

The relationship between triglyceride/high-density lipoprotein cholesterol ratio and coronary slow-flow phenomenon

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Abstract

Purpose: In this study, we aimed to investigate the relationship between high triglyceride (TG)/high-density lipoprotein cholesterol (HDL-C) ratio and coronary slow-flow phenomenon (CSFP) in patients undergoing elective coronary angiography for suspected coronary artery disease.

Methods: This prospective study included a total of 84 CSFP patients and 83 controls with normal coronary flow, as evidenced by coronary angiography. The Thrombolysis in Myocardial Infarction (TIMI) frame count (TFC) was used to measure the coronary blood flow velocity. The lipid profiles were analyzed and TG/HDL-C ratio were calculated dividing absolute TG levels by absolute HDL-C levels in peripheral blood.

Results: The median TG/HDL-C ratio was higher in the CSFP group than the control group (3.4 [2.6 to 4.9] vs. 2.3 [1.8 to 3], respectively; $p < 0.001$). The multivariate logistic regression analysis revealed that TG/HDL-C ratio was an independent predictor of CSFP (odds ratio [OR]: 1.78, 95% confidence interval [CI]: 1.59-2.32; $p = 0.001$) and TG/HDL-C ratio was positively correlated with the TFC in the CSFP group ($r = 0.311$, $p < 0.001$). The area under the receiver operating characteristic curve of TG/HDL-C for the diagnosis of CSFP was 0.73 (95% CI: 0.65-0.81; $p < 0.001$). If a cut-off value of 2.75 was used, higher levels of TG/HDL-C ratio could predict the presence of CSFP with 72% sensitivity and 71% specificity.

Conclusion: Our study results suggest that TG/HDL-C ratio is associated with CSFP and may be a useful biomarker for predicting CSFP and its severity.

Introduction

The coronary slow-flow phenomenon (CSFP) is a coronary artery disease, characterized by delayed vessel opacification in the absence of obstructive coronary artery disease [1]. It is defined angiographically and its incidence varies from 1 to 7% among the patients undergoing coronary angiography for suspected coronary artery disease (CAD) [2]. Although the exact mechanisms of CSFP are still unclear, small vessel disease, endothelial dysfunction, diffuse atherosclerosis, microvascular vasomotor dysfunction, and inflammation are implicated in its pathophysiology [3–6]. In addition, CSFP may cause transient myocardial hypoperfusion in patients with both normal coronary arteries and angina, thereby, leading to increasing the risk of CAD and worsening of the prognosis [7]. There is no definitive treatment of CSFP and traditional anti-anginal drugs are often used in the treatment. A particular attention has been paid to control hypertension and dyslipidemia in CSFP cases [8]. In some studies, statins are used to regulate cholesterol levels and take vascular inflammation under control [9].

In recent years, intimal thickening in the coronary arteries, diffuse calcification, lumen irregularity, and non-occlusive atheroma plaques have been identified in the majority of cases with CSFP [3, 10, 11]. In the light of recent findings, CSFP should be evaluated as CAD, which was earlier considered a subgroup of cardiac syndrome X [2]. Several studies have suggested that established cardiovascular risk factors may play a role in the pathogenesis of microvascular angina in healthy individuals, result in coronary

microvascular dysfunction [12]. Dyslipidemia is one of the risk factors of cardiovascular disease (CVD) [13]. It is defined as a disorder of lipoprotein metabolism, rather than elevations in total cholesterol (TC) or low-density lipoprotein cholesterol (LDL-C) alone [14]. Triglyceride (TG), LDL-C, and high-density lipoprotein cholesterol (HDL-C) are important components of the lipid fraction of the human body [14]. However, epidemiological researches have demonstrated that lipid-related ratios such as TC/HDL-C, TG/HDL-C, or LDL-C/HDL-C may be probably better predictors of CVD risk than any other single lipid marker [15–17]. Among these, the TG/HDL-C ratio was first proposed by Gaziano et al. [17] as an atherogenic index. Several studies have shown that TG/HDL-C ratio is a strong predictor of CAD such as myocardial infarction (MI), LDL phenotype B, and atherogenic risk [18, 19]. In addition, the TG/HDL-C ratio appears to be more valuable than any other single lipid marker, since it has an ability to reflect the complex interactions between the lipoprotein metabolism and to better predict plasma atherogenicity [16]. Besides its simplicity and practicality, there is a growing number of evidences supporting the predictive value of TG/HDL-C ratio in cardiovascular events and may be of clinical relevance [20, 21].

In the light of the literature data, we, in the present study, aimed to investigate the relationship between the TG/HDL-C ratio and CSFP in patients undergoing elective coronary angiography for suspected CAD and to identify whether TG/HDL-C ratio was a feasible biomarker in distinguishing CSFP cases from healthy individuals.

Materials And Methods

Study design and study population

This single-center, prospective study was conducted at Department of Cardiology of a tertiary care center between October 2017 and February 2020. A total of 84 CSFP patients who were admitted with chest pain and had myocardial ischemia as assessed by myocardial perfusion scintigraphy with positive treadmill test results and age- and sex-matched 83 controls with normal coronary flow were included. The CSFP was confirmed by coronary angiography and the Thrombolysis in Myocardial Infarction (TIMI) frame count (TFC) was used to measure the coronary blood flow velocity. Those undergoing angiography previously and undergoing surgery or mechanical revascularization for significant CAD were excluded from the study. Patients with left ventricular dysfunction (ejection fraction <50%), peripheral artery disease, congenital heart disease, chronic renal or hepatic insufficiency, chronic obstructive pulmonary disease, acute and chronic inflammatory diseases, or autoimmune disorders, and those receiving drugs affecting the lipid metabolism were also excluded. All participants were informed about the nature of the study and a written informed consent was obtained. The study protocol was approved by the institutional Ethics Committee with the Approval No. 0447. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Data collection and definitions

Baseline demographic and clinical characteristics of all participants including age, sex, body mass index (BMI; calculated as weight in kg divided by height in meters squared), and comorbidities were

recorded. Hypertension was defined as a systolic blood pressure of ≥ 140 mmHg and diastolic blood pressure of ≥ 90 mmHg or the current use of antihypertensives. Diabetes mellitus was defined as a fasting blood glucose of ≥ 126 mg/dL in two consecutive measurements or having a history of diabetes and using insulin or oral antidiabetics. Smoking was defined as current daily smoking.

Coronary angiography-based CSFP assessment

Coronary angiography was percutaneously performed using the Judkins technique. The coronary arteries were visualized at right and left oblique and caudal planes at 30 frames per second (fps). A contrast agent was injected manually during coronary angiography (6 to 10 mL of contrast agent at each position using right and left, and cranial and caudal angulations). Angiographic images were stored in 34 runs in a CD in accordance with the Digital Imaging and Communications in Medicine (DICOM) standards and the flow velocity was measured. All angiographic measurements were carried out by two cardiologists who were blind to the clinical status of the patients. The flow in coronary arteries was measured using the TFC as described by Gibson et al. [22]. The TFC was calculated from the difference between the first and last frames. The first frame was when nearly complete lumen opacification with antegrade filling, while the final frame was accepted when the contrast dye reached distal landmarks. The following distal landmarks were used for the analysis: the distal bifurcation of the left anterior descending artery (LAD) (*i.e.*, the “mustache”) (Figure 1a) and the distal bifurcation of the segment with the longest total distance in the left circumflex artery (LCX) and the first branch of the posterolateral artery in the right coronary artery (RCA) (Figure 1b) [22]. As the LAD artery is often longer than the other main coronary arteries, the LAD TFC is usually high. The longer LAD frame counts were corrected dividing by 1.7 to calculate the corrected TFC [22]. The mean TFC was accepted as 36 ± 2.5 for LAD, 22 ± 4.1 for LCX, and 20.4 ± 3.1 for RCA. The corrected cut-off value for the LAD artery was $21.1 (\pm 1.5)$ frames. Any TFC values with more than 2 standard deviations (SDs) were considered CSFP [21] (Figure 2). The mean TFC for each subject was calculated by summing the TFC for LAD, LCX, and RCA and, then, dividing this sum into 3 [22].

Biochemical analyses

Venous blood samples were drawn from each participant after an overnight (12-h) fasting. All biochemical and hematological parameters including fasting blood glucose, creatinine, urea, uric acid, aspartate aminotransferase (AST), alanine aminotransferase (ALT), TC, TG, HDL-C, and LDL-C were analyzed on the day of sample collection using a commercial autoanalyzer (c8000i; Abbott Diagnostics GmbH, Germany). For samples with a TG level of < 400 mg/dL, the LDL-C was calculated using the Friedewald formula $[(LDL-C = TC - HDL-C - (TG/5)]$ [23]. Hematological analyses were carried out using the BC-6800 Hematology Analyzer (Shenzhen Mindray Bio-Medical Electronics Co., Ltd., Shenzhen, China). The lipid profiles were analyzed and TG/HDL-C ratio were calculated dividing absolute TG levels by absolute HDL-C levels in peripheral blood.

Statistical analysis

Statistical analysis was performed using the SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). Continuous data were expressed in mean \pm SD or median (interquartile range [IQR]), while categorical data were expressed in number and percentage. The normality assumption was checked using the Kolmogorov-Smirnov test. One-way analysis of variance (ANOVA) with *post-hoc* Tukey test, independent samples *t*-test, Kruskal-Wallis and Mann-Whitney U tests were used to examine independent quantitative variables. The paired samples *t*-test and Wilcoxon test were performed to analyze dependent quantitative variables. Independent qualitative variables were examined using the chi-square test or Fisher's exact test, when the chi-square assumptions were not met. The Pearson or Spearman correlation analysis was carried out to identify the relationship between the continuous variables. The correlation between the TG/HDL-C ratio and TFC was examined using the Spearman correlation coefficient. Backward stepwise univariate and multivariate logistic regression analyses were performed to determine independent predictors of CSFP. The receiver operating characteristic (ROC) curve was used to identify sensitivity and specificity of independent predictors of CSFP. The optimal cut-off value was calculated from the point of maximal sensitivity and specificity, as described by Youden [24]. The DeLong test was used to compare predictive performance of independent predictors of CSFP. A *p* value of <0.05 was considered statistically significant at 95% confidence interval.

Results

Of the 84 CSFP patients, 52 were males and 32 were females with a mean age of 54 ± 8.9 (range, 39 to 67) years. Of the 83 control individuals, 41 were males and 42 were females with a mean age of 55.2 ± 8.5 (range, 33 to 68) years. There was no statistically significant difference in the demographic characteristics such as age, sex, BMI and risk factors for CAD such as diabetes mellitus, hypertension, or smoking between the two groups ($p>0.05$ for all). The use of antiplatelets and angiotensin-converting enzyme inhibitors (ACEI)/angiotensin receptor blockers (ARBs) was more frequent in the control group. Baseline demographic and clinical characteristics of both groups are summarized in Table 1.

Laboratory test results of the CSFP and control groups are presented in Table 2. Accordingly, there was no statistically significant difference in the mean fasting blood glucose, urea, AST, ALT, white blood cell (WBC) count, hemoglobin, and platelets between the groups ($p>0.05$ for all). However, the mean creatinine and uric acid levels were significantly higher in the CSFP group than the control group ($p=0.002$ and $p=0.004$, respectively). The mean HDL-C level was significantly lower in the CSFP patients ($p=0.001$) with significantly higher TG levels ($p<0.001$) and TG/HDL-C ratio ($p<0.001$). On the other hand, there was no statistically significant difference in the TC and LDL-C levels between the groups ($p=0.208$ and $p=0.209$, respectively). The mean corrected TFC for LAD 46 ± 5 vs. 20.4 ± 2.2 , respectively; $p<0.001$), for LCX (30.2 ± 3.4 vs. 19.7 ± 2.3 , respectively; $p<0.001$), and for RCA (28.3 ± 4.2 vs. 19 ± 2.3 , respectively; $p<0.001$) were significantly higher in the CSFP group than the control group. In addition, the mean TFC was significantly higher in these patients (34.8 ± 3 vs. 19 ± 1.6 , respectively; $p<0.001$).

Backward stepwise univariate and multivariate logistic regression analyses were performed to determine independent predictors of CSFP. The relation of CSFP with age, sex, diabetes mellitus, smoking,

creatinine, uric acid, and TG/HDL-C ratio was examined. Given the fact that TG/HDL-C ratio, TG, and HDL-C show a strong correlation with each other, these variables were excluded from the multivariate analysis. The correlation analysis results are shown in Table 3. Accordingly, there was a positive and significant correlation between the TFC and TG/HDL-C ratio and TG levels ($r=0.311$, $p<0.01$; $r=0.222$, $p=0.06$, respectively) and a negative and significant correlation between the TFC and TG/HDL-C ratio and HDL-C levels ($r=0.275$, $p=0.001$) (Figure 3). In the multivariate regression analysis, the TG/HDL-C ratio was found to be a significant independent predictor of CSFP (odds ratio [OR]: 1.78, 95% CI: 1.59-2.32; $p=0.001$) (Table 4). The ROC curve was used to evaluate the ability of TG, HDL-C, and TG/HDL-C ratio to discriminate CSFP and healthy individuals. The ROC curve showed an area under the curve (AUC) value of 0.72 (95% CI: 0.65-0.81; $p<0.001$). The sensitivity and specificity of TG/HDL-C ratio for predicting CSFP were 72% and 71%, respectively. The AUC value of TG was 0.69 (95% CI: 0.61-0.76; $p<0.001$) with 64% sensitivity and 63% specificity at values above 126.5 mg/dL. The AUC value of HDL-C was 0.66 (95% CI: 0.58-0.73; $p=0.001$) with 59% sensitivity and 60% specificity at values below 45.5 mg/dL (Figure 4). The TG/HDL-C ratio, TG, and HDL-C were compared in terms of their predictive performance using the DeLong method. The predictive performance of TG/HDL-C ratio was significantly superior to that of TG, but it was borderline significant compared to HDL-C, indicating no statistical significance.

Discussion

In the present study, we investigated the possible relationship between the TG/HDL-C ratio and CSFP in patients undergoing elective coronary angiography. Our study results showed that the mean TG/HDL-C ratio was significantly higher in the CSFP patients than those with normal coronary flow. In addition, the mean TCF was positively and significantly correlated with the TG/HDL-C ratio. The ROC curve analysis showed that the cut-off value of TG/HDL-C ratio was sufficient to discriminate CSFP and non-CSFP individuals with a high sensitivity and specificity.

The CSFP is an angiographic evidence and should be considered as a distinct entity with specific characteristics, pathogenic mechanisms, and specified diagnostic criteria [1, 2]. Although the exact pathophysiology of CSFP is still unclear, endothelial dysfunction and atherosclerosis have been thought to be involved [3, 6]. Abnormally slow flow in the coronary arteries has been proposed to be an indicator of diffuse atherosclerosis related to the endothelial damage before angiographically visible coronary lesion, indicating an early manifestation involving both the microvascular system and epicardial coronary arteries [3, 11]. In a study, Avşar et al. [25] examined the possible link between CSFP and carotid artery intima-media thickness (CIMT) and found the increased CIMT in CSFP patients. In this study, the CIMT and corrected TCF were also significantly correlated, implying that CSFP might be an early marker of both endothelial dysfunction and subclinical atherosclerosis. In another study investigating the epicardial coronary morphology and intracoronary pressure in CSFP patients using intravascular ultrasonography (IVUS) and flow rate measurements, Cin et al. [3] reported diffuse intimal thickening, widespread calcification through the vessel wall, and non-obstructive atheroma. Consistent with these findings, Pekdemir et al. [11] described longitudinally extended massive calcification along the epicardial arteries as evidenced by IVUS examination as the most common finding in CSFP patients. Furthermore, Camsari

et al. [26] found the CIMT to be associated with IVUS indices in CSFP patients. Taken together, these findings support the notion that CSFP is an indicator of microvascular diseases and diffuse, non-obstructive atherosclerotic disease of the epicardial arteries.

Endothelial dysfunction is an early indicator of atherosclerosis [27]. Endothelial-dependent, flow-mediated dilatation (FMD) of the brachial artery has been shown to reduce in CSFP patients, indicating that CSFP may play a role in the etiology of endothelial dysfunction [5]. In addition, plasma homocysteine and endothelin levels increase in CSFP patients, both which have detrimental effects on endothelial function [4, 10]. In the light of existing data, CSFP seems to be a form of early diffuse coronary atherosclerosis, predominantly characterized by microvascular endothelial dysfunction.

It has been well established that lipid abnormalities contribute to the development of atherosclerosis [10]. An extensive number of studies have demonstrated that high TC and LDL-C and low HDL-C are strongly associated with ischemic heart disease, stroke, peripheral vascular disease, and atherosclerosis [12]. Elevated LDL-C levels with high TG and low HDL-C have been shown to increase the risk of CAD than elevated LDL-C levels alone [28, 29]. Review of the literature reveals that different subfractions of the lipid particles are involved in the atherogenesis. Small dense LDL particles are more atherogenic than larger particles [28]. Less dense HDL2 particles are protective, while small dense HDL3 particles are atherogenic [30]. High TG and low HDL-C levels are strongly associated with small dense LDL-C levels [18, 28]. The TG/HDL-C ratio has been shown to be an indirect indicator of small dense LDL particles and a superior predictor of coronary heart disease than conventional lipid parameters [15, 19]. This ratio has been also considered an independent predictor of CVD and all-cause mortality [20, 21]. In their study, Keles et al. [31] evaluated whether the TG/HDL-C ratio differed between patients with chronic inflammatory disease and healthy individuals. The authors concluded that increased TG/HDL-C ratio and low FMD values might indicate endothelial dysfunction and a higher risk of atherosclerosis in these patients. Consistent with previous studies showing a link between low HDL-C and high TG levels and CSFP [32–34], we found high TG levels low HDL-C levels in the CSFP group in our study.

Review of the literature reveals only one retrospective study investigating the relationship between proportional serum lipid parameters and CSFP. In this study including 54 CSFP patients and 39 controls, Kalayci et al. [34] found higher TG, TC/HDL-C, TG/HDL-C, LDL-C/HDL-C, and non-HDL-C levels to be associated with CSFP. In addition, there was a weak, but positive correlation between the TG and TG/HDL-C ratio and mean TFC. In our prospective study, we also found a significant correlation of the high TG, TG/HDL-C ratio, and low HDL-C and CSFP. Furthermore, we showed a weak, but positive correlation between the TG levels and mean TFC and a moderate, positive correlation between the TG/HDL-C ratio and mean TFC. These findings suggest that high TG/HDL-C ratio is an independent predictor of CSFP.

In the literature, several studies have shown the link between LDL-C levels and CSFP [35–37]. In a study investigating the clinical and angiographic properties of CSFP, Yilmaz et al. [35] found LDL-C levels to be correlated with CSFP. On the other hand, no significant correlation between these two variables was

reported in some other studies [36, 37]. Similarly, in our study, the LDL-C levels were comparable between the two groups. Based on these findings, it can be speculated that TG and HDL-C levels are more valuable indicators of CSFP than LDL-C alone and TG/HDL-C ratio shows a higher correlation with the mean TFC, than TG and HDL-C levels.

Nonetheless, there are some limitations to this study. First, it has a single-center design with relatively small sample size. Second, we were unable to evaluate the atherosclerotic alterations in the coronary arteries via sophisticated imaging modalities such as IVUS or optic coherence tomography, precluding the evaluation of coexisting non-obstructive CAD in isolated CSFP patients. Of note, IVUS is not recommended in the routine daily practice for the evaluation of CSFP patients and the diagnosis is usually confirmed based on visible angiographic findings. Third, inflammatory biomarkers such as the high-sensitivity C-reactive protein, interleukin-6, and tumor necrosis factor-alpha were unable to be analyzed. Further large-scale, prospective, randomized-controlled studies are needed to confirm these findings.

Conclusions

In conclusion, the CSFP is a poorly recognized clinical entity. Our study results suggest that TG/HDL-C ratio is strongly associated with CSFP and is a significant independent predictor of CSFP. Therefore, it may be a useful biomarker for predicting CSFP and its severity. Beyond its predictive value, it may be of value as a therapeutic target owing to its simplicity and as it allows longitudinal follow-up in the clinical setting. Further studies are warranted to gain a better understanding of the pathogenesis of CSFP and the diagnostic and therapeutic value of TG/HDL-C ratio in this group of patients.

Declarations

Authors' contributions

Conceptualization: Gonul AÇIKSARI, Adem ATICI, Methodology: Gonul AÇIKSARI, Adem ATICI, Gokhan CETİNKAL Formal analysis: Adem ATICI, Gokhan CETİNKAL, Mehmet KOCAK Data collection: Fatma Betul CELİK, Adem ATICI Data interpretation: Adem ATICI, Gokhan CETİNKAL, Fatma Betul CELİK Writing: Gonul AÇIKSARI, Mustafa CALISKAN, Original draft: Fatma Betul CELİK, Adem ATICI, Mehmet KOCAK Review & editing: Mustafa CALISKAN. All authors read and approved the final manuscript.

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Tables

Table 1. Baseline demographic and clinical characteristics of participants

Variable	CSFP group (n=84)		Control group (n=83)		p value
	Mean±SD/n (%)		Mean±SD/n (%)		
Age, year	54.6 ± 8.9		55.2 ± 8.5		0.646
Sex, n (%)	Female	32 (38.1)	42 (50.6)		0.104
	Male	52 (61.9)	41 (49.4)		
BMI, kg/m ²	28.7 ± 3.5		29.1 ± 3.6		0.338
Smoking, n (%)	16 (19)		21 (25.3)		0.331
Hypertension, n (%)	38 (45.2)		39 (47)		0.821
Diabetes mellitus, n (%)	22 (26.2)		19 (22.9)		0.620
Calcium canal blocker, n (%)	16 (19)		10 (12)		0.212
Beta-blocker, n (%)	18 (21.4)		26 (31.3)		0.147
ACEI/ARB, n (%)	16 19,0%		27 32,5%		0.046
Antiplatelet, n (%)	18 21,4%		30 36,1%		0.036
OAD	15 17,9%		15 18,1%		0.971
Statin	12 14,3%		16 19,3%		0.388

Data are given in mean ± SD or number and frequency, unless otherwise stated. ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; BMI: body mass index; CSFP: coronary slow flow phenomenon; NCF normal coronary flow; SD: standard deviation.

Table 2. Laboratory test results of participants

variable	CSFP group (n=84)		Control group (n=83)		p value
	Mean±SD/n (%)		Mean±SD/n (%)		
fasting glucose, mg/dL	110.9	± 33.1	102.8	± 22.4	0.059
urea, mg/dL	30	± 9.5	30.4	± 10.8	0.872
creatinine, mg/dL	0.84	± 0.12	0.77	± 0.15	0.002
ALT, IU/L	23.2	± 10.6	20.4	± 6.8	0.122
AST, IU/L	21.9	± 8.2	21.2	± 9.5	0.176
uric acid, mg/dL	5.6	± 1.7	4.8	± 1.3	0.004
TC, mg/dL	202.5	± 40.1	194.3	± 38.2	0.208
LDL-C, mg/dL	125.2	± 34	118.2	± 34.5	0.209
HDL-C, mg/dL	43.6	± 9.	50	± 11.1	0.001
triglyceride, mg/dL	150 (109 - 206)		115(96 - 145.5)		<0.001
TG/HDL-C ratio	3.4 (2.6 - 4.9)		2.3(1.8 - 3)		<0.001
WBC, 10 ³ /mm ³	7.7	± 2.5	7.7	± 1.9	0.770
hemoglobin, mg/dL	13.7	± 1.6	13.7	± 1.6	0.934
platelet, 10 ³ /mm ³	238.9	± 62	250.3	± 67.4	0.363
IMI frame count					
LAD (corrected)	46	± 5	20.4	± 2.2	<0.001
LCX	30.2	± 3.4	19.7	± 2.3	<0.001
RCA	28.3	± 4.2	19	± 2.3	<0.001
TFC	34.8	± 3	19	± 1.6	<0.001

Data are given in mean ± SD or number and frequency, unless otherwise stated. ALT: alanine aminotransferase; AST: aspartate aminotransferase; CSFP: coronary slow flow phenomenon; hs-CRP: high-sensitivity C-reactive protein; HDL-C: high-density lipoprotein cholesterol; LCx: left circumflex coronary artery; LAD: left anterior descending coronary artery; LDL-C: low-density lipoprotein cholesterol; RCA: right coronary artery; TC: total cholesterol; TIMI: Thrombolysis in Myocardial Infarction; TFC: TIMI frame count; TG: triglyceride; WBC: white blood cell.

Table 3. Correlation analysis results

Variable	Univariate Model			Multivariate Model		
	OR	95% CI	<i>p</i>	OR	95% CI	<i>p</i>
Age	0.992	0.958-1.027	0.644			
BMI	1.01	0.91-1.13	0.855			
Sex	0.60	0.33-1.11	0.105			
Smoking	0.66	0.36-1.38	0.270			
Diabetes	1.28	0.60-2.47	0.588			
Hypertension	0.95	0.52-1.76	0.875			
Creatinine	48.42	4.28 - 548.32	0,002			
HDL-C	0.94	0.90 - 0.97	0,000			
Triglyceride	1.01	1.01 - 1.02	0,000			
Uric acid	1.45	1.13 - 1.85	0,004			
TG/HDL-C ratio	1.73	1.33 - 2.27	0,000	1.78	1.59 - 2.32	0.001

Logistic Regression (backward LR). BMI: body mass index; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TG: triglyceride; OR: odds ratio; CI: confidence interval.

Table 4. Correlation of mean TFC with other variables

	<i>r</i>	<i>p</i> value
Fasting glucose	0.115	0.154
Creatinine	0.112	0.157
Urea	0.069	0.385
Uric acid	0.109	0.166
TC	0.003	0.975
TG/HDL-C ratio	0.311	<0.001
LDL-C	0.002	0.809
HDL-C	-0.275	0.001
Triglyceride	0.222	0.006

HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; TFC: Thrombolysis in Myocardial Infarction frame count; TG: triglyceride.

Figures

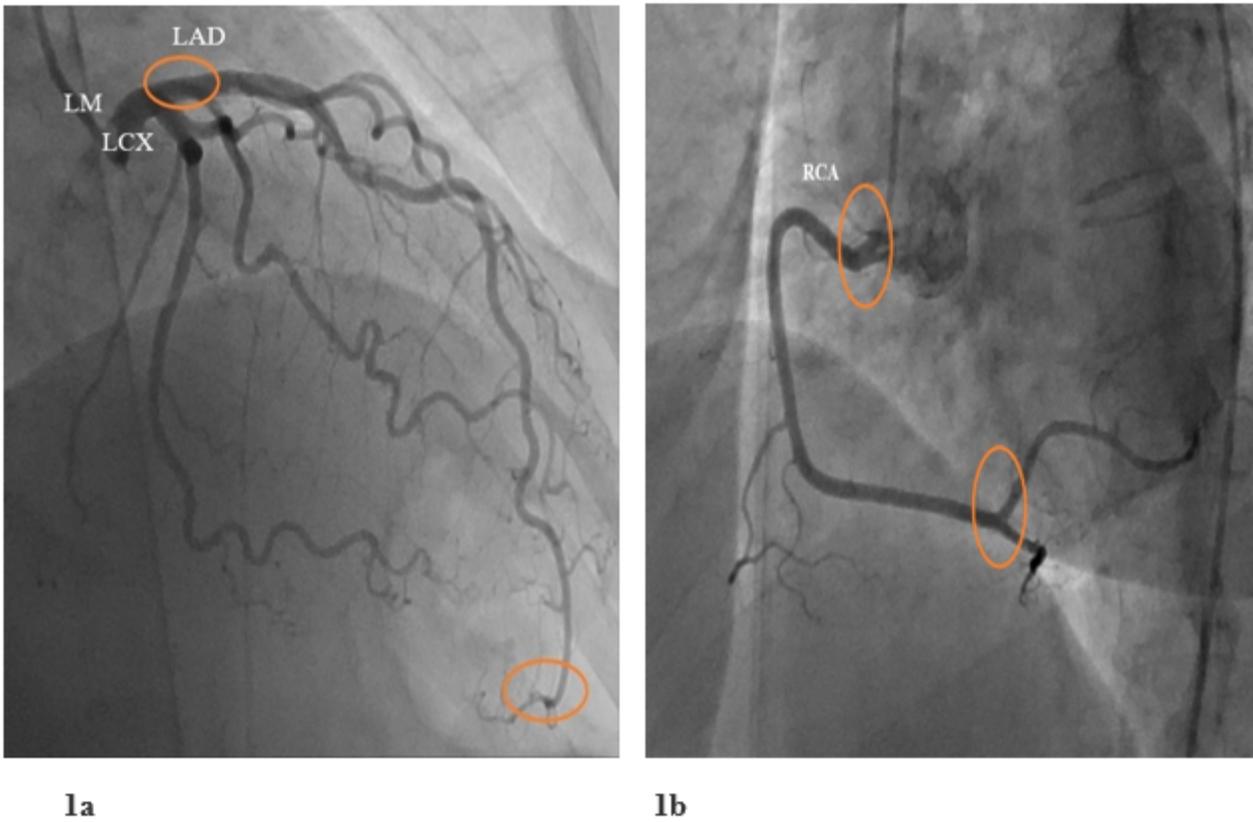


Figure 1

a: Measurement of coronary flow by TFC. The speed with which the dye reaches the distal 'pitchfork' bifurcation of LAD from the ostium is measured in frame counts. b: In RCA the flow is measured from ostium to origin of first posterolateral branch. *Abbreviations: TFC, Thrombolysis in Myocardial Infarction frame count; LAD, left anterior descending; RCA, right coronary artery; LCX, left circumflex; LM, left main.

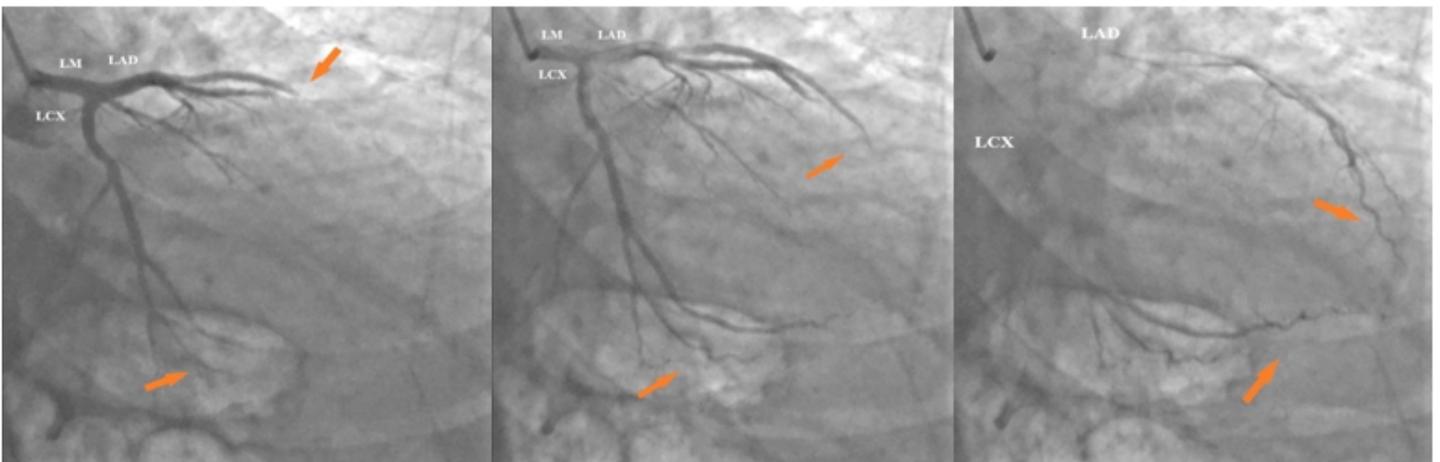


Figure 2

Coronary angiography of a 46-year-old man with CSFP of our study participant showing slow progression of contrast material in the LAD and with normal epicardial coronary arteries. TIMI frame count 55.

*Abbreviations: CSFP, coronary slow-flow phenomenon; LAD, left anterior descending; LCX, left circumflex; LM, left main; TIMI, Thrombolysis in Myocardial Infarction.

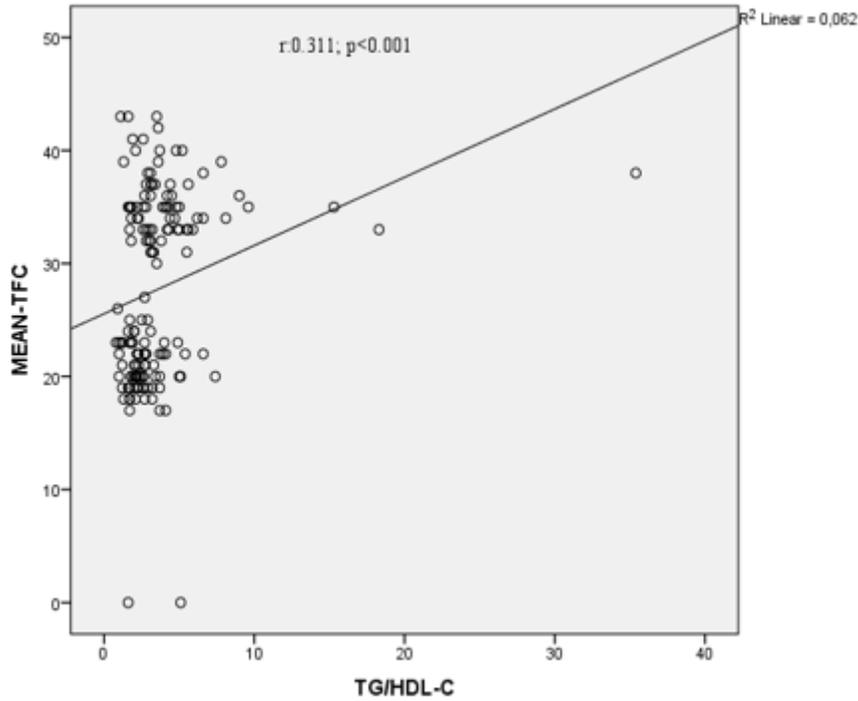


Figure 3

Correlation between TG/HDL-C ratio and the mean-TFC in CSFP patients. TFC: Thrombolysis in Myocardial Infarction frame count; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol.

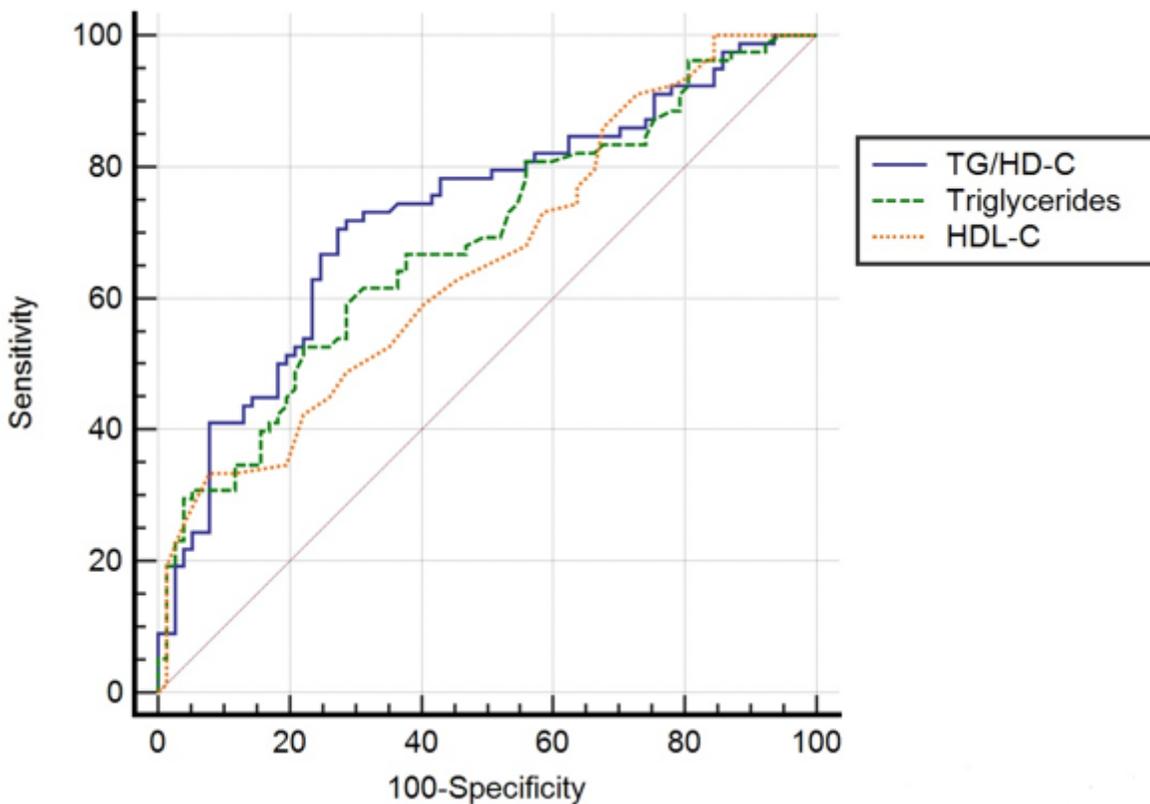


Figure 4

ROC curves showing the predictive value of TG/HDL-C ratio, TG, and HDL-C for CSFP. ROC: receiver operating characteristics; AUC: area under the curve; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; CSFP: coronary slow flow phenomenon; CI: confidence interval. Differences between areas are as follows: TG-HDL-C vs. TG: 0.444; 95% CI: 0.037-0.084; Z-score: 2.14; $p=0.03$; TG/HDL-C vs. HDL-C: 0.073; 95% CI: -0.0034-0.15; Z-score: 1.87; $p=0.06$; TG vs. HDL-C: 0.029; 95% CI: -0.0772-0.14; Z-score: 0.54; $p=0.59$).