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Relationship between peripheral arterial disease severity determined by the Glass classification and triglyceride-glucose index; novel association and novel classification system.

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Keywords: peripheral arterial disease; GLASS classification; triglyceride-glucose index; insulin resistance.

Abstract. Peripheral arterial disease is a serious clinical manifestation caused by atherosclerosis. It is one common cause of morbidity and mortality worldwide. It is commonly seen in males, and its (prevelance) increases with age. It is most prevalent with smoking, hypertension, diabetes mellitus and hyperlipidemia. Novel studies investigate the relationship between triglyceride-glucose index (TyG) and cardiovascular diseases. Studies investigating the association of this index and peripheral arterial disease and disease severity are generally done by using The Trans-Atlantic Inter-Society Consensus (TASC) classification. We aimed to study this association by using the new Global Limb Anatomic Staging System (GLASS) classification. Two hundred patients between 25 to 90 years old diagnosed with peripheral arterial disease and admitted to the hospital for peripheral arterial angiography between July 2021 and December 2021, were evaluated retrospectively with blood parameters and angiographic images. Patients were divided into two groups: moderate (group 1; n=58) and severe (group 2; n=142) according to the GLASS classification. No statistical differences were observed for comorbidities and repeated interventional procedure rates (p=0.164). Triglyceride values were found to be statistically different between groups (p=0.040). TyG was found higher in group 2 (p= 0.04). According to the binary logistic regression model, only TyG was found to have a significant effect as a diagnostic factor (p=0.011). TyG was also significantly correlated with the Rutherford (p=0.012) and GLASS classification severity (p<0.001). Peripheral arterial disease and disease severity could be easily monitored with simple calculable TyG. In this way, precautions could be taken, and morbidities could be prevented.

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Relación entre la gravedad de la enfermedad arterial periférica determinada por la clasificación GLASS y el índice de triglicéridos-glucosa; nueva asociación y nuevo sistema de clasificación.

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Palabras clave: enfermedad arterial periférica; clasificación de GLASS; indice de triglicéridos-glucosa; resistencia a la insulina.

Resumen. La enfermedad arterial periférica es una manifestación clínica importante causada por la aterosclerosis. Es una causa común de morbilidad y mortalidad en todo el mundo. Se ve comúnmente en hombres y la prevalencia aumenta con la edad. Es más común con el tabaquismo, la hipertensión, la diabetes mellitus y la hiperlipidemia. Nuevos estudios investigan la relación entre el índice de triglicéridos-glucosa (TyG) y las enfermedades cardiovasculares. Los estudios que investigan la asociación de este índice y la enfermedad arterial periférica generalmente se realizan utilizando la clasificación de TASC. Nuestro objetivo fue estudiar esta asociación utilizando la nueva clasificación de GLASS (sistema global de estadificación anatómica de extremidades). Doscientos pacientes entre 25 a 90 años con diagnóstico de enfermedad arterial periférica e ingresados al hospital para angiografía arterial periférica entre julio de 2021 y diciembre de 2021, fueron evaluados retrospectivamente con parámetros sanguíneos e imágenes angiográficas. Los pacientes se dividieron en dos grupos: leves (grupo 1; n=58) y graves (grupo 2; n=142) según la clasificación de GLASS. No se observaron diferencias estadísticas para las comorbilidades y las tasas de procedimientos intervencionistas repetidos (p = 0,164). Los valores de triglicéridos se encontraron significativamente diferentes entre los grupos (p= 0,04). El índice de triglicéridos-glucosa se encontró más alto en el grupo 2 (p= 0,04). Según el modelo de regresión logística binaria, solo el índice de triglicéridos-glucosa resultó tener un efecto significativo como factor diagnóstico (p=0,011). El índice de triglicéridos-glucosa también se correlacionó significativamente con la gravedad de la clasificación de Rutherford (p=0,012) y la clasificación de GLASS (p<0,001). La enfermedad arterial periférica y la gravedad de la enfermedad podrían controlarse fácilmente con TyG calculable simple. De esta manera, se podrían tomar precauciones y prevenir morbilidades.

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INTRODUCTİON

Peripheral arterial disease (PAD) is an important disease that arises from systemic atherosclerosis and has effected about 200 million people worldwide [1,2]. Although PAD is most commonly seen among males, its incidence in women has increased especially at ages over 50 years [3]. Its prevelance incereases with age, and the reported rate is about 20% or above in individuals who are over 80 years [4]. It is a pathology that could result in

morbidities ranging from lower extremity ulcers to limb losses. Despite the high morbidity rates, PAD tends to be asymptomatic until it reaches the advanced stage [5]. Its presentation can vary from asymptomatic phase to critical limb ischemia (CLI) and most of the patients that are admitted to hospitals suffer from intermittent claudication. The most common diagnostic test for PAD is ankle-brachial index (ABI) measurement and values ≤ 0.90 is considered as arterial stenosis and its sensitivity in diagnosing PAD is 95% [6,7]. Doppler ultrasonography generally is the first imaging method choosed for diagnosing PAD.

Despite this type of clinical course and well-known adverse outcomes, the pathophysiology of PAD has not yet been fully understood. The well-known main underlying pathology of PAD is atherosclerosis [8]. Since atherosclerosis is a common underlying pathology, the risk factors for PAD are; hypertension (HT), smoking, diabetes mellitus (DM) and hyperlipidemia [9].

Insulin resistance (IR), is usually one of the main events underlying DM, a pathology characterized by decreased insulin sensitivity of peripheral tissues [10] and the resulting chronic hyperinsulinemia is significantly associated with atherosclerotic cardiovascular disease (CVD) [11-13]. It has been detected that insulin-resistant patients endure higher cardiovascular risk than insulin-sensitive subjects [14]. According to these reports, an association with IR and vascular disease is very likely but exact pathogenesis of this relation remain controversial. The effect on the vascular area is one of the pathological mechanism evaluated in the association between DM and PAD [15]. IR related vascular damage includes functional and structural vascular injury such as; vascular wall elasticity loss (arterial stiffness), increased intima-media thickness, impaired vasodilation and vascular calcification [16].

Also the relationship between the triglycerides (TGs), CVD and atherosclerosis is still controversial. Recent studies have provided evidence that TGs and TG-rich lipoproteins are among the causes of CVD [17].

The triglyceride-glucose index (TyG), a calculated index by using fasting blood glucose and triglyceride values, has been defined as a novel marker of IR [18-20] and studies have shown a relationship between the TyG and CVD, stroke, carotid atherosclerosis and coronary artery disease (CAD) [21-23]. Although many studies have evaluated the association of this index with CAD, CVD and carotid atherosclerosis, there are currently very few data about its association with PAD and disease severity. We aimed to investigate the association between TyG and PAD severity, by using a new anatomical classification for PAD named Global Limb Anatomic Staging System (GLASS).

MATERİAL AND PATİENTS

Our study is a retrospective observational comparative study that compares results of individuals allocated into two groups according to the severity of their lesions. Two hundred patients that were between 25 and 90 years old, admitted to our outpatient clinic, diagnosed with PAD and hospitalized for peripheral arterial angiography between July 2021-December 2021 were investigated retrospectiveley. Patient data were obtained from Isparta City Hospital's hospital registration system and angiography laboratory archive. The study was approved by Suleyman Demirel University Medical Faculty Ethical Committee (Number:72867572-050.01.04-196235).

Patients that were admitted to outpatient clinic with intermittant claudication or extremity ulcers, diagnosed with PAD as a result of clinical examination (absence of palpable peripheral pulses) and low ABI measurement (ABI≤ 0.9). The Rutherford Classification was used for clinical staging of existing disease. According to Rutherford Classification, asymptomatic patients staged as "Cathegory 0", mild claudication as "Cathegory 1", moderate claudication as "Cathegory 2", severe claudication staged

as "Cathegory 3", ischemic rest pain as "Cathegory 4", minor tissue loss "Cathegory 5" and major tissue loss expressed as "Cathegory 6" [24].

Patients diagnosed with PAD as a result of clinical examination were taken to color Doppler ultrasonography (Toshiba Applio 500; Japan) and if a pathology was detected, Computed Tomographic Angiography (CTA) (Hitachi Supria; Japan) was applied for detailed evaluation. After performing CTA, patients that had peripheral arterial stenosis more than 50% were hospitalized for peripheral arterial angiography for further evaluation and treatment. Angiographies performed in Isparta City Hospital angiography laboratory (Toshiba Infinix; Japan) by the same physician with local anesthesia from right or left femoral artery approaches with 6F sheath by using Seldinger technique. Antegrad or retrograd approaches selected according to the lesions of the patients evaluated by CTA images.

Patients who underwent peripheral angiography were evaluated by novel GLASS anatomic classification in terms of PAD severity. (Table 1) GLASS classification is a new anatomic classification system using angiographic findings for severity of PAD. It was published in 2019 by joining of three

Table 1
Global Limb Anatomic Staging System (GLASS).

Aorta-Iliac Grading	
1	Stenosis of the common and external iliac artery, chronic total occlusion of either common or external iliac artery (not both), stenosis of the infrarenal aorta; any combination of these.
2	Chronic total occlusion of the aorta; chronic total occlusion of common and external iliac arteries; severe diffuse disease and/or small-caliber (<6 mm) common and external iliac arteries; concomitant aneurysm disease; severe diffuse in-stent restenosis in the aorta-iliac system.
Femoro-Popliteal (FP) Grading	
0	Mild or no significant (<50%) disease
1	Total length SFA disease <1/3 (<10 cm); may include single focal CTO (<5 cm) as long as not flush occlusion; popliteal artery with mild or no significant disease.
2	Total length SFA disease 1/3–2/3 (10–20 cm); may include CTO totaling <1/3 (10 cm) but not flush occlusion; focal popliteal artery stenosis <2 cm, not involving trifurcation.
3	Total length SFA disease >2/3 (>20 cm) length; may include any flush occlusion <20 cm or non-flush CTO 10–20 cm long; short popliteal stenosis 2–5 cm, not involving trifurcation.
4	Total length SFA occlusion >20 cm; popliteal disease >5 cm or extending into trifurcation; any popliteal CTO.
Infra-Popliteal (IP) Grading	
0	Mild or no significant (<50%) disease.
1	Focal stenosis <3 cm not including TP trunk.
2	Total length of target artery disease <1/3 (<10 cm); single focal CTO (<3 cm not including TP trunk or target artery origin).
3	Total length of target artery disease 1/3–2/3 (10–20 cm); CTO 3–10 cm (may include target artery origin, but not TP trunk).
4	Total length of target artery disease >2/3 length; CTO >1/3 (>10 cm) of length (may include target artery origin); any CTO of TP trunk.

Table 1
CONTINUATION

Inframalleolar/Pedal Grading	
0	Target artery crosses ankle into foot, with intact pedal arch
1	Target artery crosses ankle into foot; absent or severely diseased pedal arch
2	No target artery crossing ankle into foot

CTO: Chronic Total Occlusion; SFA: Superficial Femoral Artery; TP:Tibio-peroneal.

vascular societies [25]. With this new anatomic staging system, better assessment of limb ischemia and better characterization of the anatomic specifications of vascular disease could be achieved [26].

After 12 hours of overnight fasting, venous blood samples for biochemical and hematological parameter measurements were taken from the blood drawn from the antecubital vein at the first day after hospital admission for blood analysis. Biochemical analysis included the serum lipid profile and fasting glucose levels (Variant 2-Turbo, Bio-Rad; Japan).

TyG is calculated as Ln (fasting triglycerides (mg/dL) × fasting glucose (mg/dL) / 2). ABI was calculated as the ratio of highest systolic ankle pressure to highest systolic brachial pressure measured manually.

Patients diagnosed with Buerger disease, vasculitis, acute limb ischemia, systemic inflammatory diseases, chronic liver and hematological diseases; patients operated or had vascular interventions before outpatient clinic admission; patients who have known malignancy and whose index could not be calculated due to the abscence of laboratory parameters were excluded from the study.

Statistical Analysis

Statistical analyses of the study were performed with SPSS 25.0 (IBM Incorp, IL, USA) program. Descriptive measures were presented as mean±SD or median (Q1-Q3) for numerical measurements according to their normality, and frequency (percentage ratio) for categorical measurements. The normality of numerical measurements was analyzed with the Kolmogorov-Smirnov test. Independent group comparisons were performed by using the Student's t-test and the Mann-Whitney U test. Chi-square test was used to determine the relationships between the categorical variables, distribution-appropriate correlation analyzes were used to determine the relationships between numerical measurements. To determine the factors that affect the severity of PAD, univariate and multivariate logistic regression models were established. The goodness-of-fit values and significance of the model were calculated. The model was created by using the forward likelihood ratio logistic regression method for avoiding the multicollinearity problem. In order to determine the diagnostic features of the TyG index, ROC analysis was performed and diagnostic rates were calculated. A $p<0.05$ value was considered statistically significant by taking the type-I error rate as 5% throughout the study.

The power analysis of the study was performed with the GPower 9.1.2 (Universitaet Kiel, Germany) program. By calculating the triglyceride and glucose values and TgG index of the patients that were selected for the pilot study, the effect size was calculated for mild to moderate and severe patient groups ($d=0.742$). The sample size for each group was calculated as $n=54$ for the power value of 95% and margin of error of 5%. However, the moderate:severe ratio was taken as 1:2, since the number of patients with severity was observed to be higher among the patients admitted to the hospital.

RESULTS

Two hundred patients diagnosed with PAD that underwent peripheral arterial angiography were included in the study. Patients were divided into two groups for the severity of their lesions according to GLASS classification as Group 1 (moderate- G1) and Group 2 (severe- G2), (Table 2).

There was no difference for mean age, gender and comorbidities between the study groups. While chronic kidney disease (CKD) was found to be higher in the G2, CAD was found to be slightly higher in G1. Lower extremity amputation rates were found significantly higher in G2 (Table 3).

Patients were also evaluated according to the Rutherford classificiation and stastistically significant association with GLASS classification was observed ($p<0.001$). Statistically significant relationship was also found between the PAD severity determined by GLASS classification and ABI ($p<0.001$).

TyG values showed statistically significant difference between the groups. TyG was higher in severe group (G2) compared to the moderate group (G1) ($p=0.04$). When TyG comparison was studied for Rutherford classification among study groups (Table 2), TyG was observed significant higher in severe group compared to the moderate group ($p=0.012$).

There was no difference observed for serum total cholesterol, high density lipoprotein (HDL), and low density lipoprotein (LDL) values among the moderate and severe groups. The results of biochemical parameters were summarised in Table 4.

Since the TyG and PAD severity association was found significant in study groups, ROC analysis was applied to determine the index diagnostic value for PAD severity. A significant but low-level ROC curve was obtained. Diagnostic ratios were calculated as 65.5% sensitivity and 58.9% specificity (Fig. 1).

In order to determine the diagnostic factors effecting G2, a binary logistic regression model was created by taking G1 as the reference group. Demographic variables (age and gender), TyG, HDL, LDL and total cholesterol values were included in the model. Variables that could cause multicollinearity problem were excluded. The model was created by using the forward stepwise logistic regression method. The model was found significant (Omnibus $X^2=6.971$; $p=0.008$ and Hosmer-Lemeshow $X^2=10.03$; $p=0.262$). Goodness of fit was found at medium-level (Nagelkerke $R^2=0.05$). Only TyG was found to have a significant effect on the model as a diagnostic factor (OR=2.075), (Table 5).

DİSCUSSİON

In our study, we aimed to investigate the relationship between the severity of PAD, which is determined by using the GLASS classification, and the TyG. According to the best of our knowledge, our study is the first to examine the association of TyG with the severity of PAD determined by using this novel classification system; and similar to other few studies reported in the literature, we have found a significant relationship between TyG and PAD severity. Since we aimed

Table 2
Study groups divided according to GLASS and Rutherford classification.

Group 1 (Moderate)	Group 2 (Severe)
Femoropopliteal 0-2/Aorta-iliac 1	Femoropopliteal 3-4/Aorta-iliac 2
Infrapopliteal 0-2	Infrapopliteal 3-4
Pedal 0	Pedal 1-2
Rutherford Class 0-2	Rutherford Class 3-6

Table 3
Demographic spesifications and comorbidities.

		Group1 N=58 (28.3)	Group2 N=142 (71.1)	Total N=200	
Specifications	Cathegories	N (%)	N (%)	N (%)	*p*
Gender	Female	4 (6.9)	23 (16.2)	27 (13.6)	*0.095*
	Male	54 (93.1)	119 (83.8)	171 (86.4)	
Diabetes Mellitus	none	26 (44.8)	65 (45.8)	90 (45.5)	*0.885*
	Yes	32 (55.2)	77 (54.2)	108 (54.5)	
Hypertension	None	16 (27.6)	44 (31)	59 (29.8)	*0.561*
	Yes	42 (72.4)	98 (69)	139 (70.2)	
Smoker	None	37 (63.8)	98 (69)	133 (67.2)	*0.379*
	Yes	21 (36.2)	44 (31)	65 (32.8)	
Coronary Artery Disease	None	31 (53.4)	89 (63.1)	119 (60.1)	*0.216*
	Yes	27 (46.6)	52 (36.9)	78 (39.4)	
Chronic Renal Failure	None	54 (93.1)	127 (89.4)	179 (90.4)	*0.462*
	Yes	4 (6.9)	15 (10.6)	19 (9.6)	
Repeated Intervention	None	48 (82.8)	127 (89.4)	173 (87.4)	*0.164*
	Yes	10 (17.2)	15 (10.6)	25 (12.6)	
Amputation	None	52 (89.7)	107 (75.4)	159 (79.5)	*0.023**
	Yes	6 (10.3)	35 (24.6)	41 (20.5)	
Rutherford Classification	0+	5 (8.8)	0	5 (2.5)	
	1+	25 (43.9)	3 (2.1)	28 (14.1)	
	2+	21 (36.8)	4 (2.8)	25 (12.6)	
	3+	2 (3.5)	84 (59.2)	86 (43.2)	*<0.001**
	4+	1 (1.8)	41 (28.9)	42 (21.1)	
	5	3 (5.3)	8 (5.6)	11 (5.5)	
	6	0	2 (1.4)	2 (1.0)	
Age (years)	67.09±9.22	68.47±11.42			*0.207*
ABI	0.67±0.13 0.77; 0.69-0.82	0.31±0.12 0.28; 0.24-0.36			*<0.001**

*: Significant at the 0.05 level according to the Chi-Square test; +: the related Rutherford class is significantly different between the groups. ABI: Ankle-Brachial Index.

to determine this association by using novel GLASS classification, we also evaluated the GLASS classification system to understand its relationship with the PAD severity. For this purpose, we compared this system with the Rutherford classification and ABI measurements and found significant agreement between the GLASS and PAD severity.

There has been some studies that investigated multiple pathological consequences of atherosclerosis; however, PAD has been paid less attention than the other pathologies like CAD or stroke [27]. Based on the latest reports, it is estimated that 5.56% ratio of people worldwide aged 25 years and older had PAD [28]. But only 10% of PAD patients

Table 4
Biochemical parameters.

	Group1 (N=58)	Group2 (N=142)	
	Avarage±SS Median; Q1-Q3	Avarage±SS Median; Q1-Q3	*p*
Triglyceride (mg/dL)	135.33±54.29 129; 88.75-161.86	172.28±84.31 153.5; 113-210	*0.040**
Fasting Blood Glucose	132.86±45.62 116.5; 95.25-165	137.56±52.64 126.5; 94.75-173.5	*0.269*
LDL	105.22±35.39 113.5; 75.25-130.75	116.08±37.31 111.14; 88-140	*0.875*
VLDL	27.43±11.21 26; 18.25-32.24	34.03±16.42 30; 22-41.25	*0.061*
HDL	42.9±16.02 40; 34-46.75	41.73±13.53 40; 33-48	*0.907*
Total Cholesterol	170.81±38.16 174.5; 145.5-199.25	188.87±48.97 181.5; 156-220.25	*0.541*
TyG	8.96±0.54 8.9; 8.69-9.41	9.21±0.61 9.2; 8.78-9.49	*0.040**

*: Significant at the 0.05 level according to the Mann-Whitney U test.
TyG: Triglyceride-Glucose Index; LDL: Low density Lipoprotein; HDL:High density Lipoprotein; VLDL: Very Low Density Lipoprotein,

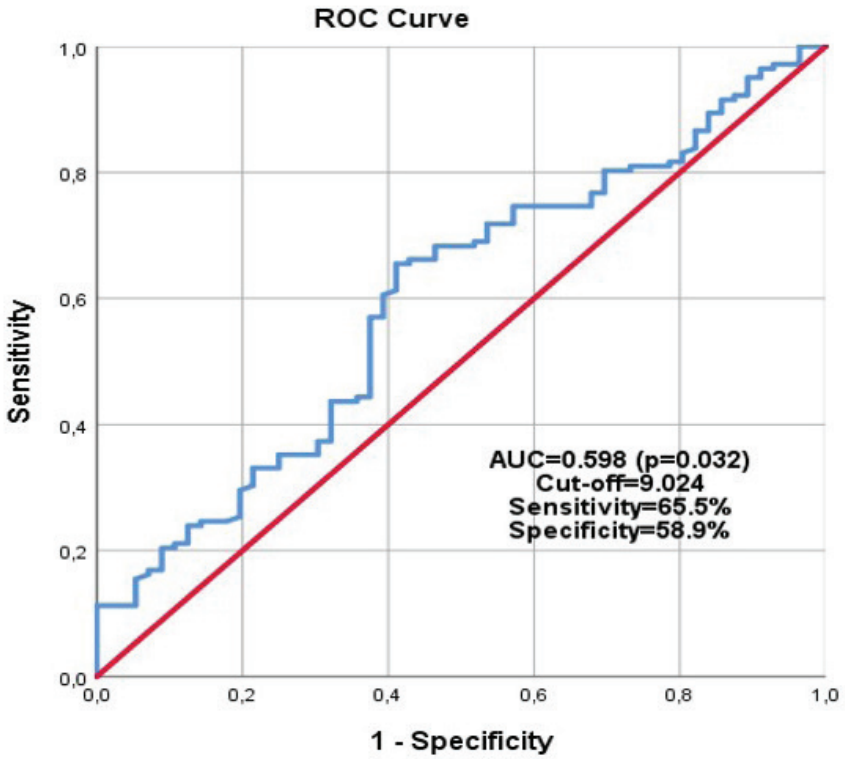

Fig. 1. Triglyceride-Glucose Index ROC curve for patients with severe lesion.

Table 5
Diagnostic factors effective on patients with severe lesion.

Factors	Beta	p	OR	%95 CI
Age	1.528	0.216		
Gender	3.002	0.083		
TyG	0.730	0.011*	2.075	1.183-6.640
LDL	2.264	0.132		
HDL	0.017	0.896		
T. cholesterol	3.193	0.074		

TyG: Triglyceride-Glucose Index; LDL: Low density Lipoprotein; HDL:High density Lipoprotein; T.Cholesterol: Total Cholesterol. *: Significant at the 0.05 level according to the Binary logistic regression analysis.

demonstrate typical symptomatology and the others remain undiagnosed [5]. Therefore, it is important to determine the appropriate biomarkers for the PAD risk and its severity. With regular measurement of the levels of these biomarkers will be important in terms of determining the risk of PAD or monitoring the course of the diagnosed disease. By this means, taking early measures could prevent the progression of the disease at early clinical stages.

Insulin is a hormone that regulates the cell metabolism, and IR is characterized by a deficit in insulin uptake by peripheral tissues. This resistance impairs glucose uptake and glycogen synthesis of tissues and creates an imbalance in lipid oxidation. As glucose homeostasis deteriorates, insulin secretion increases. Secondary to hyperinsulinemia, oxidative stress and an increase in inflammatory responses occur [29,30]. Endothelial cells get affected by this oxidative stress, endothelial function gets impaired and atherosclerosis develops in the chronic period [31]. For these reasons, IR has been seen as an important risk factor for CVD [32,33]. It has been shown that IR and hyperinsulinemia are associated with the development of HT, dyslipidemia and atherosclerosis [34,35]. But data that have reported association of IR and PAD are limited [36,37]. A cross-sectional study of 3242 adults from data in the National Health and Nutrition Examination Survey identified a positive relation between IR and PAD [26,37]. A study with 4208 participants over the age of 65 years in the Cardiovascular Health Study, found that IR was associated with a higher risk of clinical PAD [27,38]. In some reports, TyG was defined as a marker with high specifity and sensitivity for IR [11,38].

The positive relationship of TyG with CVD and atherosclerosis has been shown in many studies [39-41]. Li *et al*. reported in a retrospective study that the TyG could be used as a high risk predictor for CVD [42]. In a study conducted with 5014 healthy individuals, high levels of the TyG were shown to be associated with an increased risk of CVD [41]. In another study involving 4319 patients, a significant association of the TyG with the presence of coronary calcification was reported [39]. IR and PAD association was reported in some studies [27,36,37]. Although there are studies on the association of the TyG with coronary and carotid diseases, studies that show the relationship of the TyG and PAD severity is rare. Chiu et al. reported a significant association between the TyG and low ABI in their study [43]. Kim *et al.*, on the other hand, found that the TyG was associated with arterial stiffness and coronary artery calcification in Korean adults [44]. Among these studies, the study conducted by Duran Karaduman *et al*. showed a significant relationship between the TyG elevation and PAD severity [3]. In addition, there are studies that have investigated the predictability of the TyG for critical limb ischemia [45].

Despite all these reports, studies that examine the severity of the PAD and TyG association according to the anatomical classification systems developed for PAD, such as TASC, are very limited. In the study conducted by Duran Karaduman et al, the relationship between the TyG and PAD complexity and severity was investigated by using TASC classification [3]. In our study we found a statistically significant correlation between TyG and the severity and complexity of PAD detected with GLASS classification ($p=0.04$) similar to the findings of the reports on the association of TyG and PAD severity determined with other angiographic classification systems like TASC [3]. We also compared this novel system with Rutherford system and ABI measurements to determine the positive association of PAD severity and this system. We observed a statistically significant association ($p< 0.01$), (Table 3).

Serum lipids also play an important role in developing atherosclerosis. LDL is the best known parameter for this risk but the relationship between the TGs, CVD and atherosclerosis is still controversial. Recent studies have provided evidence on the fact that TG and TG-rich lipoproteins are among the causes of CVD [10]. It has been shown that the simultaneous presence of hypertriglyceridemia (HTG) promotes the formation of high atherogenic small dense LDL particles [46]. As a summary, there is a relation between TG levels and atherosclerosis [47,48]. In our study, TG levels were also found significantly higher in G2 ($p=0.04$).

There were some limitations of our study. The low number of patients was one of the most important limiting factor. It was mostly due to the limited number of interventional procedures performed in our clinic. In addition, the laboratory parameters that were used in the calculation of TyG were absent in the data of some patients; therefore, the index could not be calculated and these patients were compulsorily excluded from the study. This was another factor that reduced our case number. We think that the low diagnostic value of TyG detected by ROC analysis could increase if the study could be performed with more patients, and by this means the study could become more valuable.

TyG is an easily calculable index. In our study we found a significant relationship between the severity of PAD and TyG, which was determined by using the novel GLASS classification, similar to previous studies which use other anatomic classification systems. In the light of these findings, we think that this index would be a useful and simple marker for detecting the patients' disease severity for newly diagnosed or cases has been treated with medically or other invasive methods. Possible early detection of worse onset or worsening of the diagnosed disease can be predicted by routine use of this parameter, and morbidities could be prevented by applying appropriate treatments to these patients in early periods. But more large scale studies are needed to support this conclusion.

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Conflict of Interest

Authors declare no conflicts of interests

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