BMC Cardiovascular Disorders

RESEARCH

Open Access

Association between the triglyceride-glucose index and contrast-induced nephropathy in chronic total occlusion patients undergoing percutaneous coronary intervention

Serdar Söner[1*], Adem Aktan[2], Raif Kılıç[3], Hamdullah Güzel[4], Ercan Taştan[1], Metin Okşul[1], Adnan Duha Cömert[1], Mehmet Sait Coşkun[5], Hülya Tosun Söner[6] and Tuncay Güzel[1]

Abstract

Objective The triglyceride glucose (TyG) index is a biomarker of insulin resistance and is associated with an increased risk of cardiovascular events. Contrast-induced nephropathy (CIN) is an important complication that causes poor outcomes in patients undergoing percutaneous coronary intervention (PCI). In this study, we aimed to investigate the relationship between the TyG index and CIN and mortality in patients who underwent PCI due to chronic total coronary occlusion (CTO).

Methods Two hundred eighteen individuals from three separate medical centers who underwent procedural PCI between February 2010 and April 2012 and had a CTO lesion in at least one coronary artery were recruited. According to the TyG index, patients were divided into two groups. Patients with a TyG index ≥ 8.65 were included in Group 1, and patients with a TyG index < 8.65 were included in Group 2. Patients were followed up for 96 months. The main outcome was the development of CIN and mortality.

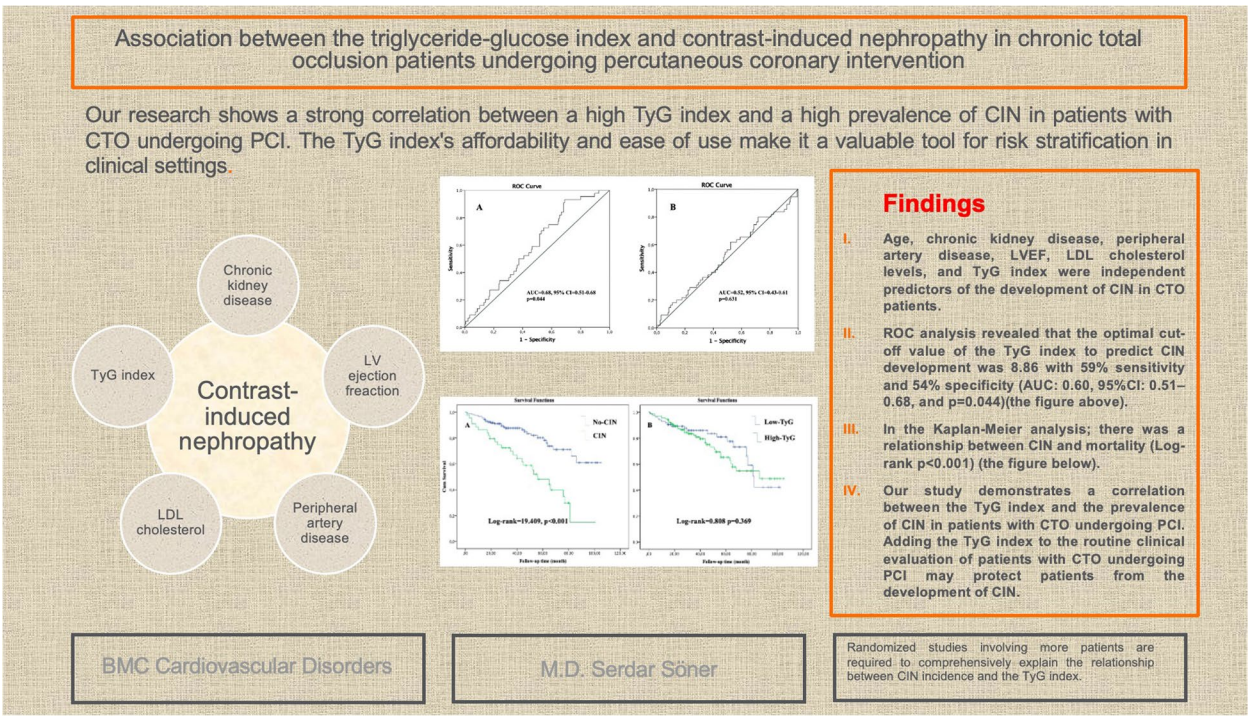
Results The mean age of the patients (65.8 ± 10.94 vs. 61.68 ± 11.4, $P = 0.009$), diabetes mellitus (60 [44.8%] vs. 11 [13.1%], $P < 0.001$), and dyslipidemia rates (52 [38.8%] vs. 21 [25%], $P = 0.036$) were higher in group 1. In multivariable logistic regression analysis, it was seen that age (OR = 1.04, 95% CI = 1.01–1.08, $P = 0.020$), chronic kidney disease (OR = 2.34, 95% CI = 1.02–5.33, $P = 0.044$), peripheral artery disease (OR = 5.66, 95% CI = 1.24–25.91, $p = 0.026$), LVEF (OR = 0.95, 95% CI = 0.92–0.99, $P = 0.005$), LDL cholesterol levels (OR = 1.00, 95%CI = 1.00–1.02, $P = 0.024$) and TyG index (OR = 2.17, 95% CI = 1.21–3.89, $P = 0.009$) were independent predictors of the development of CIN.

Conclusion Our study demonstrates a correlation between the TyG index and the prevalence of CIN in patients with CTO undergoing PCI. Adding the TyG index to the routine clinical evaluation of patients with CTO undergoing PCI may help protect patients from the development of CIN.

Keywords Insulin resistance, Contrast-induced nephropathy, Chronic total occlusion, Triglyceride-glucose index

*Correspondence:
Serdar Söner
drserdar_89@hotmail.com
Full list of author information is available at the end of the article

Graphical Abstract



Introduction

With increasing life expectancy and the elderly population, there has been a significant increase in records regarding the need for coronary angiography (CAG), percutaneous coronary intervention (PCI), and some of its negative consequences in recent years [1, 2]. And this increase is expected to continue. One of the important complications of PCI is contrast-induced nephropathy (CIN). The reported incidence of CIN with PCI varies greatly, from 3 to 19%, despite its significance [3]. Estimates from single-center studies or studies conducted before the current usage of volume expansion techniques and iso-osmolar contrast agents are likely to be the cause of this vast discrepancy.

CIN after PCI is a common and potentially fatal complication of this procedure. CIN is strongly correlated with prolonged hospitalization, increased healthcare costs, late renal and cardiovascular problems, and mortality [4, 5]. Following primary PCI, several factors may contribute to the development of CIN, including intrarenal vasoconstriction, oxidative damage, dysfunction of endothelial cells, inflammatory conditions, decreased renal blood flow, and the production of reactive oxygen species. Direct tubular epithelial cell injury stemming from contrast media is another potential mechanism. [6–9]. Since the specific pathophysiology of CIN is yet unknown, there is no proven treatment for CIN. To lower the occurrence of CIN, screening individuals for significant risk factors and implementing timely preventative measures are crucial.

Insulin resistance (IR) is the primary cause of diabetes mellitus (DM) and a common indicator of a systemic immune response and metabolic problems, which are linked to the development of atherosclerosis of the coronary arteries [10, 11]. Many studies have demonstrated that the TyG index has a relationship with many risk factors for CHD, such as hypertension, diabetes mellitus, obesity, and metabolic syndrome, and it may additionally predict the future outcomes of patients with coronary artery disease (CAD) and in-stent restenosis [12–15]. These studies have shown that the TyG index may be a predictor of poor outcomes. It is known that DM is a predictor of poor outcomes for cardiovascular diseases. However, the TyG index has not been adequately tested in selected patient groups.

Many parameters associated with coronary artery disease and poor prognosis have been previously investigated [16–18]. It has been shown in many studies that the TyG index is a predictor of the development of CIN in acute coronary syndrome, but there is no data on the

amount of contrast agent or angiography duration in these studies [19, 20]. Acute heart failure in acute coronary syndrome patients already contributes to the development of CIN due to Type 1 Cardiorenal Syndrome. We aim to eliminate this doubt by including patients who underwent elective PCI in our study. Again, in our study, we investigate the effect of long-term angiography and excessive contrast use on CIN by including patients with CTO instead of patients who used relatively variable duration and amount of contrast. In our study, we planned to investigate the effect of the TyG index on the development of CIN and mortality in CTO patients who underwent PCI.

Materials and methods

Study population

For this study, 218 individuals from three separate medical centers who underwent procedural CAG between February 2010 and April 2012 and had a CTO lesion in at least one coronary artery were recruited. The study was designed to be cross-sectional, retrospective, and multicenter. According to the Tyg Index values, patients were divided into two groups. The cut-off value for the TyG index was determined by taking into account a study investigating the relationship between triglyceride-glucose index and contrast-induced nephropathy in patients with non-ST elevation myocardial infarction who underwent percutaneous coronary intervention [20]. Patients whose Tyg index value ≥ 8.65 were included in Group 1, and Tyg index value < 8.65 in Group 2. Two cardiologists reviewed and selected the patients' CAG images. The patient's follow-up information, laboratory results, echocardiography results, and demographic information were all taken from the hospital registry. In our study, all patient data was anonymized by removing identifiable information such as names, addresses, and contact details. Each record was assigned a unique identifier, and the dataset was encrypted and securely stored on a restricted-access server. The Health Sciences University Gazi Yaşargil training and research hospital ethics committee granted study permission per the 2013 Declaration of Helsinki (25–26/04/2024). The need for informed consent was waived by the Ethics Committee due to the retrospective nature of the study, which analyzed anonymized data from hospital records. Patients with EF ≥ 40, aged within 18–90 years, and at least one coronary artery with CTO who had procedural CAG were included. EF ≤ 40, acute coronary syndrome (ACS), allergic to contrast, coronary artery bypass grafting (CABG) history, end-stage kidney disease, kidney transplantation history, low blood pressure, intra-aortic balloon pump use, rheumatoid and connective tissue diseases, cancer, current infection, and data inaccessibility were among the exclusion criteria. The patient flowchart is shown in Fig. 1. The main outcome measure for the 96-month follow-up period was CIN and mortality. The patients were called for the first check-up at the end of the first month and were called for check-ups every 3 months until the first year. After the first year, they were called for check-ups every 6 months. During the check-ups, the patients' laboratory values, clinical conditions and medication use were evaluated and recorded.

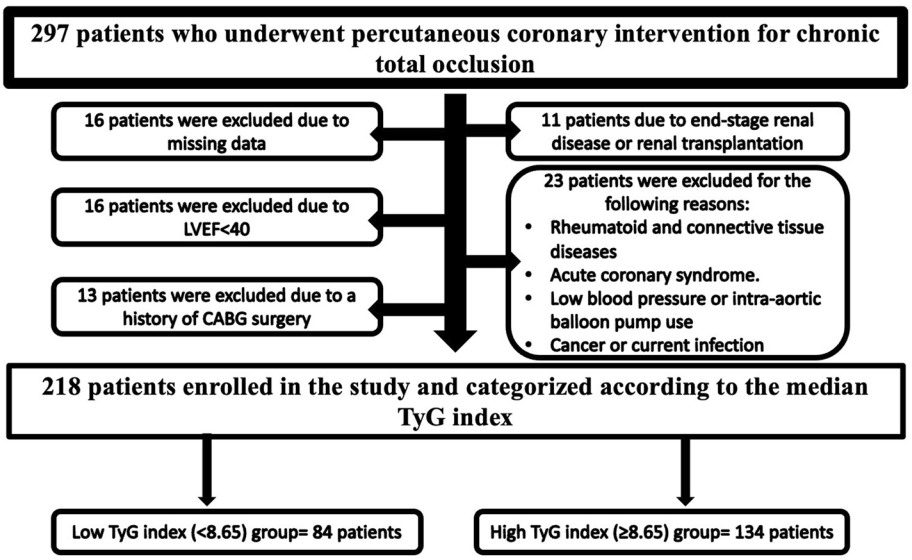


Fig. 1 Patients enrollment flowchart

Periprocedural management

For every patient in the study, a non-ionized low-osmolality contrast agent was utilized. The doctor's decision on the angioplasty procedure and the quantity of contrast agents was final. Before and after the procedure, all of the study's patients were given hydration with a serum that contained at least 1000 cm^3 of a 0.9% isotonic sodium chloride solution. Before the procedure, 300 mg of aspirin and 300 mg of clopidogrel were given to each patient. Following PCI, a minimum of one year of therapy with 100 mg/d of aspirin and 75 mg/d of clopidogrel was recommended. All of the study participants regularly got statins, beta-blockers, and angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor antagonists (ARBs), assuming no contraindications applied.

Definitions

Blood samples were obtained from the anterior region of each study patient's arm while they were in the supine position after they were admitted to the cardiology clinic. While the blood parameters were being examined at room temperature, the serum was separated using centrifugation at 3000×g cycles. Individuals whose blood pressure measurement was 90/60 or below were classed as hypotensive, while those whose measurement was 140/90 or greater were hypertensive. A patient's low-density lipoprotein (LDL) level exceeding 130 mg/dL, their total cholesterol level over 200 mg/dL, or their usage of statins were all defined as dyslipidemia. The echocardiography laboratory performed transthoracic 2D echocardiography (Vivid S6, GE Medical Systems, USA) to calculate the patients' LVEF. CIN was defined as a rise in serum creatinine concentration that occurs 48–72 h after CAG of 0.5 mg/dL, or ≥ 25%. Renal failure was defined as an eGFR (glomerular filtration rate) of less than 60 mL/min/1.73 m2, as calculated by the Cockcroft-Gault formula. A saline solution of 1 ml/kg/h was given to all patients whose creatinine clearance was less than 60 ml/min, both 12 h before and following the procedure. If their ejection fraction was less than 40%, they were given 0.5 ml/kg/h. The methodology used to determine the TyG index was Ln (fasting triglyceride [mg/dL] × fasting blood glucose [mg/dL]/2), [21].

Statistical analysis

For analysis, the IBM SPSS version 24.0 software was used. Depending on how the data were distributed, baseline continuous variables were given as means ± standard deviation or median and interquartile range (IQR). Frequency and percentage were used to characterize categorical variables. The normal distribution of variables was analyzed through Kolmogorov–Smirnov and Shapiro–Wilk tests. The association between survival and CIN development and the Tyg index over a 96-month follow-up period was examined using the Kaplan–Meier test. Depending on the distributions, the Mann–Whitney U test or Student's t-test were used to compare continuous variables. For continuous variables, univariable analysis was used; for categorical variables, the chi-square or Fisher's exact test was utilized. Using descriptive statistical analysis methods, patients were also analyzed between groups that developed CIN and those that did not. The variables influencing the development of CIN were assessed using univariable logistic regression analysis. Parameters with $p \leq 0.1$ in univariable logistic regression analyses were added to multivariable logistic regression analyses. In all cases, a *P*-value less than 0.05 was considered statistically significant.

Results

Baseline characteristics

The baseline characteristics of the study population are shown in Table 1. The mean age of the patients in group 1 was higher than in group 2 (65.8 ± 10.94 vs. 61.68 ± 11.4, $P=0.009$). Diabetes mellitus (60 [44.8%] vs. 11 [13.1%], $P<0.001$) and dyslipidemia rates (52 [38.8%] vs. 21 [25%], $P=0.036$) were higher in group 1. The rates of cerebrovascular disease, in-stent restenosis, and two or more total vessels were also higher in group 1 ($P<0.05$ for each). No significant difference was observed between the groups in terms of gender, LVEF, hypertension, smoking, chronic kidney disease (CKD), and peripheral artery disease.

Hemoglobin ($P=0.022$), glucose ($P<0.001$), total cholesterol ($P=0.002$), triglyceride ($P<0.001$), and uric acid levels ($P=0.044$) were higher in group 1. No significant difference was observed between the groups in terms of white blood cell, neutrophil, lymphocyte, platelet, creatinine, glomerular filtration rate, albumin, HDL, and LDL values.

In the Pearson correlation analysis, while a significant correlation was observed between white blood cell ($P=0.001$), glucose, triglyceride, total cholesterol values ($P<0.001$ for each), and TyG index, no significant correlation was observed between LVEF, LDL, GFR, hemoglobin values, and TyG index. Correlation analyses are shown in Table 2.

Logistic regression analyses

When patients were grouped according to the development of CIN, in univariable logistic regression analysis, age, chronic kidney disease, peripheral artery disease, LVEF, two or more total vessels, LDL cholesterol levels, and TyG index were found to be predictors of the development of CIN ($P<0.05$ for each). When the parameters

Table 1 Baseline characteristics of the total population according to the groups

Variables	TyG index ≥ 8.65 (*n* = 134)	TyG index < 8.65 (*n* = 84)	*P* value
Age years	65.8 ± 10.94	61.68 ± 11.45	**0.009**
Female gender, n (%)	39 (29.1)	20(23.8)	0.392
Ejection fraction (IQR)	50 (20)	50 (20)	0.223
Hypertension, n (%)	48 (35.8)	30 (35.7)	0.987
Diabetes mellitus, n (%)	60 (44.8)	11 (13.1)	**< 0.001**
Dyslipidemia, n (%)	52 (38.8)	21 (25)	**0.036**
Smoking, n (%)	37 (27.6)	21 (25)	0.671
Chronic kidney disease, n (%)	31 (23.1)	18 (21.4)	0.769
Cerebrovascular disease, n (%)	6(4.5)	0 (0)	**0.049**
Peripheral arterial disease, n (%)	7 (5.2)	5 (6)	0.818
In-stent restenosis, n (%)	22 (16.4)	6 (7.1)	**0.046**
Two or more total vessel, n (%)	18 (13.4)	4 (4.8)	**0.039**
Hemoglobin, gr/dL	13.8 ± 1.8	13.3 ± 1.9	**0.022**
White blood cell, 10^3/μL	10.0 ± 3.5	9.6 ± 3.5	0.540
Neutrophile, 10^3/μL (IQR)	5.81 (4.2)	5.26 (2.7)	0.136
Lymphocyte, 10^3/μL (IQR)	2.15 (1.1)	1.97(1.07)	0.165
Platelet, 10^3/μL	246 ± 71.6	247.3 ± 79.8	0.902
Glucose, mg/dL (IQR)	144 (122)	103 (29)	**< 0.001**
Creatinine, mg/dL (IQR)	0.89 (0.3)	0.88 (0.31)	0.458
Glomerular filtration rate, mL/min	80.88 ± 23.3	82.13 ± 26.95	0.717
Albumin, mg/dL	3.6 ± 0.44	3.56 ± 0.47	0.465
Total cholesterol, mg/dL	188.8 ± 9.6	168.4 ± 44.6	**0.002**
HDL, mg/dL	37.9 ± 7.9	42.5 ± 13.1	**0.002**
LDL, mg/dL	108.2 ± 37.1	102.9 ± 38.3	0.316
Triglyceride, mg/dL (IQR)	193 (106)	98 (49.25)	**< 0.001**
Uric acid, mg/dL	6.2 ± 1.85	5.61 ± 1.88	**0.044**

TyG index Triglyceride-glucose index, *HDL* High density lipoprotein, *LDL* Low density lipoprotein

Table 2 Pearson correlation tests with TyG index

Parameters	Correlation coefficient	*P* value
White blood cell	0.219	**0.001**
Hemoglobin	0.108	0.113
Ejection fraction	0.039	0.565
Glomerular filtration rate	−0.092	0.174
Glucose	0.587	**< 0.001**
Triglyceride	0.514	**< 0.001**
Total cholesterol	0.261	**< 0.001**
Low density lipoprotein	0.048	0.483

contributing to the development of CIN were put into the multivariable logistic regression model, it was seen that age (OR = 1.04, 95% CI = 1.01–1.08, $P = 0.020$), chronic kidney disease (OR = 2.34, 95% CI = 1.02–5.33, $P = 0.044$), peripheral artery disease (OR = 5.66, 95% CI = 1.24–25.91, $P = 0.026$), LVEF (OR = 0.95, 95% CI = 0.92–0.99, $P = 0.005$), LDL cholesterol levels (OR = 1.00, 95%CI = 1.00–1.02, $P = 0.024$) and TyG index (OR = 2.17, 95% CI = 1.21–3.89, $P = 0.009$) were independent predictors of the development of CIN (Table 3).

ROC curve and survival analyses

Receiver operating characteristic curve (ROC) analysis revealed that the optimal cut-off value of the TyG index to predict CIN development was 8.86 with 59% sensitivity and 54% specificity (AUC: 0.60, 95%CI: 0.51–0.68, and $P = 0.044$). However, no significant relationship was observed between the TyG index and mortality in the ROC analysis ($p = 0.631$) (Fig. 2).

Patients were grouped according to the TyG index and CIN development, and the mortality curve was created using Kaplan–Meier analysis. While there was no significant relationship between the TyG index and mortality (Log-rank = 0.808, $P = 0.369$), a significant relationship was observed between the development of CIN and mortality (Log-rank = 19.409, $P < 0.001$). Kaplan–Meier

Table 3 Logistic regression analyses of the development of contrast-induced nephropathy

Parameters	Univariable analysis		Multivariable analysis	
	OR (95%CI)	*P* value	OR (95%CI)	*P* value
Age	1.04 (1.01–1.07)	**0.007**	1.04 (1.01–1.08)	**0.020**
Female gender	0.87 (0.41–1.87)	0.730		
Hypertension	1.66 (0.85–3.26)	0.136		
Diabetes mellitus	0.63 (0.32–1.25)	0.188		
Cerebrovascular disease	0.24 (0.47-.1.23)	0.087	1.87 (0.24–14.58)	0.549
Chronic kidney disease	3.64 (1.78–7.45)	**< 0.001**	2.34 (1.02–5.33)	**0.044**
Dyslipidemia	0.75 (0.38–1.49)	0.419		
Peripheral arterial disease	4.42 (1.35–14.46)	**0.014**	5.66 (1.24–25.91)	**0.026**
Smoking	1.79 (0.88–3.63)	0.104		
Ejection fraction	0.95 (0.92–0.98)	**0.001**	0.95 (0.92–0.99)	**0.005**
Glucose	1.00 (0.99–1.00)	0.176		
Total cholesterol	1.00 (1.00–1.01)	0.257		
Hemoglobin	0.94 (0.78–1.12)	0.483		
Two or more total vessel	3.19 (1.26–8.03)	**0.014**	1.71 (0.57–5.12)	0.342
TyG index	1.91 (1.21–3.04)	**0.006**	2.17 (1.21–3.89)	**0.009**
LDL cholesterol	1.10 (1.00–1.01)	**0.028**	1.00 (1.00–1.02)	**0.024**

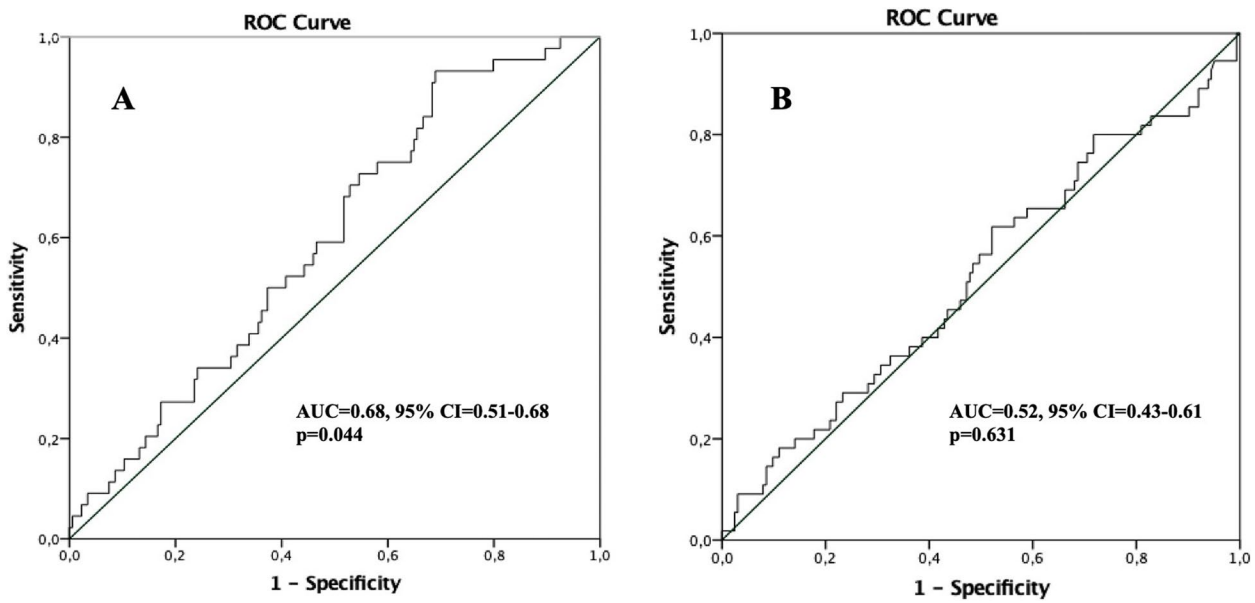


Fig. 2 ROC curve analysis of TyG index to predict the development of CIN (**A**) and death (**B**)

analyses are shown in Fig. 3. Additionally, a graphical abstract summarizing the findings of our study is schematized.

Discussion

In this study, we investigated the relationship between the TyG index and CIN development and mortality in CTO patients. According to the results of our study, the TyG index was found to be an independent predictor of CIN development. However, the relationship between the TyG index and mortality was not statistically significant.

Other results of our study showed a significant relationship between the TyG index and the development of cerebrovascular accident, dyslipidemia, advanced age, DM, in-stent restenosis, number of multiple total vessels, and uric acid levels.

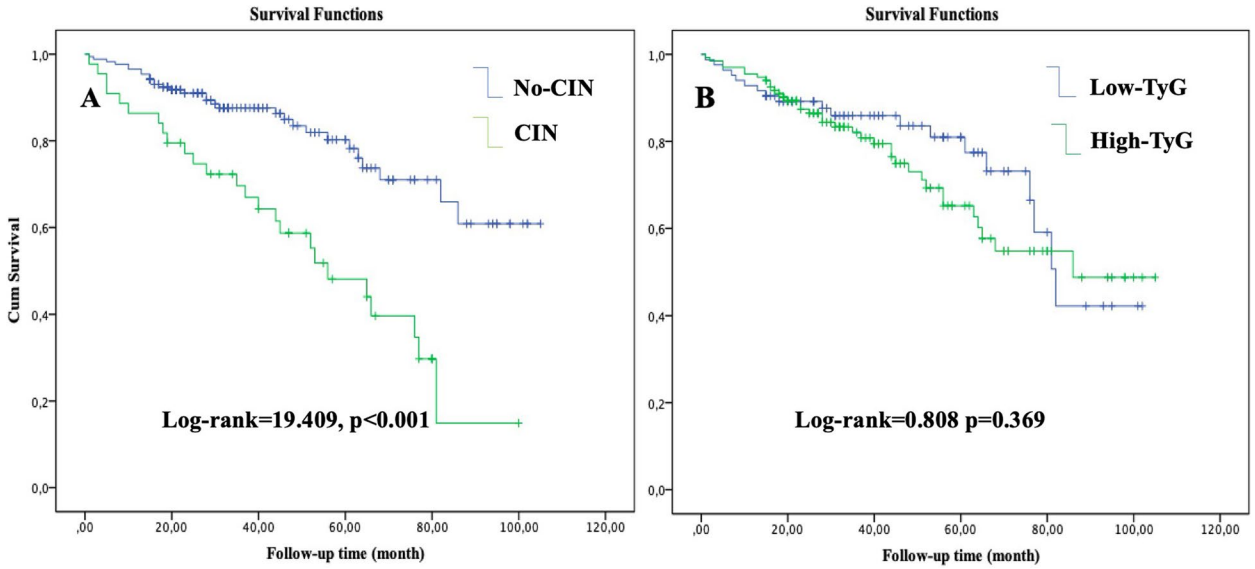


Fig. 3 Kaplan–Meier analysis of CIN development (**A**) and TyG index (**B**) for survival

Many previous studies have shown the association between TyG index and cardiovascular diseases, DM, and angina pectoris, and the prognosis of these diseases [21–29]. According to Alessandra et al., the TyG index may be utilized to measure atherosclerosis in individuals with known cardiovascular disease (CVD) and was positively correlated with a greater incidence of symptomatic CAD [30]. Additionally, Jin et al. demonstrated a positive correlation between the TyG index and subsequent cardiovascular (CV) events, such as non-fatal myocardial infarction, cerebrovascular accident, after-discharge revascularization, and total mortality [31]. These findings raise the possibility that the TyG index can be a helpful indicator for forecasting clinical consequences in patients with stable coronary artery disease. According to research by Mao et al., the TyG index may be a separate predictor of the severity of CAD as determined by the SYNTAX Score and future cardiovascular events, which are defined as the combined occurrences of non-fatal stroke, cardiac mortality, target vessel revascularization, chronic heart failure, and non-fatal myocardial infarction in non-ST-segment elevation acute coronary syndrome [32]. Similar to these studies, in our study, a significant relationship was observed between the TyG index and advanced age, diabetes mellitus, dyslipidemia, cerebrovascular disease, in-stent restenosis, and two or more total vessels.

Insulin resistance may be connected to the TyG index's negative correlation with CV outcomes, even if the exact mechanism is yet unknown. Numerous investigations conducted in the last several years have demonstrated the significance of IR in advanced plaque advancement as well as atherogenesis. This is because IR promotes the death of endothelial cells, vascular smooth muscle cells, and macrophages [33, 34]. IR may lead to several metabolic alterations that can precipitate the onset of CVD. For instance, IR may result in an imbalance in the metabolism of glucose, leading to persistent hyperglycemia. This, in turn, may produce oxidative stress and an inflammatory response, ultimately resulting in damage to vascular endothelial cells. Additionally, IR can change how fats are metabolized. This can result in dyslipidemia and the well-known lipid triad of increased plasma triglycerides, decreased plasma HDL cholesterol, and the formation of tiny, dense LDL cholesterol particles. The development of atherosclerotic plaque is facilitated by these metabolic alterations [35].

Prior research found that the use of a contrast agent decreased human renal blood flow by 50% around four hours later [36, 37]. Renal hypoxia and worsening of damage might result from renal vascular endothelial cells' increased release of different vasoconstriction factors and decreased release of vasodilatation factors following the injection of contrast agent. Since there is now no effective, proven treatment for CIN, it is important from a medical point of view to prevent CIN.

There are many studies examining the relationship between the TyG index and CIN development. The most important difference between our study and other studies is that ACS patients who underwent emergency PCI were excluded, and only CTO patients were included in the study. One study showed a strong relationship between high TyG index and the risk of developing CIN

in patients with type 2 diabetes mellitus and coronary artery disease [19]. Again, in a study including 350 non-diabetic NSTEMI patients who underwent PCI procedures, a significant relationship was observed between the TyG index and the development of CIN [20].

A research of 1772 PCI patients in China found that hyperuricemia, age > 75, eGFR < 60, anemia, and emergent PCI were independent predictors of CIN [38]. In our study, similar to the results of this study, advanced age, CKD, and hyperuricemia were predictors of the development of CIN. Unlike this study, in our study, no significant relationship was observed between anemia and the development of CIN, and emergency PCI patients were not included in the study. While the exact pathophysiological mechanism behind the deleterious consequences of hyperuricemia is yet unknown, it seems to be complex. Hyperuricemia has been associated in clinical studies with many proatherogenic processes, such as elevated oxidative stress, smooth muscular cell proliferation, inflammatory processes, and dysfunction of endothelial cells [39–41].

A previous study found a significant relationship between anemia and the development of CIN, but the effect of anemia on CIN was examined in patients with GFR = 15–60 [42]. Anemia may have already been effective in stage 3–4 CKD patients. However, in our study, anemia did not appear to be a predictor of CIN because our population did not consist only of CKD patients. CKD itself is already a predictor of CIN, and anemia may have been significant in this patient group. To understand the true impact of anemia, studies including patients with normal kidney function are needed.

LDL cholesterol can cause the endothelial B-type receptors to be upregulated, which can lead to vasospasms and decrease the flow of blood locally. As a result, the authors hypothesized that elevated LDL cholesterol levels may be linked to CIN by inducing renal vasoconstriction, a link that was supported by additional research. The results of our study also support this study. In our study, LDL cholesterol level was evaluated as an independent predictor for the development of CIN.

According to earlier research, a prolonged rise in arterial blood pressure can harm the renal vessel's ability to regulate its blood pressure. It can also lead to renal arteriole thickening and arteriosclerosis, which can cause hypertension and high glomerular capillary filtration, which can ultimately result in ischemia and sclerosis of the glomerulus [43]. The relationship between hypertension and the development of CIN is not clear. In our study, unlike this study, no significant relationship was observed between hypertension and the development of CIN. This may be due to the low number of hypertensive patients. In addition, whether hypertension is under control or not is an important confounding factor. Perhaps studies that include only controlled hypertensive patients can guide the scientific world to obtain clearer data on this subject.

The main reason why the CIN development rate in our study is higher than other studies is that patients with chronic total occlusion were included in the study, and as a result, the procedure time was prolonged, and the amount of contrast material was high. Additionally, RIFFLE criteria were used in the definition of CIN. In one study, the authors compared CIN criteria. While 18.3% of patients met the criteria for CIN, 12.2%, 10.5%, and 15.6% of the patients met the criteria for AKIN, RIFLE (CKD-EPI), and RIFLE (MDRD), respectively. They showed that the criteria that best define CIN development after STEMI are the RIFFLE criteria. [44].

A meta-analysis study including six prospective and six retrospective studies was conducted to evaluate the associations of the TyG index with cardiovascular disease and mortality risks in the general population. As a result of the study, no significant association was found between cardiovascular or all-cause mortality and TyG index [42]. However, results were different in a study of 5452 critically ill individuals with coronary artery disease. In this study, increasing TyG index was associated with 30-day and 1-year all-cause mortality [45, 46]. In our study, TyG index and all-cause mortality were investigated in parallel, and no significant association was found. This may be due to the small number of patients included in the study and the small number of deaths that occurred. Although there is no accepted cut-off value for the TyG index, it is an important finding that a high TyG index can predict CIN. The significant results in regression analyses suggest that the TyG index may be useful in predicting the risk of CIN. However, the low sensitivity and specificity values in the ROC analysis indicate that this index alone will not be sufficient to predict CIN. Incorporating the TyG index into a multiparameter risk score for CIN may increase its clinical applicability. Nevertheless, the use of the TyG index in clinical practice can be a reference for invasive cardiologists in predicting procedural complications, especially CIN. Therefore, invasive cardiologists can reduce procedural complications and protect patients from poor outcomes by considering the risk of developing CIN in patients with high TyG index. Moreover, the mortality relationship appears negative in our study. Prospective studies with large participation investigating the relationship between the TyG index and mortality may be useful. In future studies planned to be conducted on CIN using the TyG index, prospective studies with a larger patient population may be decisive in this regard.

Our study has lots of limitations. Firstly, our population consists of relatively few patients. The small sample size

in our study and the use of a cohort from approximately ten years ago may be a limitation in generalizing its effect to the current literature. Considering the wide spectrum of CTO disease, the small number of patients becomes a very important limitation. Considering that our study is limited to Turkey, it would be appropriate to consider it as a study that cannot be generalized on a global scale. Some results that are inconsistent with the current literature may be due to these reasons. Given that creatinine levels are expected to rise within three to five days after the procedure, differences in the timing of peak creatinine levels after the procedure may have led to an incorrect estimate of the true CIN rate. In addition, although we attempted to reduce this limitation by including only patients with CTO that were prolonged and used in large amounts of contrast, the fact that parameters such as the amount of contrast medium used and procedure times were not included in our data is an important limitation. Procedure time and the amount of contrast medium associated with it are parameters that alone may affect the development of CIN. The effect of some parameters that may affect the development of CIN could not be completely excluded. We did not have information on calorie intake or dietary habits, which could affect TG levels even after correcting for other important factors such as blood lipids. Another limitation of the study design is that certain patient groups, such as heart failure with low ejection fraction and rheumatological diseases, were not included, which prevents the study from being generalizable to all patient populations.

Conclusion

Our study demonstrates a correlation between the TyG index and the prevalence of CIN in patients with CTO undergoing PCI. The affordability and ease of use of the TyG index make it a valuable tool for risk stratification in clinical settings. Adding the TyG index to the routine clinical evaluation of patients with CTO undergoing PCI may help protect patients from the development of CIN. Although its use alone is not sufficient, we believe that the TyG index can be included in a risk score to predict CIN.

Acknowledgements
None.

Clinical trial number
Not applicable.

Authors' contributions
S. Söner, H.T. Söner, and T. Güzel contributed to data acquisition. A.D. Cömert, E. Taştan, and M. Okşul were responsible for the analysis. M. S. Coşkun, R. Kılıç, A. Aktan, and H. Güzel were responsible for drafting the manuscript, and all authors contributed to the concept, study design, and interpretation of the data. All authors contributed to the critical revision of the manuscript and have approved the final version for submission.

Funding
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability
Data is available upon reasonable request from the corresponding author and will be provided after anonymization. (drserdar_89@hotmail.com).

Declarations

Ethics approval and consent to participate
The Health Sciences University Gazi Yaşargil Training and Research Hospital ethics committee granted study permission per the 2013 Declaration of Helsinki (25–26/04/2024). The need for informed consent was waived by the Ethics Committee due to the retrospective nature of the study, which analyzed anonymized data from hospital records.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Cardiology, Health Science University, Gazi Yaşargil Training and Research Hospital, Diyarbakır 21070, Turkey. [2]Department of Cardiology, Mardin Artuklu University, Mardin, Turkey. [3]Department of Cardiology, Çermik State Hospital, Diyarbakır, Turkey. [4]Department of Cardiology, Düzce University Faculty of Medicine, Düzce, Turkey. [5]Department of Cardiology, Ergani State Hospital, Diyarbakır, Turkey. [6]Department of Anesthesiology and Reanimation, Health Science University, Gazi Yaşargil Training and Research Hospital, Diyarbakır 21070, Turkey.

Received: 9 November 2024 Accepted: 3 January 2025
Published online: 20 January 2025

References

1. Jentzer JC, Scutella M, Pike F, Fitzgibbon J, Krehel NM, Kowalski L, et al. Early coronary angiography and percutaneous coronary intervention are associated with improved outcomes after out of hospital cardiac arrest. Resuscitation. 2018;123:15–21. https://doi.org/10.1016/j.resuscitation.2017.12.004. (Epub 2017 Dec 6 PMID: 29223601).
2. Patel N, Patel NJ, Cohen MG. Coronary Angiography and Percutaneous Coronary Intervention After Out-of-Hospital Cardiac Arrest-Reply. JAMA Cardiol. 2017;2(5):580–1. https://doi.org/10.1001/jamacardio.2016.5788. (PMID: 28146258).
3. Tsai TT, Patel UD, Chang TI, Kennedy KF, Masoudi FA, Matheny ME, et al. Contemporary incidence, predictors, and outcomes of acute kidney injury in patients undergoing percutaneous coronary interventions: insights from the NCDR Cath-PCI registry. JACC Cardiovasc Interv. 201;7(1):1–9. https://doi.org/10.1016/j.jcin.2013.06.016. PMID: 24456715; PMCID: PMC4122507.
4. Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, Fahy M, et al. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. J Am Coll Cardiol. 2004;44(7):1393–9. https://doi.org/10.1016/j.jacc.2004.06.068. (PMID: 15464318).
5. Wi J, Ko YG, Kim JS, Kim BK, Choi D, Ha JW, et al. Impact of contrast-induced acute kidney injury with transient or persistent renal dysfunction on long-term outcomes of patients with acute myocardial infarction undergoing percutaneous coronary intervention. Heart. 2011;97(21):1753–7. https://doi.org/10.1136/hrt.2010.218677. (Epub 2011 May 20 PMID: 21602521).
6. Bartholomew BA, Harjai KJ, Dukkipati S, Boura JA, Yerkey MW, Glazier S, et al. Impact of nephropathy after percutaneous coronary intervention and a method for risk stratification. Am J Cardiol. 2004;93(12):1515–9. https://doi.org/10.1016/j.amjcard.2004.03.008. (PMID: 15194023).

7. Russo D, Minutolo R, Cianciaruso B, Memoli B, Conte G, De Nicola L. Early effects of contrast media on renal hemodynamics and tubular function in chronic renal failure. J Am Soc Nephrol. 1995;6(5):1451–8. https://doi.org/10.1681/ASN.V651451. (PMID: 8589322).
8. Goldenberg I, Matetzky S. Nephropathy induced by contrast media: pathogenesis, risk factors and preventive strategies. CMAJ. 2005;172(11):1461–71. https://doi.org/10.1503/cmaj.1040847. Erratum. In: CMAJ. 2005;173(10):1210. PMID: 15911862; PMCID: PMC557983
9. Heyman SN, Khamaisi M, Rosen S, Rosenberger C. Renal parenchymal hypoxia, hypoxia response and the progression of chronic kidney disease. Am J Nephrol. 2008;28(6):998–1006. https://doi.org/10.1159/000146075. (Epub 2008 Jul 18 PMID: 18635927).
10. Meikle PJ, Summers SA. Sphingolipids and phospholipids in insulin resistance and related metabolic disorders. Nat Rev Endocrinol. 2017;13(2):79–91. https://doi.org/10.1038/nrendo.2016.169. (Epub 2016 Oct 21 PMID: 27767036).
11. Imai Y, Dobrian AD, Weaver JR, Butcher MJ, Cole BK, Galkina EV, et al. Interaction between cytokines and inflammatory cells in islet dysfunction, insulin resistance and vascular disease. Diabetes Obes Metab. 2013;15 Suppl 3(0 3):117–29. https://doi.org/10.1111/dom.12161. PMID: 24003928; PMCID: PMC3777698.
12. Zhu Y, Liu K, Chen M, Liu Y, Gao A, Hu C, et al. Triglyceride-glucose index is associated with in-stent restenosis in patients with acute coronary syndrome after percutaneous coronary intervention with drug-eluting stents. Cardiovasc Diabetol. 2021;20(1):137. https://doi.org/10.1186/s12933-021-01332-4. PMID: 34238294; PMCID: PMC8268452.
13. Wang Y, Yang W, Jiang X. Association Between Triglyceride-Glucose Index and Hypertension: A Meta-Analysis. Front Cardiovasc Med. 2021;31(8):644035. https://doi.org/10.3389/fcvm.2021.644035. PMID: 34136539; PMCID: PMC8200397.
14. Si Y, Fan W, Shan W, Zhang Y, Liu J, Han C, et al. Association between triglyceride glucose index and coronary artery disease with type 2 diabetes mellitus in middle-aged and elderly people. Medicine (Baltimore). 2021;100(9):e25025. https://doi.org/10.1097/MD.0000000000025025. PMID: 33655974; PMCID: PMC7939227.
15. Khan SH, Sobia F, Niazi NK, Manzoor SM, Fazal N, Ahmad F. Metabolic clustering of risk factors: evaluation of Triglyceride-glucose index (TyG index) for evaluation of insulin resistance. Diabetol Metab Syndr. 2018;5(10):74. https://doi.org/10.1186/s13098-018-0376-8. PMID: 30323862; PMCID: PMC6173832.
16. Wang Z, Ye D, Ye J, Wang M, Liu J, Jiang H, et al. ADAMTS-5 Decreases in Coronary Arteries and Plasma from Patients with Coronary Artery Disease. Dis Markers. 2019;16(2019):6129748. https://doi.org/10.1155/2019/6129748. PMID: 31929842; PMCID: PMC6935801.
17. An K, Jia Y, Xie B, Gao J, Chen Y, Yuan W, et al. Alterations in the gut mycobiome with coronary artery disease severity. EBioMedicine. 2024 May;103:105137. https://doi.org/10.1016/j.ebiom.2024.105137. Epub 2024 May 3. PMID: 38703606; PMCID: PMC11087906.
18. Smith ML, Bull CJ, Holmes MV, Davey Smith G, Sanderson E, Anderson EL, et al. Distinct metabolic features of genetic liability to type 2 diabetes and coronary artery disease: a reverse Mendelian randomization study. EBioMedicine. 2023 Apr;90:104503. https://doi.org/10.1016/j.ebiom.2023.104503. Epub 2023 Mar 2. PMID: 36870196; PMCID: PMC10009453.
19. Qin Y, Tang H, Yan G, Wang D, Qiao Y, Luo E, et al. A High Triglyceride-Glucose Index Is Associated With Contrast-Induced Acute Kidney Injury in Chinese Patients With Type 2 Diabetes Mellitus. Front Endocrinol (Lausanne). 2021;22(11):522883. https://doi.org/10.3389/fendo.2020.522883. PMID: 33551987; PMCID: PMC7862330.
20. Gursoy E, Baydar O. The triglyceride-glucose index and contrast-induced nephropathy in non-ST elevation myocardial infarction patients undergoing percutaneous coronary intervention. Medicine (Baltimore). 2023;102(2):e32629. https://doi.org/10.1097/MD.0000000000032629. PMID: 36637929; PMCID: PMC9839251.
21. Hong S, Han K, Park CY. The triglyceride glucose index is a simple and low-cost marker associated with atherosclerotic cardiovascular disease: a population-based study. BMC Med. 2020;18(1):361. https://doi.org/10.1186/s12916-020-01824-2. PMID: 33234146; PMCID: PMC7687762.
22. Wu Y, Yang Y, Zhang J, Liu S, Zhuang W. The change of triglyceride-glucose index may predict incidence of stroke in the general population over 45 years old. Cardiovasc Diabetol. 2023;22(1):132. https://doi.org/10.1186/s12933-023-01870-z. PMID: 37296457; PMCID: PMC10257314.
23. Chen X, Liu D, He W, Hu H, Wang W. Predictive performance of triglyceride glucose index (TyG index) to identify glucose status conversion: a 5-year longitudinal cohort study in Chinese pre-diabetes people. J Transl Med. 2023;21(1):624. https://doi.org/10.1186/s12967-023-04402-1. PMID: 37715242; PMCID: PMC10503019.
24. Xue Y, Xu J, Li M, Gao Y. Potential screening indicators for early diagnosis of NAFLD/MAFLD and liver fibrosis: Triglyceride glucose index-related parameters. Front Endocrinol (Lausanne). 2022;2(13):951689. https://doi.org/10.3389/fendo.2022.951689. PMID: 36120429; PMCID: PMC9478620.
25. Zhao Y, Gu Y, Zhang B. Associations of triglyceride-glucose (TyG) index with chest pain incidence and mortality among the U.S. population. Cardiovasc Diabetol. 2024;23(1):111. https://doi.org/10.1186/s12933-024-02209-y. PMID: 38555461; PMCID: PMC10981836.
26. Guo D, Wu Z, Xue F, Chen S, Ran X, Zhang C, Yang J. Association between the triglyceride-glucose index and impaired cardiovascular fitness in non-diabetic young population. Cardiovasc Diabetol. 2024;23(1):39. https://doi.org/10.1186/s12933-023-02089-8. PMID: 38245734; PMCID: PMC10800072.
27. Santulli G, Visco V, Varzideh F, Guerra G, Kansakar U, Gasperi M, et al. Prediabetes Increases the Risk of Frailty in Prefrail Older Adults With Hypertension: Beneficial Effects of Metformin. Hypertension. 2024;81(7):1637–1643. https://doi.org/10.1161/HYPERTENSIONAHA.124.23087. Epub 2024 May 16. PMID: 38752357; PMCID: PMC11170724.
28. Xin F, He S, Zhou Y, Jia X, Zhao Y, Zhao H. The triglyceride glucose index trajectory is associated with hypertension: a retrospective longitudinal cohort study. Cardiovasc Diabetol. 2023;22(1):347. https://doi.org/10.1186/s12933-023-02087-w. PMID: 38102704; PMCID: PMC10725029.
29. Yang Z, Gong H, Kan F, Ji N. Association between the triglyceride glucose (TyG) index and the risk of acute kidney injury in critically ill patients with heart failure: analysis of the MIMIC-IV database. Cardiovasc Diabetol. 2023;22(1):232. https://doi.org/10.1186/s12933-023-01971-9. PMID: 37653418; PMCID: PMC10472684.
30. da Silva A, Caldas APS, Hermsdorff HHM, Bersch-Ferreira ÂC, Torreglosa CR, Weber B, et al. Triglyceride-glucose index is associated with symptomatic coronary artery disease in patients in secondary care. Cardiovasc Diabetol. 2019;18(1):89. https://doi.org/10.1186/s12933-019-0893-2. PMID :31296225;PMCID:PMC6625050.
31. Jin JL, Cao YX, Wu LG, You XD, Guo YL, Wu NQ, et al. Triglyceride glucose index for predicting cardiovascular outcomes in patients with coronary artery disease. J Thorac Dis. 2018;10(11):6137–46. https://doi.org/10.21037/jtd.2018.10.79. PMID:30622785;PMCID:PMC6297409.
32. Mao Q, Zhou D, Li Y, Wang Y, Xu SC, Zhao XH. The Triglyceride-Glucose Index Predicts Coronary Artery Disease Severity and Cardiovascular Outcomes in Patients with Non-ST-Segment Elevation Acute Coronary Syndrome. Dis Markers. 2019;11(2019):6891537. https://doi.org/10.1155/2019/6891537.
33. Di Pino A, DeFronzo RA. Insulin Resistance and Atherosclerosis: Implications for Insulin-Sensitizing Agents. Endocr Rev. 2019;40(6):1447–67. https://doi.org/10.1210/er.2018-00141.
34. Reardon CA, Lingaraju A, Schoenfelt KQ, Zhou G, Cui C, Jacobs-El H, et al. Obesity and Insulin Resistance Promote Atherosclerosis through an IFNγ-Regulated Macrophage Protein Network. Cell Rep. 2018;23(10):3021–30. https://doi.org/10.1016/j.celrep.2018.05.010. PMID:29874587;PMCID: PMC6082182
35. Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga FA. Association between insulin resistance and the development of cardiovascular disease. Cardiovasc Diabetol. 2018;17(1):122. https://doi.org/10.1186/s12933-018-0762-4.PMID:30170598;PMCID:PMC6119242.
36. Patti G. Short-term high-dose atorvastatin for periprocedural myocardial infarction prevention in patients with renal dysfunction. J Cardiovasc Med (Hagerstown). 2011;12(5):305–8. https://doi.org/10.2459/JCM.0b013e3283454faa. (PMID: 21451331).
37. Toso A, Leoncini M, Maioli M, Gallopin M, Tedeschi D, Amato M, et al. Short-term high-dose atorvastatin for periprocedural myocardial infarction prevention in patients with renal dysfunction. J Cardiovasc Med (Hagerstown). 2011May;12(5):318–21. https://doi.org/10.2459/JCM.0b013e328341024f. (PMID: 21045713).
38. Guo W, Liu Y, Chen JY, Chen SQ, Li HL, Duan CY, et al. Hyperuricemia Is an Independent Predictor of Contrast-Induced Acute Kidney Injury and Mortality in Patients Undergoing Percutaneous Coronary Intervention. Angiology. 2015;66(8):721–6. https://doi.org/10.1177/0003319714568516. (Epub 2015 Jan 23 PMID: 25616679).

39. Sautin YY, Nakagawa T, Zharikov S, Johnson RJ. Adverse effects of the classic antioxidant uric acid in adipocytes: NADPH oxidase-mediated oxidative/nitrosative stress. Am J Physiol Cell Physiol. 2007;293(2):C584–96. https://doi.org/10.1152/ajpcell.00600.2006. Epub 2007 Apr 11. Erratum in: Am J Physiol Cell Physiol. 2010;299(3):C726. PMID: 17428837.
40. Corry DB, Eslami P, Yamamoto K, Nyby MD, Makino H, Tuck ML. Uric acid stimulates vascular smooth muscle cell proliferation and oxidative stress via the vascular renin-angiotensin system. J Hypertens. 2008;26(2):269–75. https://doi.org/10.1097/HJH.0b013e3282f240bf. (PMID: 18192841).
41. Khosla UM, Zharikov S, Finch JL, Nakagawa T, Roncal C, Mu W, et al. Hyperuricemia induces endothelial dysfunction. Kidney Int. 2005;67(5):1739–42. https://doi.org/10.1111/j.1523-1755.2005.00273.x. (PMID: 15840020).
42. Murakami R, Kumita S, Hayashi H, Sugizaki K, Okazaki E, Kiriyama T, et al. Anemia and the risk of contrast-induced nephropathy in patients with renal insufficiency undergoing contrast-enhanced MDCT. Eur J Radiol. 2013;82(10):e521–4. https://doi.org/10.1016/j.ejrad.2013.06.004. (Epub 2013 Jul 1 PMID: 23827802).
43. Pan HC, Wu XH, Wan QL, Liu And BH, Wu XS. Analysis of the risk factors for contrast-induced nephropathy in over-aged patients receiving coronary intervention. Exp Biol Med (Maywood). 2018;243(12):970–5. https://doi.org/10.1177/1535370218799973.PMID:30299175;PMCID:PMC6180409.
44. Silvain J, Nguyen LS, Spagnoli V, Kerneis M, Guedeney P, Vignolles N, et al. Contrast-induced acute kidney injury and mortality in ST elevation myocardial infarction treated with primary percutaneous coronary intervention. Heart. 2018;104(9):767–72. https://doi.org/10.1136/heartjnl-2017-311975. (Epub 2017. PMID: 29092921).
45. Liu X, Tan Z, Huang Y, Zhao H, Liu M, Yu P, et al. Relationship between the triglyceride-glucose index and risk of cardiovascular diseases and mortality in the general population: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):124. https://doi.org/10.1186/s12933-022-01546-0.PMID:35778731;PMCID:PMC9250255.
46. Wang H, Fu Q, Xiao S, Ma X, Liao Y, Kang C, et al. Predictive value of the triglyceride-glucose index for short- and long-term all-cause mortality in patients with critical coronary artery disease: a cohort study from the MIMIC-IV database. Lipids Health Dis. 2024;23(1):263. https://doi.org/10.1186/s12944-024-02252-4.PMID:39175047;PMCID:PMC11340174.

Publisher's Note