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CLINICAL STUDY

Assessment of triglyceride/glucose index with respect to coronary slow flow

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ABSTRACT
BACKGROUND: Coronary slow flow (CSF) is determined by delayed opacification of the epicardial coronary arteries without obstructive disease. The triglyceride glucose index (TGI) has been suggested as a useful marker of insulin resistance. Previous studies have shown that TGI is associated with cardiovascular disease, but no study has examined the relationship between TGI and CSF.
OBJECTIVES: Therefore, the primary objective of the present study was to investigate the relationship between TGI and CSF.
METHODS: This study retrospectively evaluated patients who were admitted to our clinic with complaints of chest pain and underwent coronary angiography between January and December 2018. A total of 1100 coronary angiography images were assessed, and 72 patients with CSF were detected. Coronary flow was quantified objectively using the TIMI (thrombolysis in myocardial infarction) frame count (TFC) method as described by Gibson et al. TGI was calculated as follows: ln [fasting triglycerides (mg/dL) × fasting glucose (mg/dL)/2].
RESULTS: The CSF group had significantly higher glucose levels (mg/dl) [(114.92±30.92), (125.61±33.22), than the control and CSF groups, respectively, p=0.0001], TGI [(9.02±0.56), (9.26±0.54), p=0.0001], and triglyceride levels (mg/dl) [(170.67±110.81), (201.19±136.93), p=0.002]. There was no statistically significant correlation between TGI and left anterior descending artery TFC, circumflex artery TFC, right coronary artery TFC (r/p values; 0.24/0.06; 0.32/0.08; 0.18/0.36, respectively). TGI, HDL, HT, age, and sex were examined with a multiple logistic model, and TGI was found to be statistically significant for the risk of CSF (p=0.0001; O.R:7.459).
CONCLUSION: TGI was statistically significantly higher in the CSF group than the control group. According to the multivariate logistic regression analysis, only TGI was independently associated with the risk of CSF, but higher TGI did not predict more slow coronary flow. Prospective studies are needed to clarify the prognostic relationship of TGI and CSF in terms of future cardiovascular events *(Tab. 2, Fig. 1, Ref. 19)*. Text in PDF *www.elis.sk*
KEY WORDS: coronary slow flow, triglyceride glucose index, TIMI frame count.

Introduction

Coronary slow flow (CSF) was first described by Tambe et al in 1972 and is determined by delayed opacification of the epicardial coronary arteries without obstructive disease (1). Previous studies revealed that coronary endothelial dysfunction and microvascular disease play a pivotal role in patients with CSF. Myocardial biopsy studies have shown the presence of coronary microvascular disease in patients with CSF (2, 3). Thrombolysis in the myocardial infarction frame count (TFC) is used for the diagnosis of CSF and has been found to have a correlation with insulin resistance in patients with CSF (4). Insulin resistance is an important marker for cardiometabolic diseases, which are significantly associated with a high risk of poor cardiovascular outcomes (5).

The triglyceride-glucose (TGI) index is calculated using triglyceride and glucose values and has been reported to be significantly correlated with insulin resistance. Thus, it has been proposed as a reliable surrogate marker of insulin resistance (6). Previous studies have shown that TGI is associated with cardiovascular disease, but no study has examined the relationship between TGI and CSF. Therefore, the primary objective of the present study was to investigate the relationship between TGI and CSF.

Methods

Study population

This study retrospectively evaluated patients who were admitted to our clinic with complaints of chest pain and underwent coronary angiography between January and December 2018. A

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total of 1100 coronary angiography images were assessed, and 72 patients with CSF were detected. A control group was formed with 72 patients who were demographically similar to this group and had normal coronary angiography. This study complied with the principles outlined in the Declaration of Helsinki and was approved by the local ethics committee of Pamukkale University.

The exclusion criteria included obstructive coronary artery disease, cerebrovascular events, coronary artery bypass grafting, valvular heart disease, missing data, cardiogenic shock, chronic infectious disease, malignant tumours, taking statins or triglyceride-lowering medications, renal dysfunction with estimated glomerular filtration rate (eGFR) < 30 mL/ (min * 1.73 m^2), and treatment with renal replacement therapy. Significant coronary artery stenosis was defined as at least a 75 % reduction in the internal diameter of the right, left anterior descending, or left circumflex coronary arteries or their major branch, or a 50 % reduction in the internal diameter of the left main trunk.

Tab. 1. Demographic and laboratory findings of the study population.

Parameters	Control group Mean (min-max)	CSF group Mean (min-max)	p
Age (year)	57.5 (40–81)	54.5 (31–82)	0.377
Sex (female) n, (%)	34 (47.2)	23 (31.9)	0.061
Hypertension n, (%)	36 (50)	32 (44.4)	0.504
DM n, (%)	12 (8.6)	14 (10)	0.434
	mean± std (min–max)	mean± std (min–max)	
Glucose (mg/dl)	114.92±30.92 (69–268)	125.61±33.22 (77–253)	0.0001*
Creatinine (mg/dl)	0.84±0.17 (0.6–1.23)	0.82±0.18 (0.6–1.23)	0.438
Total cholesterol (mg/dl)	191.35±37.64 (132–26)	193.65±39.38 (72–288)	0.531
LDL (mg/dl)	112.78±31.09 (44–190)	112.53±30.37 (36–181)	0.902
HDL (mg/dl)	45.1±12.6 (27–96)	41.32±13.15 (8–83)	0.0001*
Triglyceride (mg/dl)	170.67±110.81 (45–356)	201.19±136.93 (81–400)	0.002*
HBA1C	6.09±1.26 (5–5.8)	6.14±1.29 (4.6–11)	0.053
Hemoglobin (mg/dl)	14.28±1.67 (11–17)	14.28±1.85 (9.5–19)	0.96
Thrombocyte (K/uL)	239.19±71.72 (92–389)	193.65±39.38 (27–556)	0.015*
TGI	9.02±0.56 (7.62–9.92)	9.26±0.54 (8.24–11.22)	0.0001*

CSF – coronary slow flow, HBA1C – hemoglobin A1C, HDL – high density lipoprotein, LDL – low density lipoprotein, TGI – triglyceride glucose index, * $p < 0.05$, CI – confidence interval

Data collection

Patients' files from the hospital registration system were evaluated. Demographic and clinical characteristics were recorded, including age, sex, medical information, and laboratory data. Blood samples results taken from all participants after 12 h of fasting were also recorded.

Calculation of triglyceride/glucose index

TGI was calculated as follows (5): ln [fasting triglycerides (mg/dL) × fasting glucose (mg/dL)/2].

Coronary angiography and thrombolysis in the myocardial infarction frame count calculation

Coronary angiography was performed by a femoral approach using standard Judkins techniques for all the participants in this study. Coronary arteries were imaged at right and left oblique positions using cranial and caudal angles at a rate of 25 fps. To this end, an average of 6–8 ml of opaque material was manually injected for each take. Coronary flow was quantified objectively using the TIMI (thrombolysis in myocardial infarction) frame count (TFC) method as described by Gibson et al (7).

For the TFC measurement, the starting point was chosen as the moment when the contrast agent contacted both sides of the coronary artery and began to move forward. The endpoint was the moment when the contrast agent reached the "moustache point" for the left anterior descending artery (LAD). The endpoint for the right coronary artery (RCA) was the moment when the first side branch arose in posterior lateral artery, and that for the left circumflex artery (Cx) was the moment when distal bifurcation of the longest branch was displayed.

Since LAD lasts longer, the measured value was standardized by dividing it by 1.7 (21, 22). The mean TFC for each participant was calculated by dividing the sum of the TFCs of LAD (corrected), LCX, and RCA by 3. All participants with a corrected TFC greater than 27 (two standard deviations from the published normal range) in at least one of the three epicardial coronary arteries were accepted as having CSF. Those whose TFC fell within the standard deviation of the published normal range were considered as having normal coronary flow.

Statistical analyses

All statistical analyses were performed using the software SPSS 25.0. The results for continuous variables are presented as the mean ± standard deviation, and those for categorical variables are presented as numbers and percentages. The Kolmogorov Smirnov test was used for the determination of a normal distribution. For independent group comparison, we used the independent samples t-test when parametric test assumptions were provided. We used Spearman's and Pearson's correlation analysis and logistic regression analysis to analyse the relationships between continuous variables. Statistical significance was determined with $p < 0.05$.

Results

Table 1 shows the baseline characteristics and laboratory findings of the study population. There were no statistical differences between the two groups in terms of age and sex. The CSF group had significantly higher glucose levels (mg/dl) [(114.92 ± 30.92), (125.61 ± 33.22) than the control and CSF groups, respectively, p = 0.0001], TGI [(9.02 ± 0.56), (9.26 ± 0.54), p = 0.0001], and triglyceride levels (mg/dl) [(170.67 ± 110.81), (201.19 ± 136.93), p = 0.002]. The control group had significantly higher high-density lipoprotein (HDL) (mg/dl) [(45.1 ± 12.6), (41.32 ± 13.15), p = 0.0001] and thrombocytes (K/uL) [(239.19 ± 71.72), (193.65 ± 39.38), p = 0.015]. Figure 1 shows the distribution of TGI in the control and CSF groups.

Tab. 2. The reason of coronary angiography and mean TFC values of CSF patients.

The reason of coronary angiography at CSF patient	n (%)
UAP	25 (34.7)
Non-STEMI	12 (16.6)
Stable angina	35 (48.6)
Number of arteries with CSF	n (%)
LAD	31 (41.3)
CX	2 (2.8)
RCA	10 (13.9)
LAD, CX	12 (16.7)
CX, RCA	1 (1.4)
LAD, RCA	3 (4.2)
LAD, CX, RCA	13 (18.1)
Mean TFC values	mean ± std (min–max)
LAD TFC	42.6±10 (30–90)
CX TFC	32±5.2 (27–45)
RCA TFC	30.2±3 (27–30)

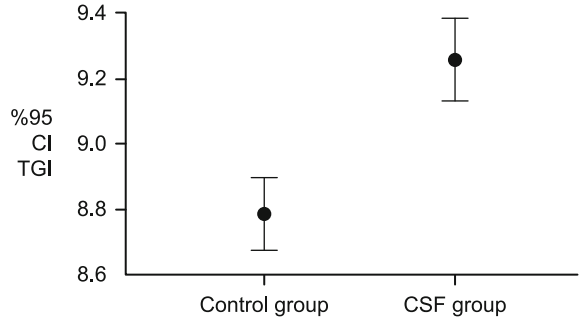

Fig. 1. The distribution of TGI at control and CSF group.

Table 2 shows the reasons for coronary angiography and mean TFC values of CSF patients. The most common reason for angiography was stable angina (n = 35, 48.6 %). CSF was most frequently detected in LAD, and its mean TFC value was 42.6 ± 10 (Tab. 2). There was no statistically significant correlation between TGI and the LAD TFC, CX TFC, or RCA TFC, (r/p values: 0.24/0.06, 0.32/0.08, and 0.18/0.36, respectively).

Univariate logistic regression models were used to determine the variables that have an impact on the risk of having CSF. The effects of TGI, age, sex, HT, diabetes mellitus, total cholesterol, LDL, HDL, TG, creatinine, and glucose variables on the risk of CSF were examined, and a multiple logistic regression model was established with statistically significant variables. TGI, HDL, HT, age, and sex were examined with a multiple logistic model, and TGI was found to be statistically significant for the risk of CSF (p = 0.0001; O.R:7.459).

Discussion

In this study, we aimed to investigate the relationship between TGI and CSF, and the results revealed that TGI was statistically higher in the CSF group than the control group. According to the multivariate logistic regression analysis, only TGI was independently associated with the risk of CSF. To the best of our knowledge, this is the first study to determine the relationship between TGI and CSF.

Insulin resistance has been suggested as an important cause of cardiovascular disease (8). Some studies have revealed that the TGI is correlated with insulin resistance, for which it has been suggested as a surrogate marker. TGI is also a better indicator than the HOMA-IR score (9, 10). One study showed a significant association between TGI and hypertension and that TGI was superior to other lipid profiles and HbA1c (11). High TGI levels were an independent predictor of an increased risk of major adverse cardiovascular events in patients with acute myocardial infarction (12), coronary artery disease (5), ST elevation myocardial infarction (13), type 2 diabetes mellitus, and acute coronary syndrome.

CSF essentially occurs because of the delayed progression of contrast agent into an epicardial coronary artery without coronary stenosis, which may involve a combination of multifactorial abnormalities, such as inflammatory status, endothelial dysfunction, subclinical atherosclerosis, and structural and functional abnormalities in coronary microcirculation. Ozcan et al showed that patients with CSF, TFC, and hs-CRP are correlated with increased insulin resistance and suggested that insulin resistance and inflammation may in part have a role in the pathogenesis of CSF.

Insulin resistance may be a cause of endothelial dysfunction in CSF. In the present study, we demonstrated that TGI was independently associated with the presence of CSF. However, there was no significant positive correlation between LAD TFC, CX TFC, RCA TFC, and TGI. Thus, we do not claim that a higher degree of slow flow or higher TFC is associated with higher TGI.

The incidence of CSF has been reported to be 1–7 % in serial angiographies and up to 5 % with acute coronary syndromes (14). In our study, the periodic prevalence of CSF was 6.5 %, which is similar to the rates in previous studies. Some studies have examined gender as a risk factor in CSF, but their results have been inconsistent (15). CSF is often detected in middle-aged men, so it is called “syndrome Y.” The male:female ratio was 2.1:1 in our study.

Chest pain, rest, or mixed-pattern angina is the most common symptom in patients admitted with CSF, but there are no special determinative findings (16). Patients admitted to the clinic most commonly have stable angina, followed by those with unstable angina. Therefore, chest pain is the most common symptom. LAD was the most common coronary artery with CSF in our study, but we did not find any specific reason for this in the literature. Although treatment is not well defined for CSF, it is typical to control hyperlipidemia and vascular inflammation with statins (17), improve endothelial function, and reduce symptoms (18, 19). CSF is a form of atherosclerosis, and good glycaemic control may be the most important issue for treatment, as supported in this study.

The current study has some limitations. The study design was retrospective, which does not allow for evaluation of the cause–effect relationship between TGI and CSF and does not supply any prognostic data in terms of future cardiovascular events. TG and fasting glucose measurements had intra-individual biological variation, which changed over time. We did not evaluate this due

to a lack of data on the relationship between TGI and all metabolic factors, such as body mass index, waist circumference, and HOMA-IR.

In conclusion, TGI was statistically higher in the CSF group than the control group. According to the multivariate logistic regression analysis, only TGI was independently associated with the risk of CSF, but higher TGI did not predict more slow coronary flow. TGI is an inexpensive and useful marker of insulin resistance and was independently associated with the presence of CSF. However, there is no specific treatment for CSF, which is a form of atherosclerosis, and good glycaemic control may be the most important issue for treatment, which is supported by our findings. Prospective studies are needed to clarify the prognostic relationship of TGI and CSF in terms of future cardiovascular events.

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