Acta Cardiologia Indonesiana

pISSN:2460-5700
eISSN:2579-4345

Web page: jurnal.ugm.ac.id/v3/jaci

Triglyceride-Glucose Index Associated with Multivessel Artery Coronary Disease (MVCD) Incidents in Patients with Coronary Artery Disease (CAD) at Sultan Agung Islamic Hospital Semarang

Muhammad Saugi Abduh[1], Ahmad Umar Alfaruq[2]

[1]Cardiovascular Division, Internal Medicine Department, Faculty of Medicine, Sultan Agung Islamic University, Semarang, Central Java, Indonesia
[2]Faculty of Medicine, Sultan Agung Islamic University, Semarang, Central Java, Indonesia

ARTICLE INFO

*Corresponding author
Email: ahmadumaralfaruq@gmail.com

Address:
Semarang, Central Java, Indonesia

Manuscript submitted: 24 May 2024
Revised and accepted: 23 Aug 2024

Keywords: Coronary Artery Disease; Multivessel Coronary Artery Disease; Stenosis; Trigleserid-Glucose Index.

ABSTRACT

Background: Coronary artery disease (CAD) patients with multivessel coronary artery disease (MVCD) have higher incidence of major adverse cardiovascular events (MACEs) than patients with single vessel coronary artery disease (SVCD). The triglyceride-glucose index (TG) is a marker of insulin resistance (IR) which has been linked to cardiovascular diseases. However, evidence on the effect of TG index on the incidence of multivessel coronary artery disease (MVCD) in coronary artery disease (CAD) is still limited.

Objective: This study aims to investigate the association between the TG index and the incidence of MVCD in CAD patients at Sultan Agung Islamic Hospital.

Methods: A total of 198 subjects suffering from CAD at Sultan Agung Islamic Hospital Semarang from March 2022 to December 2023 were divided into 2 groups, the first group being the MVCD group if the stenosis was ≥ 50% in at least two main coronary artery blood vessels and the second group is the non-multivessel coronary artery disease (non-MVCD) if the stenosis is ≥ 50% in one main coronary artery blood vessel. This research is an analytical observational study with a cross sectional design. Multivariate test was carried out using the logistic regression test.

Result: The study showed that higher TG index value (p=0.001; PR = 6.929; 95% CI = 2.209-21.736) significantly increased the risk of MVCD in CAD patients.

Conclusion: The increase of TG index is closely related to the risk of MVCD in CAD patients. This study revealed that the TG index can be a predictor of the severity in CAD patients.

INTISARI

Pendahuluan: Pasien penyakit jantung koroner (PJK) dengan penyakit arteri koroner multivessel (MVCD) memiliki insiden kejadian kejadian kardiovaskular merugikan (MACEs) yang lebih tinggi dibandingkan pasien dengan penyakit arteri koroner pembuluh tunggal (SVCD). Indeks trigliserida-glukosa (TG) merupakan penanda resistensi insulin (IR) yang dikaitkan dengan penyakit kardiovaskular. Namun, bukti mengenai pengaruh indeks TG terhadap kejadian penyakit arteri koroner multivessel (MVCD) pada PJK masih belum banyak dilakukan.

Tujuan: Penelitian ini bertujuan untuk mengetahui hubungan indeks TG dengan kejadian MVCD pada pasien PJK di RS Islam Sultan Agung.

Metode: Sebanyak 198 subjek menderita PJK di RS Islam Sultan Agung Semarang periode Maret 2022 hingga Desember 2023 dibagi menjadi 2 kelompok,

kelompok pertama adalah kelompok MVCD jika stenosis ≥ 50% pada minimal dua pembuluh darah arteri koroner utama dan kelompok kedua adalah penyakit arteri koroner non-multivessel (non-MVCD) jika stenosis ≥ 50% pada satu arteri koroner utama. Penelitian ini merupakan penelitian observasional analitik dengan desain cross sectional. Pada penelitian ini dilakukan uji multivariat dilakukan dengan uji regresi logistik. Hasil : Hasil penelitian menunjukkan bahwa semakin tinggi nilai indeks TG (p=<0.001; PR = 4.117; 95% CI = 2.284-7.424) secara signifikan meningkatkan risiko MVCD pada pasien PJK.

Kesimpulan : Peningkatan indeks TG erat kaitannya dengan risiko MVCD pada pasien CAD. Penelitian ini menunjukkan bahwa indeks TG dapat menjadi prediktor tingkat keparahan pada pasien CAD.

INTRODUCTION

Arteriosclerotic cardiovascular disease (ASCVD), including coronary artery disease (CAD), is the leading cause of death and disability worldwide[1]. Patient mortality due to CAD on the first year is 15%, and may go up to 20% after 5 years[2]. CAD patients with multivessel coronary artery disease (MVCD) have a higher incidence of major adverse cardiovascular events (MACEs) and a poorer long-term prognosis than other patients with single vessel coronary artery disease[3]. Coronary angiography remains to be the gold standard examination used to determine the severity of CAD. However, coronary angiography examination has higher risk of causing damage to the kidneys and allergic reactions because it requires high doses of contrast, so it is not suitable for patients with kidney failure or who are allergic to contrast agents[4].

Insulin resistance (IR) is recently recognized as a risk factor for CAD, especially when predisposing factor is also present, namely obesity and dyslipidemia[5]. However, the gold standard for IR, the hypoglycemic-hyperinsulinemic clamp test, is not feasible for large-scale studies due to its time-consuming and labor-intensive nature. Homeostasis model assessment of insulin resistance (HOMA-IR) is commonly used as a surrogate indicator, but is quite costly and has poor reproducibility[6]. Triglyceride-glucose (TG) index was introduced as a reliable and specific predictor of IR. It has been shown to have a good correlation with the hypoglycemic-hyperinsulinemic clamp test and HOMA-IR[7]. The TG index is particularly suitable for economically underdeveloped areas where laboratory testing may be inconvenient.

Previous studies have shown that a high TG index is linked to the development and prognosis of cardiovascular disease (CVD), even in individuals without CAD at baseline[8,9]. An increasing number of recent studies have reported on the predictive value of the TG index in CAD. To provide more reliable evidence for clinical practice, a study was conducted to summarize the relationship between the TG index, CAD risk, severity, and prognosis. In this context, the TG index is the most reliable non-invasive assessment tool for predicting CAD severity and risk stratification for patients with CAD. However, the association between the TG index and the extent of severity of CAD, as well as clinical outcomes remained unexplored in these patients. Therefore, the present study aimed to determine the association between the TG index and CAD severity in patients with CAD.

METHODS

Patient Populations

All patients that underwent coronary angiography at the Sultan Agung Islamic Hospital from March 2022 to December 2023 were enrolled. The inclusion criteria in this study were patients with CAD, between the age of 18 to 70 years, and had previously checked the fasting blood glucose, triglycerides (TG), creatinine, LDL-C, HDL-C, total cholesterol levels before having a coronary angiography (CAG) examination. Patients with severe arrhythmias, significant valvular heart disease, congenital heart disease, thyroid function disease, hematological disorders, autoimmune diseases, severe systemic diseases, unstable hemodynamics, severe trauma or after major surgery, pregnant or breastfeeding women, loss to follow up and patients who refused to participate in the study were excluded.

Data Collection and Clinical Follow-Up

The baseline demographic, laboratory results, the presence of comorbidities and coronary angiography outcomes data were retrospectively collected through medical record review, and the data extracted was revalidated by our research coordinators and physicians. This research is an analytical observational study with a cross-sectional design. A total of 198 subjects suffering from CAD at Sultan Agung Islamic Hospital Semarang from March 2022 to December 2023 were divided into 2 groups, the first group being the MVCD group if the stenosis was ≥ 50% in at least two main coronary artery blood vessels and the second group is the non-multivessel coronary artery disease (non-MVCD) if the stenosis is ≥ 50% in one main coronary artery blood vessel. The TG index is calculated as ln[fasting triglycerides (mg/dL) × fasting glucose (mg/dL)/2].

Statistical Analysis

The data were analyzed using Statistical Package for the Social Sciences (SPSS) 25 software (IBM, Chicago, USA). Categorical variables are available in the form of frequencies and percentages. A normality test was carried

out using the Kolmogorov-Smirnov test because the data consisted of > 50 samples. Continuous variables with normal data distribution are presented as mean ± standard deviation (SD). Bivariate tests with chi square tests on categorical data and unpaired t tests on numerical data with a normal distribution were carried out to determine the significance of the relationship between the incidence of MVCD and the observed variables. Variables with p<0.25 were included in the multivariate test with logistic regression testing.

RESULT

Baseline and Characteristics

A total of 198 CAD patients underwent coronary angiography at the Sultan Agung Islamic Hospital from March 2022 to December 2023 (Figure 1). The non-multivessel coronary disease group (Non-MVCD) includes 63 patients (31.8%) and the Multivessel coronary disease group (MVCD) includes 135 patients (68.2%).

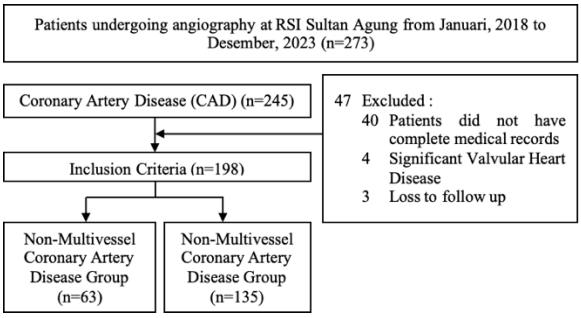

Figure 1. CONSORT Flow Chart.

Before further analysis is carried out, the characteristics of the research subjects are first explained, including demographic characteristics, lipid profile, kidney function, and accompanying comorbidities. Quantitative variables are defined in terms of average value (mean) and standard deviation, while qualitative variables are described in number/frequency and proportion of each category in percent.

DBP = Diastolic Blood Pressure, DM = Diabetes Mellitus, FBG = Fasting Blood Glucose, GFR = Glomerular Filtration Rate, HDL-C = High-Density Lipoprotein Cholesterol, HT = Hypertension, LDL-C = Low density Lipoprotein Cholesterol, RBG = Random Blood Glucose, SBP = Systolic Blood Pressure, TC = Total Cholesterol, TG = Triglyceride.

The demographic data (table 1) shows that the total of male subjects is more than females in the database, with a proportion of more than 50% out of all patients. From the anamnesis, 45.4% had diabetes mellitus (DM), 57.6% had hypertension (HT), and 51.5% had ever smoked. After analyzing the characteristics of the respondents, the data was subjected to a bivariate test to find out which variables were suitable to be tested using a multivariate test. Variables with a p-value <0.25 were subjected to a multivariate logistic regression test. The bivariate test results can be seen in Table 2.

Table 1. Baseline Characteristics

Variable	Description(n=198(%))
Age, years	58.64±10.1
Sex, n (%)	
Woman	60 (30.3%)
Man	138 (69.7%)
SBP, mmHg	154.68±37.7
DBP, mmHg	82.81±16.9
FBG, mg/dL	8.10±0.83
RBG, mg/dL	154.78±81.5
HDL-C, mg/dL	39.82±9.4
LDL-C, mg/dL	117.32±40.6
TG, mg/dL	94.70±147.32
TC, mg/dL	174.90±55.2
Creatinine, mg/dL	1.21±0.37
GFR, mL/min/1.73 m^2	63.11±19.8
Smoking History, n (%)	102 (51.5%)
DM History, n (%)	90 (45.4%)
HT History, n (%)	114 (57.6%)
HT Drugs, n (%)	114 (57.6%)
DM Drugs, n (%)	90 (45.4%)
Lipid Lowering Medication, n (%)	34 (17.1%)
TG Index	8.10±0.8

DBP = Diastolic Blood Pressure, DM = Diabetes Mellitus, FBG = Fasting Blood Glucose, GFR = Glomerular Filtration Rate, HDL-C = High-Density Lipoprotein Cholesterol, HT = Hypertension, LDL-C = Low density Lipoprotein Cholesterol, RBG = Random Blood Glucose, SBP = Systolic Blood Pressure, TC = Total Cholesterol, TG = Triglyceride.

Tabel 2. Bivariate Test.

Variable	CAD Group		p-value
	Non-MVCD (n=63)	MVCD (n=135)	
Age, years	57.61±11.3	60.60±9.1	0.033*
Sex, n (%)			0.009*
Woman	27 (42.8%)	33 (24.4%)	
Man	36 (57.2%)	102 (75.6%)	
SBP, mmHg	149.00±38.8	158.62±37.2	0.387
DBP, mmHg	82.71±16.2	83.80±17.7	0.372
FBG, mg/dL	94.38±24.1	114.06±43.8	<0.001*
RBG, mg/dL	141.76±70.4	159.15±84.5	0.240
HDL-C, mg/dL	44.04±9.8	37.82±8.3	0.240
LDL-C, mg/dL	116.04±43.7	118.40±38.7	0.450
TG, mg/dL	54.67±41.1	114.77±170.7	0.008*
TC, mg/dL	175.33±68.7	175.46±47.3	0.039*
Creatinine, mg/dL	1.03±0.2	1.29±0.4	0.030*
GFR, mL/min/1.73 m^2	72.41±22.0	59.04±17.3	0.224
Smoking History, n (%)	21 (33.3%)	81 (60.0%)	<0.001*
DM History, n (%)	27 (42.8%)	63 (46.6%)	0.616
HT History, n (%)	33 (52.4%)	81 (60.0%)	0.312
HT Drugs, n (%)	33 (52.4%)	81 (60.0%)	0.312
DM Drugs, n (%)	27 (42.8%)	63 (46.6%)	0.616
Lipid Lowering Medication, n (%)	14 (22,2%)	20 (14,1%)	0.180
TG Index	7.62±0.7	8.33±0.8	<0.001*

DBP = Diastolic Blood Pressure, DM = Diabetes Mellitus, FBG = Fasting Blood Glucose, GFR = Glomerular Filtration Rate, HDL-C = High-Density Lipoprotein Cholesterol, HT = Hypertension, LDL-C = Low density Lipoprotein Cholesterol, RBG = Random Blood Glucose, SBP = Systolic Blood Pressure, TC = Total Cholesterol, TG = Triglyceride.

The results of the bivariate test show the p-value of the variables age (0.033), gender (0.009), FBG (<0.001), TG (0.008), TC (0.039), creatinine (0.030), smoking (<0.001), Lipid-Lowering Medication (0.180) and triglyceride index (<0.001) has a p-value <0.25, so these variables are suitable for multivariate testing with logistic regression.

Tabel 3. Multivariate Logistic Regression Test.

Variable	p-value	PR	95% Cl Exp(B)	
			Lower	Upper
Age	0.208	1.025	0.352	2.213
Gender	0.791	0.883	0.986	1.065
FBG	0.443	0.993	0.977	1.010
TG	0.370	0.996	0.989	1.004
TC	0.048	0.992	0.985	1.000
Creatinine	<0.001	79.139	9.484	660.370
Lipid Lowering Medication	0.204	0.514	0.184	1.436
Indeks TG	0.001	6.929	2.209	21.736

The results of the multivariate analysis showed that the TG index variables (PR 6.929, Cl 95% 2.209-21.736) and Creatinine (79.139, Cl 95% 9.484-660.370 were predictor risk factors for MVCD. The results of this study are in line with previous research which stated that the TG index is a risk factor for the occurrence of MVCD (OR 1.496 Cl 95% 1.183-1.893 p<0.001)[10].

DISCUSSION

In this study, the results showed a significant relationship between the TG index and the presence of multivessel coronary artery disease in CAD patients. This finding is in line to previous studies, that the group with the highest TG index had a higher risk of stroke and myocardial infarction (MI)[11]. Previous studies have shown that the TG index could be an effective marker of arterial stiffness and atherosclerosis[12]. In addition, a few cohort studies discovered that the TG index was associated with the severity of stenosis and the MVCD[13]. The TG index is expected to be a useful predictor to determine the severity of CAD and the incidence of MVCD before coronary angiography (CAG) is performed in clinical practice.

IR plays a pivotal role in the pathogenesis and prognosis of several diseases, including CAD[14,15]. IR is a notable characteristic of metabolic syndrome and has been identified as an independent risk factor for CAD[16]. The association between IR and CAD involves potential molecular mechanisms, such as endothelial dysfunction, coagulation abnormalities, impaired metabolic flexibility, and dysfunction of smooth muscle cells[8,17]. Previous researches suggests that the TG index, an accurate indicator of IR, is independently associated with coronary severity across various clinical manifestations of CAD. Su et al. reported that higher TG index is associated with a heightened risk of multivessel CAD in patients with CAD[18]. In this context, the TG index has the potential to serve as a non-invasive tool to assess the complexity of CAD in dialysis patients. However, the data to support the association between the TG index and the extent and severity of CAD in this specific patient population is still limited. Further research needs to be carried out with a larger sample in a multicenter study to obtain better results.

CONCLUSION

In this study it can be concluded that the TG index and creatinine levels are the main risk factors for MVCD at Sultan Agung Islamic Hospital Semarang.

ACKNOWLEDGEMENTS

Researchers would like to thank the teaching staff at the Faculty of Medicine, Islamic Sultan Agung University.

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