Triglyceride glucose index as a marker of primary patency rate of arteriovenous fistula in diabetic hemodialysis patients

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Abstract. – OBJECTIVE: Arteriovenous fistula (AVF) structures are vital formations used for hemodialysis. Diabetes mellitus (DM) is a critical disease affecting the vascular system. The triglyceride glucose (TyG) index has been shown to be associated with major adverse cardiovascular events in patients with Type 2 DM. In this study, we aimed to investigate the effect of the TyG index on the primary AVF patency of diabetic patients.

PATIENTS AND METHODS: Between March 2018 and March 2023, patients with DM who underwent AVF surgery in our clinic due to end-stage renal disease were retrospectively included in this study. The patients who could receive hemodialysis were determined as Group 1, and those who could not were determined as Group 2.

RESULTS: A total of 189 patients were included in the study. Those who did not develop AVF primary failure were included in Group 1 [n=138, median age = 59 (22-77) years], and those who did were included in Group 2 [n=51, median age = 63 (20-81) years]. In the multivariate analysis, age >70 years (OR: 0.871, 95% CI: 0.594-0.983, p=0.039), the presence of PAD (OR: 0.582, 95% CI: 0.0.458-0.896, p=0.046), and TyG index (OR: 0.879, 95% CI: 0.591-0.916, p<0.001) were determined as independent predictors for primary AVF failure.

CONCLUSIONS: This study demonstrated that the TyG index value, calculated from blood samples taken at the time of hospital admission in hemodialysis patients with diabetes mellitus (DM), is an independent predictor of primary AVF failure following AVF surgery.

Key Words:
    Diabetes mellitus, Renal insufficiency, Hemodialysis, Glucose, Hyperlipidemia.

Introduction

Due to an increasing world population and elderly population, the number of patients with end-stage renal disease is increasing. Hemodialysis is of vital importance for these patients[1]. Arteriovenous fistula (AVF) structures are vital formations used for hemodialysis: they have fewer risks of infection and higher patency compared to arteriovenous connections made with hemodialysis catheters and grafts. Many factors, in particularly the vascular structure, can affect primary AVF patency[2].

Diabetes mellitus (DM) is a critical disease affecting the cardiovascular system, and the risk of developing kidney failure increases in these patients. Another significant problem affecting this patient group is the substantial decrease in primary patency rates of AVFs, which are frequently seen in diabetic patients compared to non-diabetic patients[3]. Various studies[4,5] have investigated the effects of some inflammatory markers on primary AVF patency. The triglyceride glucose (TyG) index is an important marker of insulin resistance and has been shown to be associated with major adverse cardiovascular events in patients with Type 2 DM[6]. In addition, one study[7] showed that this index is associated with diabetic kidney disease in Type 2 DM patients. In this current study, we aimed to investigate the effect of the TyG index on primary AVF patency of diabetic patients.

Patients and Methods

Patients with DM who underwent AVF surgery in our clinic due to end-stage renal disease between March 2018 and March 2023 were retrospectively included in this study. The data of the patients were obtained from the hospital registry system and patient files. Demographic data, preoperative blood parameters, and operative data of all patients were

recorded. Patients using antilipidemic drugs, patients with a hematological disease, patients with active malignancy, and patients with AVF in the same extremity were excluded from the study. Radiocephalic AVF in the distal arm, brachiocephalic AVF in the proximal arm, and anastomosis with the end-to-side suture technique were preferred. Patients with both arterial and vein diameters of at least 2 mm were included in the study. After the exclusion criteria, some 189 consecutive patients were included in the study. All patients included in the study had a post-operative thrill at the anastomotic line. Within three months after the operation, patients who successfully received hemodialysis from the AVF were determined as Group 1. In addition, AVF primary patency was also evaluated by Doppler ultrasonography, (Toshiba USDI709A, 7.5 mHz linear color Doppler probe) and the maturation patency in this evaluation was determined according to the flow rate and diameter[8]. The patients who could not receive hemodialysis for various reasons (thrombosis, insufficient flow) from the AVF opened within the specified time were determined as Group 2.

TyG Index Calculation

The blood parameters of all patients were evaluated using blood samples taken from their peripheral veins during hospitalization before the AVF operation. These evaluations were made on automatic analyzers (Coulter LH 780 Analyzer, CA, USA). Accordingly, the TyG index was calculated as follows: TyG index[9]= ln [fasting TG (mg/dL) x fasting glucose (mg/dL)/2].

Statistical Analysis

In this study, statistical analyses were performed using the SPSS Statistics for Windows (version 21.0, IBM Corp. Armonk, NY, USA). The p-values obtained in the test results were considered significant at <0.05. Mean and standard deviations were calculated for continuous and ordinal data using the descriptive methods. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to evaluate normality distribution. Student's t-test and the Mann-Whitney U test were used to assess normally and non-normally distributed data, respectively. Frequency and percentage analysis were conducted for nominal data, compared with the Chi-square test. Multivariate regression analysis was performed to show the effects of the TyG index on primary AVF maturation. A receiver-operating characteristic (ROC) curve analysis was performed for the TyG index to predict the primary AVF patency rate, and the area under the curve (AUC) was calculated.

Results

A total of 189 patients were included in the study. Those who did not develop AVF primary failure were included in Group 1 [n=138, median age = 59 (22-77) years], and those who did were included in Group 2 [n=51, median age = 63 (20-81) years]. While the male gender ratio was 61.6% (n=85) in Group 1, it was 70.6% (n=36) in Group 2. There were no statistically significant differences between the two groups in terms of age, gender, presence of hypertension (HT), cerebrovascular event/trans-ischemic attack history, body mass index, and smoking rates. Also, AVF locations were similar between the two groups (p=0.176) (Table I).

The preoperative blood values of the patients are shown in Table I. The two groups were similar in terms of white blood cells, hemoglobin, platelet, fasting blood glucose, HbA1c, C reactive protein, HDL-C, Triglyceride, and total cholesterol levels. TyG index and LDL-C were statistically significantly higher in Group 2 (p<0.004 and p=0.035).

Logistic regression analysis was performed to reveal the factors affecting primary AVF patency (Table II). In univariate analysis, primary AVF maturation failure was found to significantly correlate with age >70 (odds ratio [OR]: 1.126, 95% confidence interval [CI]: 1.086-1.269, p=0.022), presence of peripheral arterial disease (PAD) (OR: 0.794, 95% CI: 0.690-0.887, p=0.029), LDL-C (OR: 0.559, 95% CI: 0.342-0.740, p=0.039), and TyG index (OR: 1.176, 95% CI: 1.096-1.715, p<0.001). In the multivariate analysis age >70 years (OR: 0.871, 95% CI: 0.594-0.983, p=0.039), the presence of PAD (OR: 0.582, 95% CI: 0.0.458-0.896, p=0.046), and TyG index (OR: 0.879, 95% CI: 0.591-0.916, p<0.001) were determined as independent predictors for primary AVF failure.

For predicting primary AVF failure, the cutoff level in the ROC curve analysis was 9.2 for TyG index (AUC: 0.854, 95% CI: 0.797-0.911, log-rank p<0.001, 86.3% sensitivity and 68.9% specificity) (Figure 1).

Table I. Demographic characteristics and blood parameters of the patients.

Variables	Group 1 n=138	Group 2 n=51	*p*
Age, years	59 (22-77)	63 (20-81)	0.156
Male gender, n (%)	85 (61.6%)	36 (70.6%)	0.253
Smoking, n (%)	53 (38.4%)	21 (41.2%)	0.729
Hypertension, n (%)	107 (77.5%)	42 (82.4%)	0.472
BMI, kg/m^2	24.3 (18.9-33.8)	23.6 (17.9-34)	0.382
PAD, n (%)	26 (18.8%)	17 (33.3%)	0.035
CAD, n (%)	21 (15.2%)	11 (21.6%)	0.301
White blood cell, (10^3/μL)	6.8 (4.3-12.1)	6.9 (4.1-11.7)	0.338
Hemoglobin, mg/dL	9.9 (8.3-12.7)	9.6 (8.7-11.9)	0.441
Platelet (10^3/μL)	182 (86-246)	185 (79-228)	0.615
Fasting blood glucose, (mg/dL)	144 (129-376)	159 (121-508)	0.024
HbA1c	7.2 (6.7-9.8)	7.4 (6.6-9.6)	0.239
CRP, mg/dL	2 (1-18)	3 (2-13)	0.414
HDL-C, mg/dL	44 (26-45)	41 (27-38)	0.196
LDL-C, mg/dL	127 (75-194)	132 (84-183)	0.035
Triglyceride, mg/dL	134 (108-336)	147 (100-350)	0.161
Total cholesterol, mg/dL	198 (114-325)	204 (109-338)	0.095
TyG index	8.7 (6.6-10.8)	9.9 (7.1-11.6)	<0.001
Location of AVF			0.176
Brachiocephalic, n	28	6	
Radiocephalic, n	110	45	

BMI: body mass index, PAD: peripheral artery disease, HbA1c: glycated hemoglobin, CRP: C-reactive protein, HDL: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, BUN: blood urea nitrogen, TyG: triglyceride glucose, AVF: arteriovenous fistula.

Discussion

In patients receiving hemodialysis, arteriovenous fistulas are very important in terms of patient comfort, less risk of infection, and long-term use. However, maturation problems may occur after AVF operations. The most important factor in this problem is thrombosis due to insufficient vascular remodeling and intimal hyperplasia[10]. Patients with DM constitute a special patient group in hemodialysis patients undergoing AVF operation, as in many other cases. To the best of our knowledge, this current study is the first in the literature to reveal the negative effect of TyG index value on primary AVF patency. In addition to this contribution, we showed that being over 70 years of age and the presence of PAD are independent predictors of primary AVF patency failure.

DM is an important disease that affects vascular structures. In these patients, vasodilation disorder and increased thrombogenicity occur as a result of endothelial dysfunction[11]. Neointimal hyperplasia arising in the vascular bed is the most common complication of diabetes-related intima and is a result of intimal hyperplastic remodeling.

Table II. Binary logistic regression analysis to predict primary arteriovenous fistula maturation failure.

Variables	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	*p*	Odds ratio	95% CI	*p*
Age>70 years	1.126	1.086-1.269	0.022	0.871	0.594-0.983	0.039
Male gender	1.441	0.789-1.745	0.237	--	--	--
Hypertension	1.090	0.890-1.238	0.496	--	--	--
PAD	0.794	0.690-0.887	0.029	0.582	0.458-0.896	0.046
LDL-C	0.559	0.342-0.740	0.039	1.190	0.885-1.449	0.258
HbA1c	1.641	0.933-2.875	0.392	--	--	--
TyG index	1.176	1.096-1.715	<0.001	0.879	0.591-0.916	<0.001

PAD: peripheral artery disease, LDL-C: low-density lipoprotein cholesterol, HbA1c: glycated hemoglobin, TyG: triglyceride glucose.
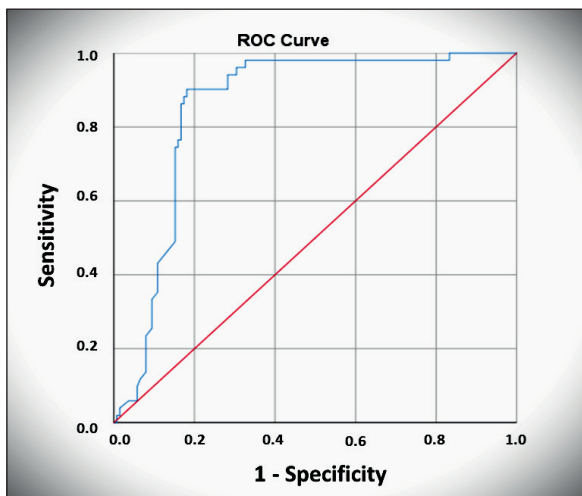
Figure 1. ROC and AUC for TyG index for predicting primary arteriovenous fistula patency (cut-off: 9.2, AUC: 0.854, 95% CI: 0.797-0.911, *p*<0.001, 86.3% sensitivity and 68.9% specificity).

Jeon et al[1] aimed to control intimal hyperplasia in AVF maturation, and they showed that both maturation and AVF patency could be positively affected by using cilostazol for this purpose. In response to the increased shear stress seen during AVF maturation, arterial flow rate and quality of venous drainage are predictors of anastomotic patency. In this mechanism, one of the main factors threatening AVF patency is increasing intimal hyperplasia due to DM[12-14]. A study by Afsar and Elsurer[15], which included 233 patients retrospectively, investigated the effect of the presence and severity of DM on primary AVF patency. In this study, the authors showed high HbA1c values and the presence of PAD as independent predictors of primary AVF failure. Unlike this study, we included only patients with DM, and in our case, the HbA1c value was higher in Group 2, but this difference was not statistically significant. However, similar to this study, we showed that the presence of PAD is indeed an independent predictor of AVF failure. PAD is frequently seen in diabetic patients, and endothelial dysfunction and structural changes in these patients may have affected fistula patency[16].

Hyperlipidemia plays an important role in the emergence of vascular diseases. Etiologically, inflammation begins due to lipid structures accumulating in the vascular bed, and cytokines are activated. Thus, the events predisposing to the atherosclerotic process and plaque rupture begin[17,18]. High LDL-C is a condition that negatively affects the vascular structure. In one study[19] that included 101 patients retrospectively, the effect of LDL-C elevation on primary AVF patency was investigated. In this study[19], in which 45.5% of the patients had DM, high LDL-C values were shown as an independent predictor of AVF failure. In another study[20] in which 118 patients were included prospectively and the patients were followed for 14 months, it was revealed that keeping the LDL-C value below 130 positively affects AVF patency. In our current study, we found that high LDL-C values were significantly correlated with primary AVF failure.

In patients with renal failure, the most common lipid abnormality is high triglyceride levels[21]. Recently, the triglyceride and TyG index values obtained with glucose have been investigated as a prognostic marker in cardiovascular diseases. The high level of this value indicates a metabolically unhealthy state[22]. The relationship between high TyG index values and carotid artery plaque formation has been shown in patients with DM. In another study[23], the relationship between a high TyG index value and coronary artery disease was revealed in patients with DM[24]. In yet another study[25] conducted on diabetic patients with heart failure, it was shown that there is a positive correlation between low TyG index values and prognosis. In this current study, we revealed for the first time that preoperative high TyG index values in hemodialysis patients with DM are an independent predictor of primary AVF failure.

Limitations

Our major limitation in this study is the retrospective study design. In addition, our study reports a single-center experience, and thus, studies with a greater number of patients are needed.

Conclusions

In this study, we demonstrated that the TyG index value, derived from blood samples taken at the time of hospital admission in hemodialysis patients with DM, serves as an independent predictor of primary AVF failure following AVF surgery. Consequently, this allows for the identification of patient groups at higher risk for AVF failure. Based on these findings, appropriate treatment and follow-up protocols can be established.

Ethics Approval

The study follows the Declaration of Helsinki and its later amendments, and it was approved by Bursa Yuksek Ihtisas Training and Research Hospital Clinical Research Ethics Committee (2011-KAEK-25 2022/08-27).

Informed Consent

Written informed consent was obtained from the patients before their interventions.

Conflict of Interest

The authors declare they have no conflict of interest.

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None.

Authors' Contributions

All authors contributed significantly to the conception and design, acquisition of data, analysis, and interpretation of data, drafting of the article or revising it critically for important intellectual content, and final approval of the version to be published.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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