










## Could the Triglyceride-Glucose Index Be a Predictor in the Diagnosis of Coronary Ectasia?

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### ABSTRACT

**Objective:** The goal of this study is to elucidate the relationship between the Triglyceride-Glucose (TyG) index, an indicator of insulin resistance (IR), and coronary artery ectasia (CAE) in patients without diabetes mellitus (DM) undergoing coronary angiography. The primary objective is to determine whether TyG index levels are independently associated with CAE, suggesting the TyG index could serve as a potential screening tool for this condition.

**Materials and Methods:** A retrospective study conducted between May 2022 and July 2023 included 1,680 patients, comprising 92 in the CAE group and 1,588 in the control group. Demographic, clinical, and biochemical parameters, including the TyG index, were assessed. Propensity Score Matching (PSM) was employed to address potential confounding factors.

**Results:** In the CAE group, the TyG index was significantly elevated ( $9.0 \pm 0.5$  vs.  $8.5 \pm 0.4$ ,  $p < 0.001$ ). After PSM, the TyG index remained higher in the CAE group ( $9.0 \pm 0.4$  vs.  $8.4 \pm 0.5$ ,  $p < 0.001$ ). Multivariable regression identified the TyG index as an independent predictor for CAE. Diagnostic performance, assessed by Receiver Operating Characteristic (ROC) analysis, demonstrated increased sensitivity and specificity post-PSM.

**Conclusion:** This study reveals a significant correlation between increased TyG index levels and CAE, regardless of traditional risk factors. The TyG index emerges as a potential predictor for CAE, offering diagnostic insights even in the absence of DM. These findings underscore the clinical relevance of the TyG index in identifying individuals at risk for CAE and its potential role in optimizing screening and treatment strategies.

**Keywords:** Cardiovascular disease, coronary artery ectasia, insulin resistance, triglyceride-glucose index.



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### INTRODUCTION

Coronary Artery Ectasia (CAE) is recognized as a variation of coronary artery disease (CAD).<sup>1</sup> It is characterized by a significant enlargement of the epicardial coronary artery, expanding to at least one and a half times the size of adjacent sections.<sup>2</sup> Angiographic studies have shown that the occurrence of CAE varies, with its prevalence estimated to be between 0.3% and 5%.<sup>3,4</sup> Although the risk factors

for CAE are similar to those for atherosclerosis, the underlying causes of CAE are not fully understood.<sup>5</sup> It is suggested that a key mechanism contributing to the development of CAE is the increased activation of matrix metalloproteinases (MMPs).<sup>5,6</sup> Recent studies have indicated that insulin might contribute to the elevated expression of MMPs.<sup>7,8</sup> However, the impact of insulin resistance (IR) on the pathogenesis of CAE requires further detailed research and clarification.

Despite the frequent observation of atherosclerosis in individuals with CAE, the prevalence of diabetes mellitus (DM) in these patients is notably lower compared to others.<sup>9</sup>

IR is recognized as a risk factor for DM, often manifesting years before the onset of DM.<sup>10</sup> Additionally, IR has been independently associated with major cardiovascular events, including its role in the atherogenic lipoprotein profile, the development of atherosclerotic deposits, and the intensity of CAD.<sup>9,11,12</sup> Atherosclerosis, characterized by the accumulation of fatty deposits within the walls of arteries, is identified as a key element in the progression of CAE.<sup>13</sup> Furthermore, the burden of atherosclerotic plaque can alter blood flow dynamics and compromise vascular integrity, thereby further facilitating the development and progression of CAE.<sup>1</sup> Given its potential impacts on atherosclerosis and MMPs, which are intimately associated with CAE, IR might play a pivotal role in the emergence of CAE.

The Triglyceride-Glucose (TyG) index has emerged as a notable indicator for IR and metabolic syndrome, which are associated with an increased risk of cardiovascular disorders and type 2 DM.<sup>10</sup> Various studies have explored the utility of the TyG index as a predictor of these health issues and as a tool for identifying individuals at increased risk.<sup>14,15</sup> Research has consistently demonstrated a substantial correlation between the TyG index and the development of atherosclerosis.<sup>16,17</sup> Yet, there are few studies that have highlighted its association with CAE.<sup>18</sup>

Given the established role of the TyG index in forecasting atherosclerosis and CAE's common linkage with atherosclerosis,<sup>15</sup> we propose that the TyG index might be a significant indicator in predicting CAE. Therefore, the objective of this research is to investigate the link between the TyG index and CAE in patients undergoing coronary angiography (CAG) without DM.

## MATERIALS AND METHODS

All methods adhered to the ethical guidelines of the overseeing committee on human research (both institutional and national) and conformed to the most recent iteration of the Helsinki Declaration (2013). This retrospective study was conducted from May 2022 to July 2023. The study received

approval from the local ethics committee (Ankara Etlik City Hospital, Ethics Committee for Clinical Research No. 1, Approval Date: 03/05/2023, No: AESH-EKI-2023-158).

### Study Population

Between October 2022 and May 2023, we reviewed all CAG images conducted in our clinic's angiography laboratory. We included patients diagnosed with CAE who were advised to undergo medical follow-up as the case group. For the control group, we selected patients with normal coronary arteries and similar baseline characteristics. Our study encompassed patients aged between 18 and 85 who underwent CAG. We excluded patients with a diagnosis of DM, a history of CAD, those who had experienced acute coronary syndrome, or patients who had undergone coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI). We specifically excluded patients with a history of CABG, prior PCI, and those newly designated for PCI, aiming to narrow our research focus and questions. This approach enabled us to focus on a population that was more closely aligned with the objectives of our study. We excluded groups with distinct treatment protocols and outcomes, which were not central to our investigation of responses to medical treatments. A total of 1,680 patients participated in the study: 1,588 in the control group and 92 in the CAE group.

### Study Protocol

We collected demographic, clinical, and imaging information from the electronic medical records of the patients. Biochemical parameters were analyzed using venous blood samples collected during outpatient evaluations after a 12-hour fasting period. All samples were processed in the same laboratory using the same equipment. The patients were divided into two groups: the case group, comprising patients diagnosed with CAE, and the control group, consisting of patients without any coronary lesions. To ensure similarity in baseline characteristics, the groups were randomized (Table 1). Measurements of CAE were conducted by the same operator.

To balance traditional cardiovascular risk factors such as advanced age, a predominantly male demographic, and a higher incidence of hypertension in the CAE group, we utilized propensity score matching (PSM). Each participant was assigned a propensity score based on factors such as age, gender, comorbidities, and disease severity using logistic regression. Then, individuals in the treatment group were matched with those in the control group based on their propensity scores, ensuring comparability. The adequacy of the matching was assessed by examining the standardized mean differences before and after matching. This approach aimed to mitigate the impact of confounding variables on the estimates of treatment effects.

**Table 1.** Characteristic findings of patients with and without CAE after PSM analysis

Variables	All population n=184	Control group n=92	CAE group n=92	p
Age, years	61.5±9.8	60.8±7.8	62.1±11.5	0.367
Gender, n (%)				
Female	45 (24.5)	21 (22.8)	24 (26.1)	0.607
Male	139 (75.5)	71 (77.2)	68 (73.9)	
BMI, kg/m <sup>2</sup>	27.0±2.6	26.9±2.7	27.1±2.6	0.609
Hypertension, n (%)	143 (77.7)	70 (76.1)	73 (79.3)	0.595
CVE, n (%)	14 (7.6)	8 (8.7)	6 (6.5)	0.782
AF, n (%)	20 (13.0)	12 (13.0)	8 (8.7)	0.478
Drugs, n (%)				
ACEi	126 (68.5)	63 (68.5)	63 (68.5)	0.999
Loop diuretics	95 (51.6)	45 (48.9)	50 (54.3)	0.461
CCB	74 (40.2)	39 (42.4)	35 (38.0)	0.548
Warfarin	18 (9.8)	11 (12.0)	7 (7.6)	0.458
DOAC	7 (3.8)	4 (4.3)	3 (3.3)	0.999
Laboratory findings				
WBC count, x10 <sup>3</sup>	8.5±2.6	8.0±2.6	8.9±2.6	0.030*
PLT count, x10 <sup>3</sup>	277.8±75.4	281.8±77.6	273.7±72.7	0.467
Hemoglobin, mg/dL	14.0±1.9	14.0±1.4	13.9±2.3	0.182
Fasting glucose, mg/dL	91.9±12.4	88.3±11.3	95.6±12.3	<0.001*
HDL, mg/dL	45.0±10.9	48.8±9.4	41.3±11.1	<0.001*
LDL, mg/dL	115.3±36.4	108.1±35.6	122.4±40.0	0.005*
TG, mg/dL	147.0 (85.0–189.0)	89.0 (80.0–154.0)	187.0 (138.2–258.0)	<0.001*
TyGi	8.7±0.6	8.4±0.5	9.0±0.5	<0.001*
ESR, mm/hr	6.4 (3.8–12.6)	6.4 (3.8–12.0)	6.3 (4.0–10.0)	0.365
CRP, mg/L	5.7 (4.0–8.5)	5.4 (3.5–8.5)	5.7 (3.8–9.8)	0.358
Creatinin, µg/dL	0.9±0.3	0.8±0.2	1.0±0.5	<0.001*
Uric acid, mg/dL	5.8±1.1	5.6±0.9	6.7±6.0	0.001*
GFR, mL/min/1.73m <sup>2</sup>	83.8±22.5	88.7±17.4	79.0±25.9	0.003*
TSH, µU/mL	1.6 (1.2–2.0)	1.6 (1.1–2.0)	1.5 (1.1–2.1)	0.905
Ectasia artery, n (%)				
LAD	28 (15.2)	–	28 (30.4)	–
Cx	19 (10.3)	–	19 (20.7)	–
RCA	45 (24.5)	–	45 (48.9)	–
Ectasia size, n (%)				
Small	41 (22.3)	–	41 (44.6)	–
Medium	48 (26.1)	–	48 (52.2)	–
Giant	3 (1.6)	–	3 (3.3)	–
Discharge drugs, n (%)				
ASA	77 (41.8)	31 (33.7)	46 (50.0)	0.025*
BB	91 (49.5)	32 (34.8)	59 (64.1)	<0.001*
Statin	80 (43.5)	35 (38.0)	45 (48.9)	0.137
Clopidogrel	26 (14.1)	9 (9.8)	17 (18.5)	0.135

Data are mean±standard deviation or median (IQR), or number (%). \*: P<0.05 indicates statistical significance. ACEi: Angiotensin-converting enzyme; AF: Atrial fibrillation; ASA: Acetylsalicylic acid; BB: Beta blocker; BMI: Body-mass index; CAE: Coronary artery ectasia; CAG: Coronary angiography; CCB: Calcium-channel blocker; CRP: C-reactive protein; Cx: Circumflex artery; CVE: Cerebrovascular event; DOAC: Direct oral anticoagulant; ESR: Erythrocyte sedimentation rate; GFR: Glomerular filtration rate; HDL: High-density lipoprotein; LAD: Left anterior descending artery; LDL: Low-density lipoprotein; PLT: Platelet; PSM: Propensity score matching; RCA: Right coronary artery; TG: Triglyceride; TSH: Thyroid-stimulating hormone; TyGi: Triglyceride-glucose index; USAP: Unstable angina pectoris; WBC: White blood cell.

### Coronary Angiography and Measurements

Coronary angiography was performed on all participants using the General Electric Healthcare (GE) Innova™ IGS 530 equipped with AutoRight™ CAG devices (Chicago, Illinois, United States). We calculated the measurements of normal and ectatic vessels using specialized software (InnovaSpin™, one-touch analysis, GE Healthcare). CAE is identified by the abnormal dilation of the coronary artery lumen, manifesting either in a localized or diffuse manner, where the diameter exceeds that of the healthy neighboring segments or the patient's largest coronary artery diameter by 1.5 times.<sup>19</sup> Coronary aneurysms are categorized based on their luminal diameter into three groups: small (<5 mm), medium (5–8 mm), and giant (>8 mm).<sup>20</sup>

### Biochemical Analysis

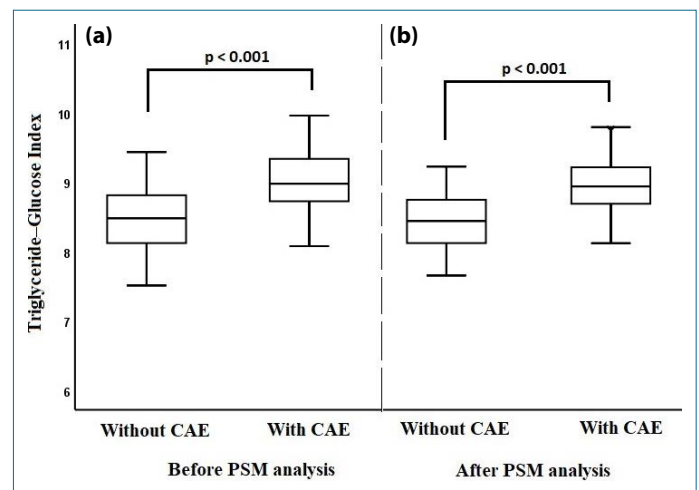
Patients' venous blood samples were analyzed using a Beckman Coulter LH 780 device (Mervue, Galway, Ireland) and a Hitachi Modular P800 autoanalyzer (Roche Diagnostics Corp., Indianapolis, IN, USA). We measured hemoglobin levels using the photometric method, leukocyte counts via the optical laser scattering method, and platelet counts through the impedance method. High-sensitivity C-reactive protein (hs-CRP) levels were determined with the immunoturbidimetric method, while fasting blood glucose and lipid parameters were measured employing the enzymatic colorimetric method. All venous blood samples were collected in the morning after an average fasting period of 8–12 hours. The Friedewald formula was used to calculate low-density lipoprotein cholesterol (LDL-C).<sup>21</sup> All TyG index measurements were calculated using the formula:  $\text{Ln}[\text{triglyceride} [\text{mg/dL}] \times \text{glucose} [\text{mg/dL}]/2]$ .<sup>22</sup>

### Echocardiographic Examination

All participants underwent routine echocardiography prior to discharge. The echocardiographic assessments were performed using the Vivid™ E80 device (GE Healthcare, Chicago, Illinois, United States) for all patients. Ejection fraction measurements were determined using the Biplane Modified Simpson's method.<sup>23</sup>

### Statistical Analysis

All data were analyzed using the Statistical Package for the Social Sciences (SPSS) v20 software package (IBM Corp., Armonk, NY, USA). Numerical data that adhered to a normal distribution, as verified by the Kolmogorov-Smirnov test, are presented as mean±standard deviation. Conversely, variables not following a normal distribution are depicted as median (interquartile range: 25<sup>th</sup>–75<sup>th</sup> percentiles). Comparisons between two groups were made using the Student's t-test for variables with normal distribution and the Mann-Whitney U test for variables that were not normally distributed. Categorical variables were expressed as numbers and



**Figure 1.** Distributions of TyGi According to the Presence of Coronary Ectasia. **(a)** Distribution of TyGi in groups before propensity match (PSM) analysis **(b)** Distribution of TyGi in groups after PSM analysis.

percentages, with comparisons between groups conducted using the Chi-square test and Fisher's exact test. Multivariable logistic regression analysis, employing the backward Wald technique, was utilized to identify potential independent predictors of coronary artery ectasia (CAE). Receiver operating characteristic (ROC) curve analysis was employed to evaluate diagnostic accuracy, with results including the area under the curve (AUC), standard error (SE), and measures of sensitivity and specificity. The optimal TyG index threshold for predicting CAE was determined using the Youden index method. A significance level of  $p < 0.05$  (\*) was set for all statistical analyses.

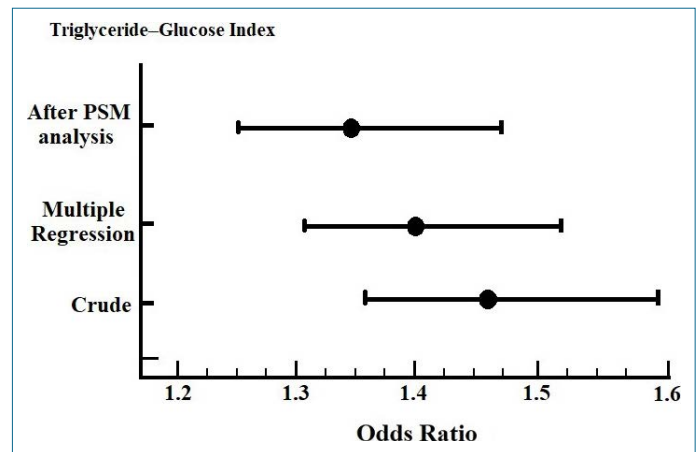
### RESULTS

The mean age of the study population was  $57.9 \pm 9.2$  years, with the majority being male (62.3%). Hypertension was the most commonly observed condition in the study population (55.9%). The predominant reason for performing CAG was chest pain (97.6%). The prevalence of CAE was found to be 5.5%. In the CAE group, ectatic segments were observed in 45 (48.9%) patients in the right coronary artery (RCA), 28 (30.4%) patients in the left anterior descending (LAD) artery, and 19 (20.7%) patients in the circumflex (Cx) artery. Ectasia size was classified as medium in 48 (52.2%) patients, small in 41 (44.6%) patients, and giant in 3 (3.3%) patients.

In the CAE group, the mean age, the proportion of males, the incidence of hypertension, and the mean TyG index ( $8.5 \pm 0.4$  vs.  $9.0 \pm 0.5$ ,  $p < 0.001$ ) were significantly higher compared to the control group (Fig. 1). Additional laboratory results, along with admission and discharge medical treatments, are detailed in Appendix 1. Potential risk factors for CAE were identified

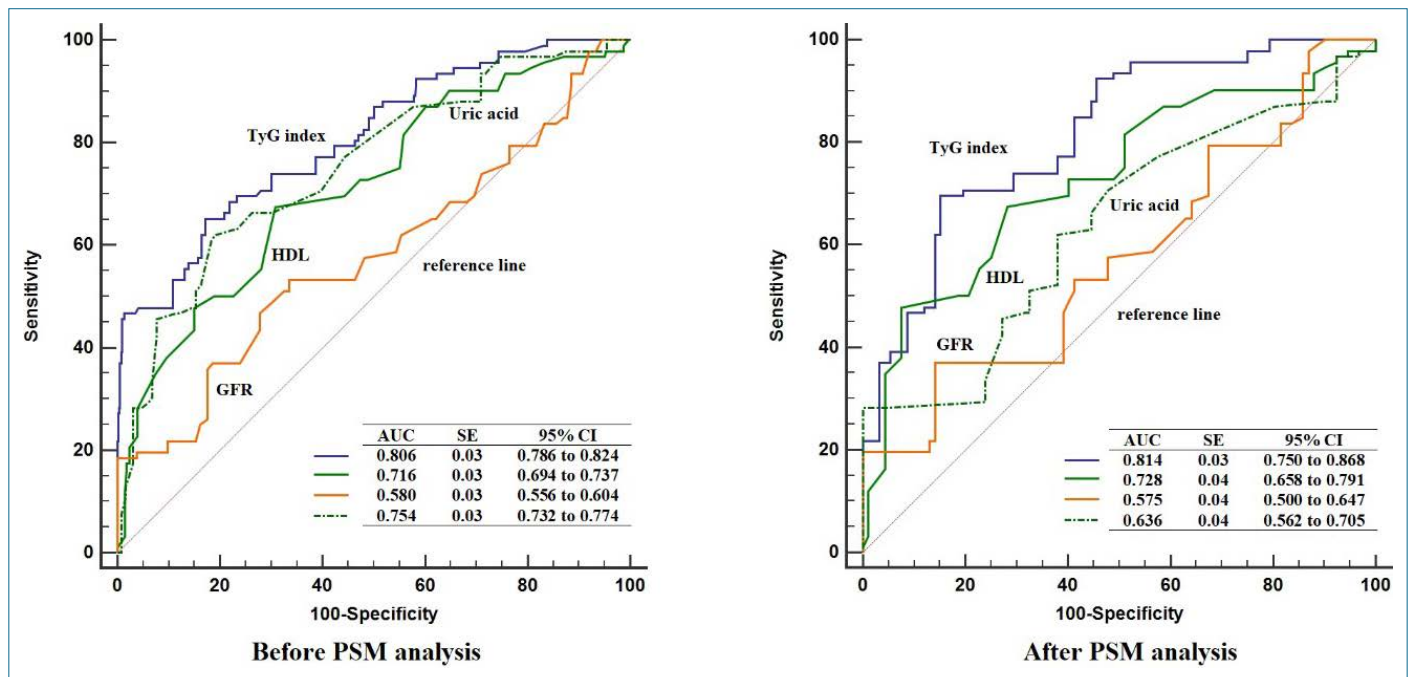
as increased age, male gender, hypertension, a history of medication use, elevated levels of White Blood Cells (WBC), fasting glucose, Low-Density Lipoprotein (LDL), triglycerides, TyG index, CRP, creatinine, and uric acid, as well as decreased levels of High-Density Lipoprotein (HDL) and Glomerular Filtration Rate (GFR). In the multivariable regression analysis that included these potential risk factors, the TyG index emerged as a predictor for CAE (Odds Ratio [OR]=1.47, 95% Confidence Interval [CI]=1.36–1.58,  $p<0.001$ ), alongside age, male gender, the use of loop diuretics, the use of calcium-channel blockers, and levels of HDL, uric acid, and GFR (Appendix 2).

Age, gender, body mass index, comorbid conditions, and medications used were considered as potential confounding factors. Consequently, a Propensity Score Matching (PSM) analysis was conducted to balance these variables between the two groups, employing 1:1 matching utilizing the nearest neighbor matching method with calipers set at 0.2, corresponding to a width of 0.25 times the standard deviation of the logit.<sup>24</sup> Following PSM analysis, 92 individuals from both the CAE and control groups were matched (Table 1). Even after the PSM analysis, the TyG index remained higher in the CAE group compared to the control group ( $9.0\pm 0.4$  vs.  $8.4\pm 0.5$ ,  $p<0.001$ ) (Fig. 1). Other laboratory parameters are presented in Table 1. Independently of other risk factors, it was determined that prior to PSM, a one-unit increase in the TyG index increased the likelihood of CAE by 1.47-fold, whereas after PSM, this likelihood rose to 1.35-fold (Table 2, Fig. 2).



**Figure 2.** The Relationship Between a One-Unit Increase in TyG Index Before and After PSM Analysis and the Probability of CAE. A one-unit increase in TyGi independently raises the likelihood of CAE by 1.40 before PSM, and 1.35 after PSM.

Before PSM analysis, regarding the diagnostic performance of the TyG index in predicting CAE, it was found to have a sensitivity of 65.2% and a specificity of 82.8%, with a cut-off value  $>8.9$  ( $AUC\pm SE=0.806\pm 0.02$ , 95% CI=0.786–0.824). However, after PSM analysis, it proved to be a more reliable predictor with a sensitivity of 70.0% and a specificity of 84.8%, using a cut-off value  $>8.8$  ( $AUC\pm SE=0.814\pm 0.01$ , 95% CI=0.750–0.868) (Fig. 3).



**Figure 3.** Diagnostic Performance of TyG Index in Predicting CAE. (a) Before PSM analysis (b) After PSM analysis.



**Table 2.** Independent predictors of CAE after PSM analysis

Variables	Univariable regression			Multivariable regression		
	OR	95% CI	p	OR	95% CI	p
WBC	1.14	1.01–1.28	0.033*	–	–	–
Fasting glucose	1.06	1.03–1.09	<0.001*	–	–	–
HDL	0.93	0.9–0.96	<0.001*	0.96	0.91–0.99	0.050*
LDL	1.01	1.0–1.02	0.012	–	–	–
TG	1.02	1.02–1.03	<0.001*	–	–	–
TyGi	1.29	1.19–1.40	<0.001*	1.35	1.24–1.48	<0.001*
Creatinine	1.31	1.13–1.52	<0.001*	–	–	–
Uric acid	1.59	1.19–2.12	0.002*	1.65	1.14–2.40	0.009*
GFR	0.98	0.96–0.99	<0.001*	0.96	0.94–0.98	<0.001*
Nagelkerke R <sup>2</sup> =0.426; p<0.001						

\*: P<0.05 indicates statistical significance. CI: Confidence interval; OR: Odds ratio; GFR: Glomerular filtration rate; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; TG: Triglyceride; TyGi: Triglyceride-glucose index.

## DISCUSSION

This study represents the first single-center investigation of its scale to explore the relationship between the TyG index and CAE, according to the available literature. In patients with CAE, we observed an impaired lipid profile characterized by low HDL, high LDL, increased triglyceride levels, and elevated fasting blood glucose levels. The TyG index was significantly higher in the CAE group compared to the control group, establishing it as an independent predictor of CAE. Notably, the TyG index demonstrated exceptional diagnostic capability in distinguishing CAE from control cases, even after adjusting for traditional risk factors.

The prevalence of CAE is influenced by various factors, including geographical location, ethnicity, age, sex, and the presence of cardiovascular risk factors. It is crucial to acknowledge that CAE is often incidentally diagnosed during CAG for suspected CAD or related symptoms, implying that the prevalence figures reported in studies might not accurately reflect the condition's true incidence in the broader population. Prevalence rates reported in studies from different countries vary: for example, a study in China identified a prevalence of 2.8% among CAG patients,<sup>25</sup> while research from Saudi Arabia reported a 6% prevalence.<sup>26</sup>

The pathophysiology of CAE is intricate and remains incompletely understood, encompassing a blend of genetic, inflammatory, and atherosclerotic factors. Atherosclerosis, characterized by the buildup of fatty plaques within the arterial walls, is believed to be a significant contributing factor to CAE.<sup>27</sup> Additionally, endothelial dysfunction, genetic

predisposition, inflammation, matrix metalloproteinases, immune system dysfunction, and hemodynamic factors have all been implicated in the development of CAE.<sup>28</sup> The interplay of these factors can weaken arterial walls, disrupt the regulation of normal vascular tone, and lead to arterial dilation and ectasia. However, the precise mechanisms and the individual contributions of these factors may vary, highlighting the need for further research to achieve a comprehensive understanding of the underlying pathophysiology of CAE.

The relationship between CAE and IR has increasingly captured the attention of cardiovascular researchers. IR, characterized by a reduced sensitivity of cells to insulin, is implicated in the development of a multitude of cardiovascular conditions. The work of Zhang et al.<sup>29</sup> has illuminated the potential link between insulin levels and the development of CAE. Their findings indicate that individuals with CAE have higher insulin levels, suggesting a common mechanism underlying the condition's emergence. Notably, their study found that the severity of lesions varies among patients, with those exhibiting elevated insulin levels also displaying more severe disease manifestations. Cao et al.<sup>30</sup> conducted a comparison of fasting insulin and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) levels among patients with CAE, arteriosclerosis, and those with normal coronary arteries. Their findings revealed significantly higher levels in CAE patients, along with positive associations between fasting glucose, HOMA-IR, and the severity of CAE. These findings suggest a plausible connection between IR and the progression of CAE. CAE may be viewed as an exaggerated vascular remodeling response to atherosclerotic lesions.<sup>27</sup> These findings

underscore the complex relationship between IR, glucose metabolism, and vascular remodeling in CAE, offering potential avenues for therapeutic approaches. Understanding these connections could pave the way for developing targeted interventions and gaining a deeper understanding of the mechanisms underlying CAE. Furthermore, IR can lead to systemic metabolic disturbances, including dyslipidemia, hypertension, and chronic inflammation, all recognized risk factors for CAE. Although the precise mechanisms underlying the relationship between CAE and IR are still under investigation, existing evidence suggests that IR may serve as a significant pathophysiological link between metabolic abnormalities and the development of CAE. Further studies are required to unravel the complexities of this association and to explore its clinical implications for risk stratification and management strategies in individuals with CAE. In our investigation, we observed that the CAE group displayed a less favorable lipid profile and elevated glucose levels. Additionally, higher levels of inflammatory indicators, such as CRP, Erythrocyte Sedimentation Rate (ESR), and uric acid, were noted in the CAE group. These observations align with prior research findings. The TyG index has been identified as an indicator of IR in numerous studies in the literature.<sup>31,32</sup> Increased IR, as indicated by a significantly higher TyG index, was observed in the CAE group. The association between unfavorable lipid profiles and inflammation has been demonstrated in various studies, suggesting that elevated IR, impaired lipid profile, and an unfavorable inflammatory profile are widely recognized. Thus, these metabolic conditions might be potential contributors to the development of CAE in our patients.

In our recent study investigating the relationship between CAE and the TyG index, we found that the TyG index was significantly higher in the CAE group and emerged as a predictor in multivariable regression analysis. Considering the presence of traditional cardiovascular risk factors such as advanced age, a predominantly male demographic, and a higher incidence of hypertension in the CAE group, propensity score matching (PSM) was utilized to mitigate these confounding factors. The analysis revealed that the TyG index exhibited better diagnostic performance compared to pre-PSM assessment, suggesting that the TyG index has high sensitivity and specificity in detecting the presence of CAE. Moreover, the TyG index is a readily calculable parameter in outpatient settings, offering ease of use and valuable insights into the likelihood of CAE. However, traditional risk factors in cardiovascular diseases, including advanced age, male gender, smoking, sedentary lifestyle, poor lipid profile, and inadequate blood sugar control, should not be overlooked. Preventable risk factors should be identified early and addressed appropriately.

## Limitations

One limitation of our study was the absence of HOMA-IR values, due to the restriction that this parameter can only be requested by internal medicine specialists within our hospital.

In our study, we compared patients with CAE to those with normal coronary arteries only, limiting our ability to determine whether the increased TyG index is specifically associated with CAE or if it may also be linked to atherosclerosis. Including a control group of patients with atherosclerosis but without CAE would enable a more comprehensive analysis in future studies. Another constraint was the single-center nature of our study, which was confined to patients attending the cardiology outpatient clinic. Consequently, this limitation may affect the generalizability of the results to the broader population. The inclusion of various cytokines and other inflammatory parameters could have enhanced our study by providing a more comprehensive understanding of the inflammatory states of our patients. However, due to the lack of these parameters in routine tests and concerns about associated costs, such data were not available. The exclusion of patients with ST-Elevation Myocardial Infarction (STEMI), those who had previously undergone invasive interventions, and patients slated for invasive procedures following CAG, was a further limitation. However, this exclusion was a deliberate choice to enable a clearer analysis of specific responses to particular treatment protocols and health outcomes within our selected sample. Nonetheless, it is essential for future studies to include these groups to further elaborate on our findings and assess the applicability of the results to a wider patient population.

## CONCLUSION

High levels of the TyG index are considered an independent predictor for the presence of CAE, which is believed to arise from the atherosclerotic process. The TyG index exhibits high diagnostic performance even among patient groups with similar traditional cardiovascular risk factors. Identifying the TyG index, already established as an independent predictor of atherosclerosis, as a predictor in CAE—a significant modality—is important for screening purposes and optimizing treatment in this patient demographic. The ease and speed of calculating the TyG index in an outpatient clinic setting are highly beneficial for clinicians.

**Ethics Committee Approval:** The Ankara Etlik City Hospital Clinical Research Ethics Committee granted approval for this study (date: 03.05.2023, number: AEŞH-EKI-2023-158).

**Author Contributions:** Concept – AK, CT; Design – VOT; Supervision – AHA; Resource – OA, MA; Materials – AK; Data Collection and/or Processing – OG, YT; Analysis and/or Interpretation – AK, YBS; Literature Search – AK; Writing – AK; Critical Reviews – AHA, VOT.

**Conflict of Interest:** The authors have no conflict of interest to declare.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

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**Appendix 1.** Characteristic findings of the research cohort

Variables	All population n=1680	Control group n=1588	CAE group n=92	p
Age, years	57.9±9.2	57.7±9.0	62.1±11.5	0.001*
Gender, n (%)				
Female	633 (37.7)	609 (38.4)	24 (26.1)	0.018*
Male	1047 (62.3)	979 (61.6)	68 (73.9)	
BMI, kg/m <sup>2</sup>	26.9±2.5	26.9±2.4	27.1±2.6	0.207
Hypertension, n (%)	939 (55.9)	866 (54.5)	73 (79.3)	<0.001*
CVE, n (%)	94 (5.6)	83 (5.2)	6 (6.5)	0.764
AF, n (%)	89 (5.3)	79 (5.0)	8 (8.7)	0.186
Drugs, n (%)				
ACEi	824 (49.0)	761 (47.9)	63 (68.5)	<0.001*
Loop diuretics	443 (26.4)	393 (24.7)	50 (54.3)	<0.001*
CCB	214 (12.7)	179 (11.3)	35 (38.0)	<0.001*
Warfarin	19 (1.1)	12 (0.8)	7 (7.6)	<0.001*
DOAC	12 (0.7)	9 (0.6)	3 (3.3)	0.003*
Laboratory findings				
WBC count, x10 <sup>3</sup>	8.2±1.9	8.1±1.8	8.9±2.6	0.006*
PLT count, x10 <sup>3</sup>	276.6±61.3	277.4±60.5	273.7±72.7	0.580
Hemoglobin, mg/dL	14.2±1.5	14.1±1.4	13.9±2.3	0.419
Fasting glucose, mg/dL	89.9±11.6	89.6±11.5	95.6±12.3	<0.001*
HDL, mg/dL	48.6±10.4	49.1±10.2	41.3±11.1	<0.001*
LDL, mg/dL	113.4±37.9	112.8±37.8	122.4±40.0	0.003*
TG, mg/dL	116.5 (80.0–158.5)	109.0 (80.0–156.2)	187.0 (138.2–258.0)	<0.001*
TyGi	8.5±0.5	8.5±0.4	9.0±0.5	<0.001*
ESR, mm/hr	5.2 (4.0–10.0)	5.2 (4.0–9.0)	6.3 (4.0–10.0)	0.356
CRP, mg/L	4.7 (3.0–7.6)	4.6 (3.0–7.6)	5.7 (3.8–9.8)	0.048*
Creatinine, µg/dL	0.8±0.2	0.8±0.2	1.0±0.5	<0.001*
Uric acid, mg/dL	5.1±1.1	5.0±1.1	6.7±6.0	<0.001*
GFR, mL/min/1.73m <sup>2</sup>	87.9±16.6	88.5±15.8	79.0±25.9	0.010*
TSH, µU/mL	1.6 (1.2–2.2)	1.6 (1.2–2.2)	1.5 (1.1–2.1)	0.669
Ectasia artery, n (%)				
LAD	28 (30.4)	–	28 (30.4)	–
Cx	19 (20.7)	–	19 (20.7)	–
RCA	45 (48.9)	–	45 (48.9)	–
Ectasia size, n (%)				
Small	41 (44.6)	–	41 (44.6)	–
Medium	48 (52.2)	–	48 (52.2)	–
Giant	3 (3.3)	–	3 (3.3)	–
Discharge drugs, n (%)				
ASA	449 (26.7)	403 (25.4)	46 (50.0)	<0.001*
BB	496 (29.5)	437 (27.5)	59 (64.1)	<0.001*
Statin	377 (22.4)	332 (20.9)	45 (48.9)	<0.001*
Clopidogrel	32 (1.9)	15 (0.9)	17 (18.5)	<0.001*

Data are mean±standard deviation or median (IQR), or number (%). \*: P<0.05 indicates statistical significance. ACEi: Angiotensin-converting enzyme; AF: Atrial fibrillation; ASA: Acetylsalicylic acid; BB: Beta blocker; BMI: Body-mass index; CAE: Coronary artery ectasia; CAG: Coronary angiography; CCB: Calcium-channel blocker; CRP: C-reactive protein; Cx: Circumflex artery; CVE: Cerebrovascular event; DOAC: Direct oral anticoagulant; ESR: Erythrocyte sedimentation rate; GFR: Glomerular filtration rate; HDL: High-density lipoprotein; LAD: Left anterior descending artery; LDL: Low-density lipoprotein; PLT: Platelet; PSM: Propensity score matching; RCA: Right coronary artery; TG: Triglyceride; TSH: Thyroid-stimulating hormone; TyGi: Triglyceride-glucose index; USA: Unstable angina pectoris; WBC: White blood cell.

**Appendix 2.** Independent predictors of CAE in the research cohort

Variables	Univariable regression			Multivariable regression		
	OR	95% CI	p	OR	95% CI	p
Demographic findings						
Age	1.05	1.03–1.08	<0.001*	1.07	1.02–1.11	0.002*
Gender						
Female	ref			ref		
Male	1.76	1.09–2.84	<0.001*	3.90	1.71–8.92	<0.001*
Hypertension	3.20	1.92–5.36	<0.001*	–	–	–
Drugs						
ACEi	2.36	1.50–3.71	<0.001*		–	–
Loop diuretics	3.62	2.36–5.54	<0.001*	13.87	6.52–29.51	<0.001*
CCB	4.83	3.09–7.57	<0.001*	8.32	4.1–16.91	<0.001*
Warfarin	10.82	4.15–28.17	<0.001*	–	–	–
DOAC	5.91	1.57–22.23	<0.009*	–	–	–
Laboratory findings						
WBC	1.21	1.1–1.34	<0.001*	–	–	–
Fasting glucose	1.06	1.04–1.08	<0.001*	–	–	–
HDL	0.92	0.89–0.94	<0.001*	0.94	0.91–0.98	0.005*
LDL	1.02	1.01–1.05	0.005*	–	–	–
TG	1.03	1.02–1.03	<0.001*	–	–	–
TyGi	1.47	1.36–1.59	<0.001*	1.40	1.30–1.52	<0.001*
CRP	1.03	1.01–1.06	0.045*	–	–	–
Creatinine	1.32	1.22–1.44	<0.001*	–	–	–
Uric acid	1.84	1.58–2.14	<0.001*	1.91	1.63–2.24	<0.001*
GFR	0.97	0.96–0.98	<0.001*	0.98	0.97–0.99	0.031*
Nagelkerke R <sup>2</sup> =0.487; p<0.001						

\*: P<0.05 indicates statistical significance. CI: Confidence interval; OR: Odds ratio; ACEi: Angiotensin-converting enzyme; CCB: Calcium-channel blocker; CRP: C-reactive protein; DOAC: Direct oral anticoagulant; GFR: Glomerular filtration rate; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; TG: Triglyceride; TyGi: Triglyceride-glucose index.