenosis[13]. Thrombosis, intimal hyperplasia and atherosclerosis are involved in the pathogenesis of vein graft disease. While the frequency of thrombosis is high in the early postoperative period, atherosclerosis plays a dominant role in the later period[14]. It is known that insulin resistance is effective in the development of atherosclerosis, and it has been shown that the risk can be reduced with treatments that reduce insulin resistance[15]. The aim of this study is to investigate the relationship between tg-glucose index, which can give information about the insulin resistance, and SVGD.

Material and Methods

418 patients who underwent coronary angiography in our clinic between January 2019 and January 2021 and had a history of coronary artery bypass graft were included in the study. Patients were divided into two groups: those with 50% or more stenosis in at least one of the saphenous vein grafts as the SVGD group, and those without stenosis as the control group. Systolic heart failure, left ventricular ejection fraction <40% ; Hypertension was defined as patients' systolic and diastolic blood pressure >140/90 mmHg or the patient's use of any anti-hypertensive medication. Diabetes mellitus (Type 2 DM) was defined as having a previous diagnosis of DM or using anti-diabetic medication or a fasting blood glucose >126 mg/dL or HbA1 c >6.5%. At least 8-hour fasting venous blood samples were taken from the patients and analyzed using appropriate methods. Routine biochemistry, complete blood values, and lipid profile results were recorded. Tg-glucose index was calculated using the formula ln (fasting tg X fasting glucose/2). Patients with a diagnosis or suspicion of coronavirus-19, hematological disease or malignancy, chronic liver failure, autoimmune disease, and rheumatological disease or incomplete laboratory results were excluded from the study.

The study was approved by the local Clinical Research Ethics Committee of our hospital (20.5.2021/1412) and the study protocol was prepared in accordance with the ethical rules of the 1975 Helsinki Declaration.

Statistical Analysis

All statistical analyses were performed with SPSS 17 (SPSS, Inc., Chicago, Illinois, USA) and MedCalc v. 19.6.1. Continuous variables were exoressed as mean ± standard deviation (mean ± SD) or median (interquartile range); categorical variables were expressed as numbers and percentages. Comparison of continuous variables between groups was performed using t-test and Mann-Whitney U test or the χ^2 test or Fisher's Exact test for categorical variables. Whether the continuous variables had a normal distribution was analyzed using the Shaphiro-Wilk test. Variables with a p value of ≤0.01 in the univariate analysis were included in the multivariate analysis. Results are expressed as relative risk and 95% confidence interval (CI). A p value of less than 0.05 was considered statistically significant.

Results

The mean age of the patients included in the study was 66.8±6.7 (74.1% male). 185 patients with 50% or more stenosis in at least one of the saphenous vein grafts were included in the SVGD group, and 233 patients without stenosis were included in the control group. There was no statistically significant difference between SVGD group and control group in terms of basal demographic characteristics. The mean ejection fraction values of the patients in the SVGD group were lower than the control group (51.6±9.0% & 55.9±6.5, p<0.001); serum creatinine, CRP, triglyceride, glucose and tg-glucose index values were found to be higher than the control group (p=0.041, p=0.003, p<0.001, p<0.001 and p<0.001, respectively). The demographic characteristics of the patients included in the study and the comparison of laboratory results are summarized in Table 1.

Multivariate regression analysis (Model 1) in which triglyceride, glucose values and other variables were taken and another regression analysis (Model 2) in which triglyceride and glucose values were excluded and other variables were taken with Tg-glucose index were used to analyze variables that could predict SVGD. According to Model 1, low ejection fraction, serum triglyceride and glucose values were found to be predictors for SVGD; In model 2, tg-glucose index and again low ejection fraction were found to be associated with SVGD (Table 2).

Table 1. *Comparison of demographic properties and laboratory results of groups*

	SVGD group (n=185)	Control group (n=233)	p
Age, years	67.3±4.3	66.4±8.2	0.237
Female, n (%)	48 (25.9)	60 (25.7)	0.985
Diabetes Mellitus, %	57	56.8	0.999
Hypertension, %	71.8	73	0.836
ESRD or GFR ≤45 ml/min/1.73 m^2, %	4.2	3.2	0.726
Systolic BP, mm Hg	127.4±17.3	122.9±12.4	0.108
Diastolic BP, mm Hg	78.8±9.7	74.0±8.3	0.497
LVEF, %	51.6±9.0	55.9±6.5	0.001
Hemoglobin, g/dL	13.2±1.8	13.1±1.8	0.646
WBC, 10^3/mL	8.4±2.1	8.5±2.0	0.529
PLT, 10^3/mL	232.2±66.5	238.1±62.2	0.356
Glucose, mg/dL	162.9±71.1	123.2±41.5	<0.001
Urea, mg/dL	42.3±17.6	38.6±14.2	0.186
Creatinine, mg/dL	1.0±0.7	0.9±0.4	0.041
LDL, mg/dL	126.9±35.5	124.8±35.0	0.545
HDL, mg/dL	38.6±8.2	39.2±7.3	0.481
Triglyceride, mg/dL	210.1±105.2	170.1±97.8	<0.001
CRP, median (IQR)	5.6 (14.5)	2.5 (5.6)	0.003
Tg-glucose index	5.1±0.2	4.8±0.2	<0.001
Albumin, g/dL	3.8±0.4	3.8±0.3	0.146
Acetylsalicylic acid,%	80.8	85.7	0.335
Statin, %	62.7	63.4	0.912
Beta blocker, %	86.1	86.5	0.942
ACEI/ARB, %	77.6	69.8	0.195

ACEI, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blockers; BP, blood pressure; CRP, C-reactive protein; ESRD, end stage renal disease; GFR, glomerular filtration rate; HDL, high density lipoprotein cholesterol; LDL, low density lipoprotein cholesterol; LVEF, left ventricle ejection fraction; Tg, triglyceride; PLT, platelets; WBC, white blood cell count.

Table 2. *Univariate and multivariate regression analysis*

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p	OR (95% CI)	p
Glucose	1.013 (1.009–1.017)	<0.001	1.013 (1.006–1.019)	<0.001*
Triglyceride	1.004 (1.002–1.006)	<0.001	1.006 (1.002–1.009)	0.002*
EF	0.933 (0.900–0.968)	<0.001	0.927 (0.888–0.967)	<0.001**
CRP	1.017 (1.017–1.029)	0.004	1.004 (0.980–1.029) –	0.726
Creatinine	1.646 (1.067–2.539)	0.024		
Tg-glucose index	25.03 (10.77–58.13)	<0.001	48.86 (14.05–169.91)	<0.001**

CRP, C-reactive protein; EF, ejection fraction; Tg, triglyceride.
* Model 1: EF, triglyceride, glucose, CRP.
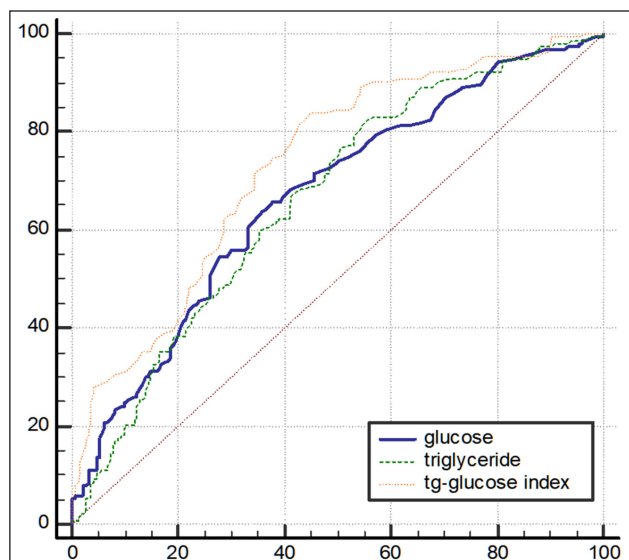** Model 2: EF, tg-glucose index, CRP.

Figure 1. *ROC curve analysis of glucose, triglyceride and tg-glucose index.*

Pairwise comparison of ROC curve analysis showed that the predictive power of tg-glucose index of SVGD was better than serum triglyceride and glucose levels (tg-glucose index and glucose: difference between area under curve [AUC]: 0.0650, SE: 0.0310, z statistics 2.097 and p=0.0360; tg-glucose index and triglyceride: difference between AUC: 0.0700, SE: 0.0237, z statistics: 2.954 and p=0.0031; triglyceride and glucose: difference between AUC: 0.00492, SE: 0.0426, z statistics 0.115 and p=0.9081) (Fig. 1).

Discussion

The most important results of this study are; 1) Insulin resistance is associated with coronary artery disease, and this relationship is also valid for SVGD, 2) The risk of stenosis in SVGs of patients with low ejection fraction is higher than those with normal EF, 3) Serum triglyceride and glucose values and tg-glucose index, which is a biomarker calculated using serum triglyceride and glucose levels and gives information about insulin resistance, was found to be higher than control patients, 4) Tg-glucose index was better than serum glucose and triglyceride levels in predicting SVGD in ROC curve analysis, 5) Tg-glucose index which can be calculated using routine biochemistry studies, is associated with SVGD and is a biomarker that can be used to determine the SVGD in daily practice.

Insulin resistance is a condition that may result in type 2 DM, coronary artery disease, polycystic ovary syndrome, metabolic syndrome, and obesity-related malignancy[16]. Insulin resistance, which is assumed to be chronic inflammation in pathogenesis, leads to the formation of a vicious circle as it leads to an increase in the inflammatory process. Its relationship with coronary artery disease can be explained by the fact that increased serum glucose and insulin levels trigger oxidative stress and cause dyslipidemia due to its effect on lipid metabolism[17]. Nitric oxide (NO), which is known to be an important vasodilator and anti-oxidative molecule, stimulates glucose transport in muscle and adipose tissue and increases glucose oxidation while reducing hepatic glycogen synthesis. In insulin resistance state, the NO synthesis stimulated by insulin is selectively impaired[18]. In patients with a high Tg-glucose index, arterial stiffness was also detected higher and this indicates that the level of nitric oxide in this group may be lower[19]. In addition, the level of ntric oxide is inversely related to the severity of the disease in patients with acute coronary syndromeand the fact that it was found to be even lower in those who underwent coronary bypass compared to those who underwent percutaneous intervention; suggests that the triglyceride glucose index may be higher in these patients[20]. SVGD develops on the basis of thrombosis or intimal hyperplasia in the early postoperative period and atherosclerosis in the period after 1 year. Therefore, it is possible to think that risk factors of atherosclerosis such as DM, HT, smoking and age are also valid for SVGD.

Within 10 years after coronary artery bypass operation using SVG, up to 20% of patients need revascularization[21]. Lesions and restenosis evaluated as noncritical in coronary angiography cause chronic angina in most of the patients. Although DM, which is a major risk factor for atherosclerosis, has been identified as an independent risk factor for SVGD in some studies, there are also studies suggesting that this theory is not valid[22,23]. In our study, patients in the group with and without SVGD were found to be similar in terms of the frequency of DM. The thesis that high blood glucose level is inversely related to SVG patency, whether DM is diagnosed or not, was also demonstrated in our study.

Kubiak et al. found that patients with SVG stenosis had a lower ejection fraction in the study in which optical coherence tomography was used[24]. Our study also supports these results.

The relationship between high serum LDL and low HDL and SVGD has been emphasized in studies[25,26].

The results of our study do not support these data. In obtaining these results; it should be kept in mind that the LDL levels of the patients in both groups were above the targeted value and that the rate of statin use was 63%. The result that the frequency of SVGD is higher in patients with high triglycerides compared to the control group was also shown in our study.

Tg-glucose index is a biomarker that can be calculated from routine biochemistry tests and can provide indirect information about insulin resistance. The fact that the insulin level can be calculated according to the HOMA-IR value without the need increases the usability rate of this index. The relationship of high tg-glucose index with the presence, severity and prognosis of coronary artery disease has been demonstrated in many studies. Mao et al. conducted a study of 791 non-ST elevation acute coronary syndrome patients and followed all patients for 12 months and showed that high tg-glucose index was a risk factor for the development of major cardiovascular events[27]. Another study in which 2840 patients evaluated with coronary computed tomographic angiography were included. In the study, it was found that the tg-glucose index was associated with coronary artery disease[28].

Our study also shows that the tg-glucose index is significantly higher in patients with SVGD compared to controls and is better in predicting the disease than glucose and triglyceride levels.

This study has multiple limitations such as being single centered and retrospective. The HOMA-IR level could not be calculated because the insulin level was not routinely studied in the patients, and the tg-glucose index and the HOMA-IR level could not be compared. The data in our study should be supported by prospective, multicenter and studies including comparative results.

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