



Association of atherogenic index and mean platelet volume with coronary slow flow phenomenon

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Abstract

Background: Coronary slow flow phenomenon is defined by delayed opacification of the coronary arteries in the absence of significant stenotic lesions in the epicardial vessels. This study investigated the association between atherogenic index and mean platelet volume (MPV) in patients with coronary slow flow.

Methods: This retrospective analysis was conducted by reviewing the medical records of patients who underwent coronary angiography at Erzurum City Hospital. Individuals diagnosed with coronary slow flow constituted the study group, whereas patients with normal coronary flow were included as the control group. Coronary perfusion was evaluated using the TIMI frame count method. The atherogenic index was derived from triglyceride and HDL cholesterol concentrations, and MPV was obtained from routine complete blood count measurements.

Results: Patients with coronary slow flow exhibited significantly higher atherogenic index and MPV values compared to the control group. Furthermore, a statistically significant positive correlation was found between TIMI frame count and both atherogenic index and MPV.

Conclusion: These results suggest a relationship between atherogenic index, MPV and coronary slow flow phenomenon. These routinely available biomarkers may have potential clinical utility and may contribute to a better understanding of the underlying pathophysiological mechanisms.

Keywords

coronary slow flow, atherogenic index, mean platelet volume

Introduction

The coronary slow flow phenomenon (CSFP) is characterised by delayed distal coronary vessel opacification during angiography in the absence of obstructive epicardial coronary artery disease, flow-limiting coronary dissection, distal embolisation or angiographically evident thrombus. [1]. Since it was first identified, CSFP has been linked to a range of clinical presentations, including stable angina, symptoms resembling acute coronary syndromes, reduced exercise capacity and rhythm disturbances [2]. Although its exact underlying mechanisms remain unclear, endothelial dysfunction, impairment of the coronary microcirculation, inflammation and enhanced platelet activity are believed to play central roles in its pathogenesis [3].

Endothelial dysfunction together with early or subclinical atherosclerosis is considered an important contributor to CSFP development. In this context, abnormalities in lipid metabolism and elevated atherogenic risk have gained attention. The atherogenic index, which is calculated using triglyceride (TG) and high-density lipoprotein cholesterol (HDL-C) levels, is considered as a reliable marker of cardiovascular risk and atherosclerotic burden [4]. Higher values of this index are thought to reflect the presence of small,

dense low-density lipoprotein (LDL) particles as well as impaired endothelial function [5].

Another important factor in CSFP pathophysiology is platelet activation. Mean platelet volume (MPV), an indicator of platelet size and activity, serves as an indirect marker of platelet function and has been associated with thrombotic risk and adverse cardiovascular outcomes [6]. Because larger platelets exhibit greater metabolic and enzymatic activity, elevated MPV levels may contribute to impaired microvascular coronary perfusion [7].

Although previous studies have examined the relationship between CSFP and various lipid parameters as well as platelet indices, research evaluating both the atherogenic index and MPV together remains limited [8]. Therefore, the present study aims to assess atherogenic index and MPV levels in patients with CSFP and to investigate their association with coronary flow velocity.

Materials and methods

1. Study design and patient selection

This retrospective study was conducted by reviewing medical records of patients who underwent coronary angiography at Erzurum City Hospital, Erzurum, Türkiye, between January 2022 and December 2024. During this period, 247 individuals underwent coronary angiographic evaluation and those without significant epicardial coronary artery stenosis were subsequently assessed in detail.

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After applying the predefined inclusion and exclusion criteria, 182 patients with complete clinical and laboratory data were enrolled in the study. Among them, 92 patients diagnosed with CSFP constituted the study group, while 90 patients with normal coronary flow were included as the control group.

Eligibility criteria included age 18 years or older, absence of $\geq 50\%$ stenosis in the epicardial coronary arteries on angiography, and availability of complete clinical and laboratory records. Patients with a prior history of coronary artery disease, previous myocardial infarction, heart failure, significant valvular heart disease, cardiomyopathy, haematological disorders, active infection, chronic inflammatory disease, malignancy, hepatic or renal dysfunction or those using medications that could affect platelet activity or lipid metabolism were excluded from the study.

2. Coronary angiographic evaluation

Coronary angiography was performed in all patients using the standard Judkins technique. Angiographic data were independently evaluated by two experienced interventional cardiologists who were blinded to the clinical and laboratory information of the participants. Coronary flow was measured using the thrombolysis in myocardial infarction (TIMI) frame count method. Due to its longer anatomical trajectory, the frame count for the left anterior descending artery was appropriately adjusted. CSFP was defined as a TIMI frame count above the established normal range in at least one epicardial coronary artery.

3. Laboratory measurements

Venous blood samples were obtained from all participants after an overnight fast and prior to coronary angiography. Complete blood count parameters were analysed using an automated haematology analyser, and MPV values were recorded. Serum levels of TGs, total cholesterol, HDL-C and LDL cholesterol were measured using standard laboratory techniques. The atherogenic index of plasma (AIP) was calculated as $\log_{10}(\text{TG}/\text{HDL-C})$, where TG and HDL-C concentrations were expressed in mmol/L.

4. Ethical approval

Ethical approval for this retrospective study was granted by the Local Clinical Research Ethics Committee (Date: 10/12/2025, Decision No: 2025/12-295). Due to the retrospective design of the study, the requirement for obtaining informed consent was waived. The study was carried out in accordance with the ethical standards outlined in the Declaration of Helsinki.

5. Statistical analysis

All statistical analyses were performed using SPSS software version 27.0.1.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Shapiro–Wilk test. Continuous variables with normal distribution were expressed as mean $\pm$ standard deviation and compared using Student's *t*-test. Variables not showing normal distribution were presented as median (interquartile range) and compared using the Mann–Whitney *U* test.

Categorical variables were expressed as numbers and percentages and compared using the Chi-square test. Correlations between continuous variables were evaluated using Pearson correlation analysis. A *p*-value < 0.05 was considered statistically significant.

Results

A total of 182 patients were analysed in this study, comprising 92 individuals in the CSFP group and 90 in the control group. The mean age was 55.1 ± 9.4 years in the CSFP group and 53.6 ± 8.9 years in the control group, with no statistically significant difference between the groups ($p = 0.268$). The proportion of male participants was also comparable between the CSFP and control groups (64.1% vs 62.2%, $p = 0.782$). In addition, there were no significant intergroup differences regarding the prevalence of hypertension, diabetes mellitus or smoking status ($p = 0.742$, $p = 0.697$ and $p = 0.768$, respectively) (Table 1).

Regarding laboratory parameters, TG levels were significantly elevated in the CSFP group compared with the control group [171 (142–198) mg/dL vs 136 (112–163) mg/dL, $p < 0.001$]. In contrast, high-density lipoprotein (HDL) cholesterol levels were significantly lower in patients with CSFP (40.2 ± 7.9 mg/dL vs 46.1 ± 8.6 mg/dL, $p < 0.001$). No statistically significant differences were observed in total cholesterol or LDL cholesterol levels between the groups ($p = 0.214$ and $p = 0.341$, respectively).

The atherogenic index was significantly higher in the CSFP group compared with controls (0.56 ± 0.19 vs 0.43 ± 0.17 , $p < 0.001$). Similarly, MPV was also increased in the CSFP group (10.2 ± 0.8 fL

Table 1 - Demographic, clinical and laboratory characteristics of coronary slow flow and control groups

Parameter	Coronary slow flow (<i>n</i> = 92)	Control group (<i>n</i> = 90)	<i>p</i> value
Age (years)	55.1 ± 9.4	53.6 ± 8.9	0.268
Male gender, <i>n</i> (%)	59 (64.1)	56 (62.2)	0.782
Hypertension, <i>n</i> (%)	41 (44.6)	38 (42.2)	0.742
Diabetes mellitus, <i>n</i> (%)	29 (31.5)	26 (28.9)	0.697
Smoking status, <i>n</i> (%)	45 (48.9)	42 (46.7)	0.768
TG (mg/dL)	171 (142–198)	136 (112–163)	< 0.001
HDL-C (mg/dL)	40.2 ± 7.9	46.1 ± 8.6	< 0.001
LDL cholesterol (mg/dL)	121.4 ± 32.6	116.8 ± 30.9	0.341
Total cholesterol (mg/dL)	198.6 ± 41.3	191.2 ± 39.8	0.214
Atherogenic index	0.56 ± 0.19	0.43 ± 0.17	< 0.001
MPV (fL)	10.2 ± 0.8	9.6 ± 0.7	< 0.001
Platelet count ($\times 10^3/\mu\text{L}$)	248 ± 61	242 ± 58	0.481
TIMI frame count	29.1 ± 4.3	18.7 ± 3.8	< 0.001

HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein; MPV, mean platelet volume; TG, triglyceride; TIMI, thrombolysis in myocardial infarction.

Table 2 - Correlation analysis between TIMI frame count and laboratory parameters

Parameter	Correlation coefficient (r)	p value
Atherogenic index	0.31	0.004
MPV	0.28	0.009
TG level	0.26	0.015
HDL-C	-0.24	0.021

HDL-C, high-density lipoprotein cholesterol; MPV, mean platelet volume; TG, triglyceride; TIMI, thrombolysis in myocardial infarction

vs 9.6 ± 0.7 fL, $p < 0.001$), whereas platelet counts did not differ significantly between the two groups ($p = 0.481$).

The TIMI frame count, reflecting coronary flow velocity, was markedly higher in patients with CSFP compared to the control group (29.1 ± 4.3 vs 18.7 ± 3.8 , $p < 0.001$).

Correlation analysis demonstrated a significant positive relationship between TIMI frame count and atherogenic index ($r = 0.31$, $p = 0.004$), MPV ($r = 0.28$, $p = 0.009$) and TG levels ($r = 0.26$, $p = 0.015$). Conversely, HDL cholesterol levels showed a significant negative correlation with TIMI frame count ($r = -0.24$, $p = 0.021$) (Table 2).

Discussion

In this retrospective analysis, both the atherogenic index and MPV were found to be significantly elevated in patients with CSFP compared with individuals exhibiting normal coronary flow. Moreover, both parameters showed significant correlations with TIMI frame count, indicating that disturbances in lipid metabolism and enhanced platelet activation may have a combined role in the development of CSFP.

Although the precise mechanisms underlying CSFP have not been fully clarified, microvascular dysfunction and endothelial impairment are widely accepted as central contributors. Prior research has demonstrated that CSFP is associated with increased oxidative stress, systemic inflammation and reduced endothelium-dependent vasodilation [9,10]. These alterations may ultimately result in functional impairment of the coronary microcirculation.

The atherogenic index, which reflects the balance between atherogenic and protective lipid fractions, has emerged as a useful marker in cardiovascular risk stratification. It has been previously linked to subclinical atherosclerosis, endothelial dysfunction and microvascular abnormalities [11,12]. In the present study, the higher atherogenic index observed in the CSFP group, together with its positive association with TIMI frame count, supports the hypothesis that dyslipidaemia may adversely affect coronary microvascular perfusion.

Platelet activation also represents a key element in the pathophysiology of CSFP. MPV, as an indirect indicator of platelet reactivity, has been associated with heightened thrombotic potential and vascular dysfunction. Earlier studies have reported that increased MPV is related to endothelial injury and impaired microcirculatory function [13,14]. Consistent with these findings, our

results demonstrate elevated MPV levels in CSFP patients and a significant positive correlation with TIMI frame count, suggesting a potential role of platelet hyperreactivity in reduced coronary flow.

Evidence examining the combined relationship of atherogenic index and MPV in CSFP remains limited. The relatively modest correlation coefficients observed in this study may be attributed to factors such as population variability, the retrospective and single-centre design, and potential unmeasured confounders. Nevertheless, the statistically significant associations observed support a link between these haematologic and metabolic parameters and CSFP [15].

Although the correlation coefficients observed in the present study were modest, CSFP is a multifactorial disorder involving endothelial dysfunction, microvascular abnormalities, inflammatory processes and platelet activation. Therefore, moderate correlations may still be clinically meaningful when interpreted within the broader pathophysiological context. These findings suggest that AIP and MPV may serve as complementary biomarkers reflecting different mechanisms associated with coronary slow flow rather than standalone diagnostic markers.

While previous studies have separately investigated lipid-related parameters and platelet activation markers in patients with CSFP, studies simultaneously evaluating both AIP and MPV in the same patient population remain limited. The present study contributes to the existing literature by demonstrating associations between both metabolic and haematological markers and coronary slow flow. The combined assessment of these readily available biomarkers may provide a more comprehensive understanding of the mechanisms underlying CSFP.

Previous studies have suggested that CSFP is not merely an angiographic finding but may be associated with adverse clinical outcomes, including recurrent angina, repeated hospital admissions, arrhythmias, acute coronary syndrome-like presentations and major adverse cardiovascular events (MACE). Several reports have also demonstrated an increased risk of cardiovascular morbidity and impaired long-term prognosis among patients with CSFP. Although the present study was not designed to evaluate clinical outcomes, the observed associations between AIP, MPV and coronary flow abnormalities may have potential implications for future risk stratification and warrant further investigation in prospective outcome-based studies.

Limitations

This study has several limitations that should be taken into account. First, its retrospective nature restricts the ability to infer causal relationships. In addition, being conducted at a single centre may limit the generalisability of the findings to broader populations. Another limitation is the lack of direct assessment of inflammatory biomarkers and endothelial function parameters, which may contribute to the pathophysiology of CSFP. Furthermore, multivariable logistic regression analysis was not performed because of the retrospective design and limited sample size. Therefore,

the independent predictive value of atherogenic index and MPV could not be determined after adjustment for potential confounding variables. Future prospective studies with larger populations are needed to evaluate whether these parameters independently predict CSFP. Nevertheless, the use of simple, routinely available and cost-effective laboratory indices enhances the clinical relevance and practical usefulness of the findings.

Although the correlations observed between TIMI frame count and both AIP and MPV were modest, CSFP is a multifactorial disorder involving endothelial dysfunction, microvascular abnormalities, inflammation and platelet activation. Therefore, moderate correlations may still be clinically meaningful when interpreted within the complex pathophysiology of the disease. These findings suggest that AIP and MPV should not be considered standalone diagnostic markers but may serve as complementary indicators reflecting different mechanisms contributing to coronary slow flow.

Furthermore, multivariable logistic regression analysis was not performed; therefore, independent predictors of CSFP could not be identified and the potential effects of confounding variables could not be fully adjusted.

Conclusion

The findings of this study demonstrate that both the atherogenic index and MPV have significantly increased in patients with CSFP compared with individuals with normal coronary flow. The observed associations between these parameters and TIMI frame count indicate that abnormalities in lipid metabolism and enhanced platelet activation may contribute to the underlying pathophysiology of CSFP.

Considering that these markers are simple, widely available and cost-effective, they may have potential value as supportive biomarkers in routine clinical evaluation. Nevertheless, further evidence from large-scale, prospective and multicentre studies is required to confirm these associations, clarify causality and evaluate their prognostic significance in clinical outcomes.

Conflict of interest

The authors declare no conflict of interest.

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Author Contributions

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Declaration of Interests

The author has no relevant financial or non-financial interests to disclose.

Availability of Data and Materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical Approval Statement

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University of Health Sciences, Erzurum Faculty of Medicine Scientific Research Ethics Committee. (Date: 10.12.2025/ Decision No.: 2025/12-295).

Informed Consent

Due to the retrospective design of the study, the requirement for informed consent was waived by the Ethics Committee.

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