JOURNAL OF CLINICAL MEDICINE OF KAZAKHSTAN (E-ISSN 2313-1519)
Original Article DOI: https://doi.org/10.23950/jcmk/13502

No-reflow phenomenon and triglyceride-glucose index in acute myocardial infarction

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Received: 2023-03-25.
Accepted: 2023-07-18

J Clin Med Kaz 2023; 20(4):27-32

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Abstract

Objective: The objective of this research was to evaluate the association between the measured triglyceride/glucose index (TyG) and the occurrence of no-reflow phenomena in patients with acute ST-elevation myocardial infarction (STEMI) following primary percutaneous coronary intervention (PCI).

Material and methods: This study comprised 242 patients who were treated with primary PCI for acute STEMI. The values of triglycerides and glucose at the time of admission were derived from the patient's file. Using coronary angiography records, the grade of post-procedural thrombolysis in myocardial infarction (TIMI) flow was determined.

Results: After PCI, patients were divided into two groups based on their TIMI flow grade: the normal coronary flow group (n=202) and the reduced coronary flow (no-reflow) group (n=40). The group with no-reflow had a poorer left ventricular ejection fraction and a higher prevalence of diabetes compared to the group with normal coronary flow. Individuals with a lower grade of TIMI flow had a substantially higher TyG index (9.7±0.25 vs. 8.8±0.5, p=0.001). The receiver operating characteristic (ROC) curve revealed that the optimal cut-off point of the TyG index for predicting no-reflow was >9.2 with specificity of 72.8% and sensitivity of 97.5% (area under the curve = 0.884; 95% confidence interval, 0.837-0.921; p=0.001).

Conclusion: At admission, patients with STEMI who experienced no reflow after primary PCI had a higher TyG index. In such cases, the TyG index can be utilized as a predictor of no-reflow.

Key words: acute myocardial infarction, percutaneous coronary intervention, no reflow phenomenon, triglyceride-glucose index

Introduction

Despite advancements in mechanical and pharmacologic reperfusion treatment, acute myocardial infarction (AMI) continues to be one of the primary causes of mortality. AMI is most effectively treated with primary percutaneous coronary intervention (PCI) [1]. The advancement of myocardial necrosis is prevented by balloon angioplasty of the epicardial coronary artery responsible for infarction. Thus, acute mechanical problems and readmissions resulting from heart failure can be reduced. Unfortunately, achieving epicardial coronary artery patency does not necessarily result in acute and long term advantages. In many patients with AMI after primary PCI efficient myocardial perfusion is not really obtained. This is one of the most important reasons for this. The failure to achieve adequate myocardial perfusion despite the patency of the epicardial coronary artery is known as no-reflow. While reported in non-ST-elevation myocardial infarction and elective PCI, specifically saphenous vein grafting, no-reflow occurs more frequently in AMI. It has been demonstrated that the "no-reflow" phenomenon, a significant complication following PCI, is related to a poor prognosis in patients [2].

Although the reasons for no-reflow creation are debatable, a number of studies have linked it to coronary artery spasm, atherosclerotic plaque embolization, and severe abnormalities of glucose metabolism [3-5]. Many investigations have shown that the triglyceride/glucose (TyG) index is a new measure of insulin resistance and

is also connected with coronary atherosclerosis, glucose and lipid metabolism problems, and microvascular endothelial dysfunction [6–10]. The establishment of the "no-reflow" syndrome after PCI is also facilitated by these pathologic pathways. In this study, we sought to determine the association between the TyG index and the "no-reflow" phenomenon in AMI patients who underwent PCI.

Material and methods

Study population

Between June 2021 and June 2022, 390 patients hospitalized with AMI at the Kahramanmaraş Sutcu Imam University Faculty of Medicine Hospital were enrolled in the retrospective-cohort study. 34 patients with a history of previous myocardial infarction, 29 patients with a history of previous PCI, 31 patients with a history of coronary artery bypass grafting, 2 patients with confirmed familial hypertriglyceridemia, 11 patients receiving statin and triglyceride-lowering therapy prior to admission, 9 patients with hepatic failure, 17 patients with renal failure, and 15 patients receiving glycoprotein IIb/IIIa antagonists during PCI were excluded from the study (Figure 1).

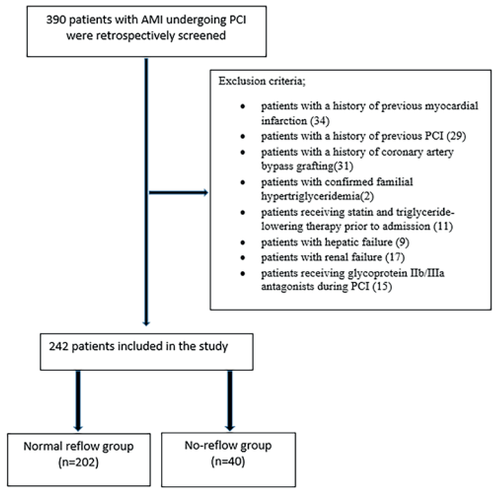

Figure 1 - Flowchart shows the patient selection process.

The study included 242 AMI patients with applying to our center. The research group comprised patients who received acetylsalicylic acid, additional antiaggregant loading (clopidogrel, prasugrel, or ticagrelor), and anticoagulant treatment (unfractionated heparin or low molecular weight heparin) prior to PCI. In accordance with the degree of TIMI blood flow after PCI, the patients included in the research were classified into two categories: no-reflow and normal coronary flow. There were 40 patients in the no-reflow group and 202 individuals in the normal blood flow group.

Exclusion criteria

Individuals having PCI or coronary artery bypass grafting with a previous history of myocardial infarction or decompensated heart failure, patients with verified familial hypertriglyceridemia; patients taking statins and triglyceride-lowering treatment prior to admission, patients with significant hepatic and renal impairment (transaminase equal to or higher than 2 times the normal value, GFR<60ml/ minx1. 73m), utilizing glycoprotein IIb/IIIa antagonists during PCI were excluded. The study procedures were evaluated and approved by the local medical ethics commission and adhered to the Declaration of Helsinki's recommendations.

Diagnostic criterion

Acute myocardial infarction was characterized as chest discomfort accompanied by new ST-segment alterations and myocardial necrosis markers that were at least twice the upper normal value [11]. TIMI flow grade; TIMI 0 (no flow after lesion), TIMI 1 (flow after lesion but partial filling of the distal vascular bed), TIMI 2 (flow after lesion with complete but delayed vascular distal bed filling), and TIMI 3 (normal coronary flow after lesion) [8]. Normal coronary flow was defined as TIMI 3 flow after PCI, while the no-reflow phenomenon was defined as angiographic blockage of coronary flow in the absence of dissection and thrombus and TIMI 2 flow [12].

Research methods

Examining patient information and patient files registered in the hospital's digital records enabled the collection of the fundamental features of the research population. By looking at the patient information and patient files in the hospital's digital records, it was possible to determine whether the patients had hypertension or diabetes mellitus if they smoked, and if they had been to the hospital before.

Blood samples were collected from the patients during hospitalization before coronary angiography. During hospitalization, laboratory data, including basic biochemistry tests and hemogram parameters were collected. The TyG index was computed with the method Ln [fasting triglycerides (mg/dl) x fasting glucose (mg/dl)/2] [13]. The left ventricular ejection fraction (LVEF) values of the research population were retrospectively evaluated using the modified biplanar Simpson technique. Two competent cardiologists who were blinded to the research data assessed the coronary angiography images of the study group and reported TIMI flow grades.

Statistical analysis

For data administration and analysis, version 24 of the SPSS program (SPSS Inc., Chicago, IL, USA) was utilized, and a p value of 0.05 was considered statistically significant. Continuous variables are reported as mean standard deviation (SD) or median and interquartile ranges (IQR) where applicable for categorical variables. The independent sample t test and, in the absence of a normal distribution, the median Mann-Whitney U test were utilized to compare the means. When applicable, the chi-square test was employed to evaluate categorical data. For regularly distributed variables, the Pearson correlation test was employed in correlation analysis, whereas the Spearmen correlation test was utilized for non-normally distributed variables. ROC (Receiver Operating Characteristics) curve analysis was used to determine the appropriate cutoff point of the TyG index for no-reflow prediction. Area under the curve (AUC) was computed using a 95% confidence range for the prediction of no-reflow. Using univariate analysis, the correlation between factors and no-reflow was determined. In a multivariate logistic regression model with a backward stepwise approach, statistically significant univariate variables and other possible confounders were employed to discover independent prognostic determinants of no-reflow.

Results

After the registry data were reviewed, the study group was split into two groups, those with normal coronary flow (patients with TIMI 3 flow, n: 202), and those with no-reflow (patients with TIMI 0, 1, and 2 flow, n: 40). Table 1 displays the baseline parameters, laboratory results, and vessel characteristics of both groups receiving PCI.

Table 1 Comparison of basic characteristic parameters between groups

	Patients with no-reflow (n:40)	Patients with normal coronary flow (n:202)	p
Basic characteristics			
Age, ± SD, years	67 ±12	64 ±12	0.921
Male/Female, n	28/12	136/66	0.854
Atrial Fibrillation, n (%)	10 (%25)	37 (%18.3)	0.374
Diabetes Mellitus, n (%)	23 (%57.5)	57 (%28.2)	0.002
Hypertension, n (%)	34 (%85)	182 (%90)	0.837
Smoking, n (%)	19 (%47.5)	88 (%43.5)	0.654
LVEF, mean ± SD, %	41±8	44 ±8	0.043
Laboratory findings			
Glucose, median (IQR), mg/dL	191 (171.25-209.75)	111 (95-157.25)	<0.001
Total cholestrol, (IQR), mg/dL	180 (158-206.5)	174 (149-205.25)	0,348
Triglyceride, (IQR), mg/dL	185.5 (168.25-193)	143 (95-174.25)	<0.001
LDL, mean ± SD, mg/dL	118.7 ±39.3	127.0±41.0	0.232
HDL, mean ± SD, mg/dL	36.7 ±9.9	41.9 ±9.6	0.003
Creatinine, mean ± SD, mg/dL	1.10 ± 0.69	1.43 ±6.0	0.451
BUN, median (IQR), mg/dL	20.6 (15.25-32)	17 (13.75-22.25)	0.037
Sodium, mean ± SD, mmol/L	137.8 ± 6.3	137.9 ±5.1	0.884
Potassium, mean ± SD, mmol/L	4.4±0.7	4.3±2.7	0.978
Hemoglobin, mean ± SD, g/dL	13.5±4.1	13.0±1.9	0.195
Hematocrit, mean ± SD, (%)	40.1±9.2	39.3 ±5.4	0.439
Platelet, median (IQR), 109/L	222 (173.75-309.25)	221 (186-272)	0.508
RDW, mean ± SD, %	44.3±6.3	44.1±5.6	0.863
MPV, mean ± SD, fL	10.4±0.9	10.9±2.3	0.022
TyG index	9.7 ±0.25	8.9±0.5	<0.001
Vessel undergoing percutaneous coronary intervention			
LAD, n (%)	15 (%37,5)	96 (%47.5)	0.298
CX, n (%)	10 (%25,0)	60 (%29.7)	0.703
RCA, n (%)	15 (%37,5)	46 (%22.7)	0.071
Stent diameter, mean ± SD, mm	2.98±0.23	2.93±0.28	0.211
Stent length, mean ± SD, mm	28.3±6.6	25.8±4.9	0.090

Continuous variables are presented as mean ± SD or median (IQR), categorical variables are presented as frequency (%). LVEF: left ventricular ejection fraction; LDL: low density lipoprotein; HDL: high density lipoprotein; BUN: blood urea nitrogen; RDW: red cell distribution width; mean platelet volüme; TyG: Triglyceride-Glucose; LAD: left anterior descending artery; CX: circumflex artery; RCA: right coronary artery.

In terms of age, gender, atrial fibrillation, presence of hypertension, and smoking, there was no significant difference between the no-reflow group and the normal coronary flow group. Regarding the coronary artery in which PCI was done and the diameter-length ratio of the stent, there was no difference between the two groups. Diabetes mellitus (DM) was more prevalent in the no-reflow group [23 (57.5%) vs 57 (28.2%), p=0.002]. Comparing the LVEF values acquired from transthoracic echocardiography reports for each patient revealed that the no-reflow group had lower LVEF values (41.8 vs. 44.8, p = 0.043).

When the laboratory results of both groups were examined, the group with no-reflow had higher glucose levels [191 (171.25-209.75) vs. 111 (95-157.25), p=0.001]. In the group with no-reflow, triglyceride levels were higher [180 (158-206.5) vs. 143 (95-174.25), p=0.001] In the group with normal coronary flow, BUN levels were lower than in the group with no-reflow (17 (13.75-22.25) vs. 20.6 (15.25-32), p=0.037). MPV was lower in the no-reflow group (10.4±0.9 vs. 10.9±2.3, p=0.022). The TyG index was greater in the no-reflow group (9.7±0.25 vs. 8.9±0.5, p=0.001).

In all patients, the TyG index was favorably correlated with fasting glucose, total cholesterol, and hemoglobin, and negatively correlated with HDL (Table 2). TyG index was negatively correlated with TIMI flow grade obtained from the evaluated coronary angiography images (r=-497, p<0.001).

Table 2 Correlation coefficients for TyG index

Variables correlated with the TyG index	R	p
Glucose	0.743	<0.001
Total cholesterol	0.142	0.028
HDL	-0.175	0.006
Hemoglobin	0.155	0.016

TyG: Triglyceride-Glucose; HDL: high density lipoprotein.

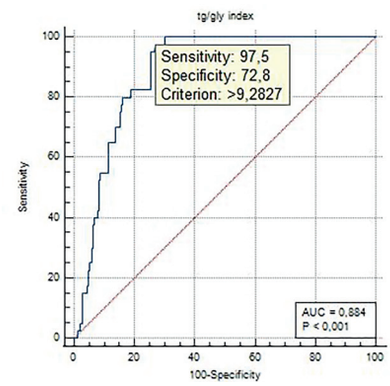

Figure 2 - Receiver operator characteristic (ROC) Curve of TyG Index to predict no-reflow.

Table 3 Univariate and multivariate logistic regression analysis results for no-reflow phenomenon

Variables	Univariate analysis						Multivariate analysis					
	B	S.E	WALD	P	OR	CI	B	S.E.	WALD	P	OR	CI
Stastistically significant variables												
TyG index	0.361	0.550	4.282	<0.001	1.819	1.698-1.767	0.013	0.678	4.996	<0.001	1.915	1.837-1.921
LVEF	0.046	0.220	4.306	0.038	1.047	1.003-1.093	0.071	0.030	5.543	0.019	1.073	1.012-1.138
BUN	0.027	0.011	5.694	0.017	1.028	1.005-1.051	0.035	0.017	4.249	0.039	1.036	1.002-1.071
MPV	0.375	0.179	4.360	0.037	0.687	0.484-0.977	0.529	0.260	4.136	0.042	0.589	0.354-0.981
Glucose	0.020	0.004	30.638	<0.001	1.020	1.013-1.028						
Diabetes Mellitus	1.229	0.356	11.914	0.001	3.418	1.701-6.868						
Triglyceride	0.015	0.004	16.543	<0.001	1.015	1.008-1.023						
HDL	0.059	0.020	9.027	0.003	0.943	0.908-0.980						

TyG: Triglyceride-Glucose; LVEF: left ventricular ejection fraction; BUN: blood urea nitrogen; MPV: mean platelet volüme; HDL: high density lipoprotein.

In multiple regression analysis with forward stepwise method, TyG index, LVEF, BUN and MPV remained to be associated with an predictor of no-reflow occurence after adjustment for variables found to be statistically significant in univariate analysis and correlated with TyG index (Table 3).

The receiver operating characteristic (ROC) curve indicates that the ideal cut-off point of the TyG index for predicting no-reflow is >9.2 with a specificity of 72.8% and a sensitivity of 97.5% (area under the curve =0.884; 95% confidence interval [CI], 0.842-0.926; p=0.001) (Figure 2). ROC curve analyses comparing the predictive values of TyG index, glucose and triglyceride showed that the sensitivity of TyG index was higher (Figure 3).

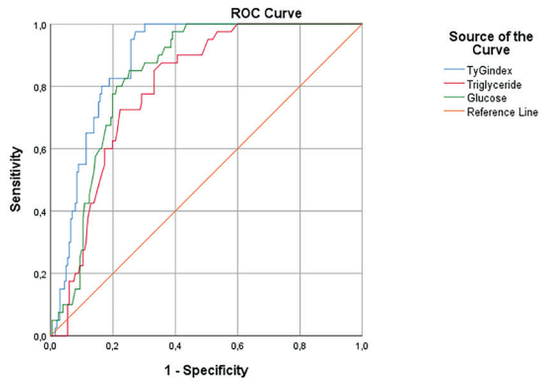

Figure 3 - ROC curve analyses comparing the predictive values of TyG index, glucose and triglycerides

Discussion

In our investigation, the TyG index was considerably higher in AMI patients who exhibited no-reflow phenomena following primary PCI. Furthermore, diabetes mellitus was more prevalent among individuals with no-reflow.

Insulin resistance plays a crucial role in the pathogenesis of the metabolic syndrome, a significant cardiovascular disease risk factor, by causing reduced glucose metabolism, impaired insulin action, and changes in hepatic lipid metabolism. The TyG index can be used to inexpensively test insulin resistance in clinical settings [6, 14, 15].

High fasting glucose is seen as a sign of insulin resistance originating in the liver, while elevated triglyceride levels are regarded as the source of insulin resistance originating in fat cells. Hence, the TyG index is a crucial indication of insulin resistance [16]. Insulin resistance is known to enhance vulnerability to thrombosis through several pathways, particularly endothelial dysfunction; there is evidence that plasminogen activator inhibitor-1 level is elevated in atherosclerotic lesions of type 2 diabetes patients [17].

In addition to its detrimental effects on endothelial function, hyperglycemia is known to promote thrombosis susceptibility [18]. In plasma, triglycerides are quickly changed from very low density lipoprotein cholesterol (VLDL) to low density lipoprotein cholesterol (LDL). LDL cholesterol is quickly glycosylated under conditions of high blood glucose to create the advanced glycation end products-LDL (AGE-LDL) complex, an advanced glycation end product [19]. It has been demonstrated that AGE-LDL has a high atherogenic impact and is related to no-reflow in patients following PCI [20, 21].

The TyG index is a novel composite score that incorporates two risk indicators, fasting glucose and triglycerides. Many studies have demonstrated the association between the TyG index and cardiovascular diseases (CVD), stroke, and CVD risk factors [21, 22]. In STEMI patients having PCI, a greater TyG index has been associated with an increased risk of significant adverse cardiac and cerebrovascular events [23, 24]. Based on these research, the TyG index, an indication of insulin resistance, can be used as a marker for atherosclerosis. In the era of reperfusion, many efforts have been made to limit the magnitude of myocardial infarction by early reperfusion with primary PCI or thrombolytic drugs; yet, while door-to-balloon timings have improved dramatically, gains in in-hospital mortality have lagged.

The success of reperfusion is governed by variables such as the severity of ischemia, the duration of reperfusion, the patency of the epicardial artery connected with the infarct, distal thromboembolism, and inadequate microvascular flow [25]. It has been demonstrated that no-reflow phenomena in the cardiac microcirculation is related to a bad long-term prognosis [26]. Recent investigations suggest that inflammation, vasospasm, and thrombosis in the microvascular bed may be among the reasons for the no-reflow phenomenon, even if its mechanism is not entirely understood [27, 28]. Diabetes mellitus is considered to be an immunologic reaction rather than a metabolic problem, and inflammation is implicated in the pathogenesis of DM patients' common microvascular consequences [29].

The no-reflow has been associated with hyperglycemia, hypercholesterolemia, and thrombus load [30, 31]. In our study, the fact that glucose levels were higher, HDL cholesterol levels were lower, and the number of patients with a diagnosis of DM was greater in the group with no-reflow supported the influence of the risk variables listed. Tartan et al. demonstrated that individuals with metabolic syndrome were more likely to have no-reflow than those without metabolic syndrome [5]. In this study, we found that the TyG index was favorably connected with fasting glucose and total cholesterol, but negatively correlated with HDL. The study by Tartan et al. is supported by metabolic syndrome components such as triglycerides, fasting blood glucose, and HDL levels in the no-reflow group [5]. In

accordance with the findings of the study by Park et al., TyG indices of 8.50 or higher are related to an elevated cardiovascular risk [32]. In our study, the no-reflow group had a higher TyG index.

There are some limitations in this study. First, our study was retrospective in method. Second, it included a relatively small number of patients and was performed in a single center. Third, clinical variables such as total ischemic time before hospital arrival, Killip scores, and MI severity according to troponin levels were not measured. The results of the study cannot be generalized to other populations and patients undergoing PCI.

Conclusion

According to the findings of our investigation, the TyG index was related to no-reflow in AMI patients receiving PCI. The TyG score shows considerable predictive value in patients with no reperfusion after AMI and can be used to stratify individuals at high risk of no reperfusion before PCI. This suggests that the TyG index could be a useful tool for identifying patients who are at a higher risk of no reflow before undergoing PCI, allowing for earlier intervention and potentially improving outcomes. It is potential as a predictor of no-reflow in patients undergoing PCI warrants further investigation in larger and more diverse patient populations.The TyG index is a simple and cost-effective measure that can be easily calculated from routine laboratory tests, making it a feasible tool for clinical use. It is potential as a predictor of no-reflow in patients undergoing PCI warrants further investigation in larger and more diverse patient populations.

Disclosures: There is no conflict of interest for all authors.

Acknowledgements: None.

Funding: None.

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