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# The role of triglyceride/glucose index in predicting coronary artery disease severity

**Ahmet Rifki Cora, Ersin Celik**

*Isparta City Hospital, Department of Cardiovascular Surgery, Isparta, Turkey*

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**Abstract**

Triglyceride-glucose index is a novel marker for metabolic disorders and insulin resistance and is known to be in close association with the presence, prognosis, and severity of coronary artery disease. However, few reports were evaluated the predictability of the Triglyceride-glucose index for the severity of coronary artery disease and the need for coronary intervention in patients undergoing coronary angiography. We aimed to evaluate this predictability in our study. This study was a retrospective observational cohort study. 310 patients diagnosed with coronary artery disease that underwent coronary angiography between April 2019 and March 2020 were randomly selected from the hospital database and evaluated. Index was calculated as Ln (fasting triglyceride (mg/dl) × fasting glucose (mg/dl) / 2). Patients were divided into two groups according to final treatment as Medical or Intervention. While glucose values differed significantly between the groups that underwent medical treatment and interventional treatment, triglyceride measurements were found quite close to each other. However, the value of the Triglyceride-Glucose index differed significantly between the groups (p=0.001). The index was found as 9.15±0.69 in the patients who underwent interventional treatment, and it was found to be lower as 8.91±0.54 in the medical treatment group. While total cholesterol, LDL, and HDL differed significantly between the groups. Creatinine, glomerular filtration rate; and ejection fraction values differed significantly between the groups. Triglyceride-Glucose index that can simply be calculated from routine blood parameters, could be a predictive parameter for complex coronary lesions that could need advanced interventions; yet further investigations are needed.

**Keywords:** Triglyceride-Glucose Index, Coronary Artery Disease, Intracoronary Intervention

## Introduction

Acute coronary syndrome (ACS) remains the leading cause of morbidity and mortality worldwide. The Global Registry of Acute Coronary Events (GRACE) study showed that the mortality rate of ACS patients after 1 year of admission to the hospital is approximately 15% [1]. Because of these high mortality and morbidity rates, early risk stratification is important to diagnose and treat coronary artery disease (CAD).

Insulin resistance (IR) is a well-known cause of metabolic disorders and systemic inflammation [2]. In addition to being a risk factor for CAD, it is also associated with a worse prognosis [3-5]. IR is described as decreased insulin sensitivity of peripheral tissues characterized by decreased uptake and oxidation of glucose [5]. This mechanism plays an important role in the pathogenesis of diabetes and thus, cardiovascular diseases (CVD) [5]. Also, IR results in hyperinsulinemia [6], and this induces neointimal hyperplasia and promotes vascular smooth muscle cell proliferation, and endothelial dysfunction results in atherosclerosis [7,8].

Although the role of IR is directly related to atherosclerosis, the role of hypertriglyceridemia (HTG) in the development of CAD is still controversial [9,10]. According to some reports, HTG is seen as an independent risk factor for developing glucose metabolism disorders [11]. Plasma triglyceride (TG) levels are strongly associated with elevated glucose levels because of the relations between fat, muscle, and function of pancreatic β-cells [12,13]. In the light of these reports, TG was revealed as an independent risk factor for developing especially Type-2 Diabetes Mellitus (T2DM), and a high range of fasting glucose resulting in DM was found to be related to atherosclerosis [14,15].

Triglyceride-Glucose Index (TyG) is a novel marker that identifies IR with high sensitivity and specificity [16,17]. It is also seen as a marker for identifying metabolic syndrome. This index is calculated as Ln (fasting triglyceride (mg/dl) × fasting glucose (mg/dl)/2). Increasing evidence has demonstrated that TyG

***Corresponding Author:** Ahmet Rifki Cora, Isparta City Hospital, Department of Cardiovascular Surgery, Isparta, Turkey
E-mail: drahmetcora@gmail.com

is significantly associated with hypertension, atherosclerosis, and progression of atherosclerosis [18-21]. Some reports have shown a relationship between TyG and CVD, such as coronary calcification, stroke, and carotid atherosclerosis [16,22-24]. Also, in some studies, it has been shown that TyG is associated with a future risk of CVD among healthy individuals [25].

There are plenty of reports about the association of TyG with CAD, but we have found few reports that evaluate the predictability of this index for CAD severity and the need for coronary intervention in patients diagnosed with CAD that are undergoing coronary angiography. We aimed to evaluate the predictability of TyG in our study.

## Materials and Methods

Our study was a retrospective observational cohort study. 310 patients diagnosed with CAD and underwent coronary angiography between April 2019 - March 2020 were randomly selected from the Isparta City Hospital database and evaluated. Ethical permission was taken from the Suleyman Demirel University Ethical committee (24.09.2021/296). Patients were divided into two groups according to final treatment as Medical (n=169) and Intervention (n=141).

After 12 hours of overnight fasting, venous blood samples for biochemical and hematological parameter measurements were made from the blood drawn from the antecubital vein on the first day after hospital admission. The biochemical analysis included the serum levels of triglyceride, lipid profile, fasting glucose levels (Variant 2-Turbo, Bio-Rad; Japan), urea, creatinine (Advia 2400, Siemens; Germany) and complete blood count included hemoglobin, white blood cell, neutrophile, monocyte, lymphocyte, platelet counts (Advia 2120, Siemens; Ireland) evaluated. TyG is calculated as Ln (fasting triglyceride (mg/dl) × fasting glucose (mg/dl)/2).

For patients needed coronary intervention during coronary angiography are defined as 'severe' coronary artery disease.

Inclusion criteria were 18≥age years old, diagnosis of coronary artery disease through a treadmill test or myocardial perfusion scintigraphy, and exact diagnosis by coronary angiography. Exclusion criteria were a history of coronary bypass, history of malignancy, history of trauma or bleeding at least in the last 3 months, and severe hepatic dysfunction.

The demographic specifications of the patients are summarized in Table 1.

### Statistical Analysis

Before the study, the power analysis was performed with the GPower 9.1.2 program. Since two independent groups were going to be treated with medical and interventional treatments, a pilot study was conducted to determine the TyG of five patients from each group. The effect size for the one-way table was calculated as 0.394 by choosing the t-test as the test family, and the Independent Samples t-Test as the statistical test. The minimum sample size for each group was calculated as 111, by accepting the error rate as 5% and the power value as 0.90.

Since the coefficient of variation of the TyG values was quite low, more patients who met the inclusion criteria were reached within the planned period. The study was completed with a total of 310 patients –169 patients in the medical treatment group and 141 patients in the interventional treatment group.

Statistical analyses of the study were performed by SPSS 20.0 (IBM Inc, Chicago, IL, USA) software. The normality of the continuous variables was checked by the Kolmogorov-Smirnov test. Since the distributions were generally seen to be normal, descriptive measures were presented as mean±SD for numerical data and frequency (percentage) for categorical data. The comparisons of the two independent groups were made with Student's t-test. The Chi-square test was used to determine the relationships between the categorical data. By performing ROC analysis, the area under the curve was determined and the cut-off value was calculated. Diagnostic ratios were calculated for each of the diagnosis-related groups created. The $p<0.05$ value was considered statistically significant for the type-I error rate of 5% in the entire study.

## Results

A total of 310 patients were included in the study. 45.5% of these patients were those who underwent interventional treatment, and 60% were male. The mean age was 61.58±11.78 years; the youngest patient was 30 years old, and the oldest patient was 92 years old. Age and gender were found to have significant differences between the study groups ($p<0,001$). The mean age (64.68 years) and male ratio (70.9%) were higher in the interventional treatment group. Among the comorbid diseases, only diabetes mellitus (DM) was found to be significantly higher in the interventional treatment group ($p<0.001$). Chronic renal failure (CRF) and peripheral

**Table 1.** Demographic Specifications of Patients

| Spesifications | Cathegories | Medical n(%) | Intervention n(%) | Total n(%) | p |
|---|---|---|---|---|---|
| Gender | Male | 86 (50.9) | 100 (70.9) | 186 (60.0) | <0.001 |
| | Female | 83 (49.1) | 41 (29.1) | 124 (40.0) | |
| DM | none | 109 (64.5) | 62 (44.0) | 171 (55.2) | <0.001 |
| | yes | 60 (35.5) | 79 (56.0) | 139 (44.8) | |
| CRF | none | 168 (100.0) | 139 (98.6) | 307 (99.4) | 0.122 |
| | yes | 0 (0.0) | 2 (1.4) | 2 (0.6) | |
| PAD | none | 168 (100.0) | 140 (99.3) | 308 (99.7) | 0.275 |
| | yes | 0 (0.0) | 1 (0.7) | 1 (0.3) | |
| AGE | Year | 59.00±11.62 | 64.68±11.25 | **<0.001** | |

Crf: Chronic Renal Failure. DM: Diabetes Mellitus. PAD: Peripheral Arterial Disease

artery disease (PAH) comorbidity rates did not differ significantly between the study groups.

ROC analysis was applied to determine the diagnostic rates of the TyG. For the ROC curve, the AUC=0.596 (p=0.004) was found 95%, and the reliability level was found between 0.532 and 0.660 (Figure 1). Although it was low, it was decided that the diagnostic ratios of the TyG could be calculated because it was at an acceptable level and the AUC was found statistically significant; and afterward, the cut-off value was found as 9.6682. The sensitivity value of the TyG was calculated as 24.82% and the specificity value as 91.72% for the medical and interventional treatment groups that were created according to the cut-off value (Table 2).

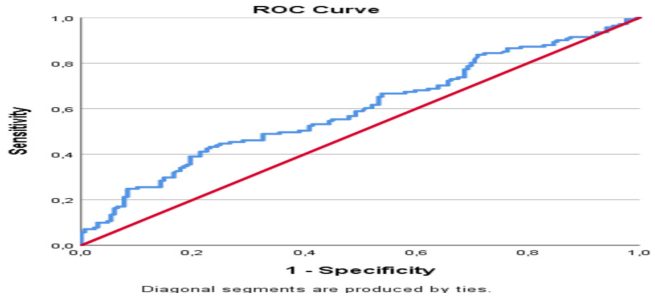


**Figure 1-** ROC Curve for Specificity and Sensitivity of TyG Values

**Table 2.** Specificity and Sensitivity Ratios of TyG for Cut-off Value

| **AUC=0.596 (p=0.004)** | **Cut-off=9,6682 mg/dL** | **0.532 – 0.660** |
|---|---|---|
| **Diagnostic Rates** | **Ratio** | **95% CI** |
| Sensitivity | %24.82 | %17.94-32.79 |
| Specifity | %91.72 | %86.49-95.40 |
| Positive Predictive Value | %71.43 | %58.38-61.90 |
| Negative Predictive Value | %59.39 | %56.83-61.90 |
| Accuracy | %61.29 | %55.62-66.74 |

While glucose values differed significantly between the groups that underwent medical treatment and interventional treatment, TG measurements were found quite close to each other. However, the value of TyG differed significantly between the groups (p=0.001). The TyG was found as 9.15±0.69 in the patients who underwent interventional treatment, and it was found to be lower than 8.91±0.54 in the medical treatment group. While total cholesterol, LDL, and HDL differed significantly between the groups in lipid biochemistry, VLDL did not differ. Also, creatinine, glomerular filtration rate (GFR); and ejection fraction (EF) values differed significantly between the groups. (Table 3).

**Table 3.** Laboratory Results and Echocardiographic Findings

| | | **Medical Follow-Up (n=169)** | **Invasive Procedure (n=141)** | |
|---|---|---|---|---|
| **AGE** | Year | 59.00±11.62 | 64.68±11.25 | <0.001 |
| **GLUCOSE** | mg/dL | 112.66±42.43 | 135.12±66.16 | <0.001 |
| **TG** | mg/dL | 169.20±101.07 | 165.24±105.66 | 0.687 |
| **TyG** | | 8.91±0.54 | 9.16±0.7 | 0.001 |
| **LDL** | mg/dL | 111.95±31.96 | 99.52±38.76 | <0.001 |
| **HDL** | mg/dL | 44.35±12.19 | 40.58±11.05 | 0.002 |
| **VLDL** | | 33.92±20.54 | 34.70±25.41 | 0.804 |
| **T.CHOL** | mg/dL | 187.44±42.02 | 172.26±45.66 | 0.001 |
| **CREATIN** | mg/dL | 0.79±0.22 | 0.95±0.39 | <0.001 |
| **GFR** | | 92.63±16.67 | 80.52±21.36 | <0.001 |
| **TROPONIN** | ng/L | 77.00±660.83 | 2457.25±8404.45 | <0.001 |
| **HB** | g/dL | 14.04±1.68 | 13.43±1.86 | 0.006 |
| **HTC** | % | 42.00±4.63 | 40.47±5.35 | 0.013 |
| **PLT** | 10^3/µL | 261012±68344 | 261000±87931 | 0.361 |
| **EF** | % | 58.22±8.90 | 52.86±6.92 | <0.001 |

Laboratory and Echocardiographic Findings

## Discussion

In our study, we aimed to investigate the predictive role of TyG for the severity of existing CAD and the need for coronary intervention among patients that are undergoing coronary angiography.

TyG was reported to be associated with CVD in many studies. This index was first studied as a marker of IR [26-28]. Also, it was reported as a useful predictor and indicator of T2DM and metabolic syndrome, both of which were associated with cardiometabolic risks [29,30]. Recent studies have reported that this index might also be an indicator of severe CAD [31]. Mao et al reported that TyG had independently predicted the CAD severity in 438 patients with non-ST segment elevation acute coronary syndrome [17].

Also, it was indicated as associated with in-stent restenosis in some reports [32-34].

It is not easy to understand the exact relationship between the TyG and CAD severity. However, we considered that this relationship could be associated with IR for some reasons reported in the literature [35]. It was shown that TyG is a good marker of IR and has high sensitivity and specificity to identify metabolic syndrome [35]. IR is insulin insensitivity, and resultant hyperinsulinemia [6] induces neointimal hyperplasia and vascular smooth muscle proliferation [7,8]. We thought that these mechanisms could result in endothelial injury results in atherosclerosis and severe arterial stenosis, and also, they could play an important role in the complexity of coronary lesions. Complex lesions generally need coronary interventions like stent implantation. Many studies showed a relationship between TyG and CAD severity [32,33,35,36]. These studies proved a positive relationship of this index with the severity of coronary lesions; however, according to our knowledge, there is a very limited number of studies in the literature showing the predictability and association of TyG for coronary artery intervention. Therefore, in our study, we aimed to investigate the predictability of the TyG for coronary artery intervention (like coronary stent implantation) among our patients who underwent coronary angiography in our hospital and found a statistically significant relationship between these two parameters ($p=0.001$) in the patients diagnosed with CAD and underwent coronary angiography.

In addition to finding statistically significant results for the relationship between TyG and CAD severity, we have also found a significant relationship between severity of coronary lesions and DM, EF, GFR, troponin I, creatinine levels.

DM has reached epidemic proportions worldwide and is the most potent independent risk factor for CAD (37). CAD is a major cause of death in diabetic patients (38), and DM is associated with two to four times increased mortality risk from heart diseases (39). In the United States, about 1/3rd of patients undergoing percutaneous coronary intervention procedures were with DM and 25% of patients undergoing coronary artery bypass surgery were diabetic (38). As in the literature, we found DM especially among a group of patients that need coronary intervention for the treatment of CAD as expected.

As known by the majority, the severity of CAD could be associated with early-onset or previous acute coronary ischemia. For this reason, after these ACS histories, EF of these patients could be affected, and a decrease in EF values could be seen among these patients as in our study. Also, many of these patients have subendocardial or transmural myocardial infarction and for these reasons, we conclude that the early onset of ACS in the patients that were included in our study is the cause of elevated troponin levels and statistical significance of the values.

Metabolic syndrome and DM play an important role in chronic or acute renal failure (40) and DM is the major independent risk factor for CAD (37). For this reason, it can be concluded that most severe CAD patients have DM and some with DM patients have impaired kidney functions with elevated serum creatinine and decreased GFR values (40,41). In our study, we also found increased serum creatinine levels and low GFR levels in the intervention group, which indicates severe CAD, with DM like what was reported in previous studies.

Yet, there were some limitations of our study; the first one was that our study was a single-center retrospective study. For this reason, this study could not enough to prove the real relationship between TyG and CAD lesion severity that needs coronary intervention. The second limiting factor was the low number of patients and the short examination period. When we retrospectively examined the patient data of our hospital, we saw that there was no standard for the blood tests demanded of each patient that was undergoing coronary angiography. As a result, we could not calculate the value of TyG for a large group of patients, and this was the biggest reason for having only a limited number of patients and a limited study period.

## Conclusion

In conclusion, TyG that can simply be calculated from routine blood parameters could be a predictive parameter for complex coronary lesions that could need advanced interventions like coronary stent implantation. And maybe adding this parameter to worldwide accepted models for CAD (like the Framingham model) can enhance the predictive value of these models. But further investigations are needed to support this conclusion.

**Conflict of interests**
*The authors declare that there is no conflict of interest in the study.*

**Financial Disclosure**
*The authors declare that they have received no financial support for the study.*

**Ethical approval**
*Suleyman Demirel University Medical Faculty Ethical Commitee 24.09.2021 date 296 number.*

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