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Coronary Slow Flow Phenomenon: A Single-Center Analysis of Prevalence and Risk Factors

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Abstract

Background: Coronary slow flow phenomenon (CSFP) is a syndrome characterized by delayed progression of the injected contrast through the epicardial coronary arteries, in the absence of significant stenosis. It is associated with myocardial ischemia, life-threatening arrhythmias, sudden cardiac death, and recurrent acute coronary syndromes.

Objective: This study aimed to determine the prevalence of CSFP and its risk factors**.**

Methods: This cross-sectional study was conducted on all patients undergoing diagnostic coronary angiography because of clinical suspicion of cardiovascular disease in Mashhad Ghaem Hospital from March 2019 to March 2020. The individual information checklist was completed, and the diagnosis of the CSFP was made on the basis of corrected TIMI frame count > 27 frames.

Results: In the present study, among 1112 patients undergoing coronary angiography, 7.5% had the criteria of CSFP. Statistical tests indicated a significant association between male sex and smoking (p-value < 0.05) with CSFP. The association between hypertension and CSFP was not significant in univariate analysis but became significant after adjustment. Factors such as age, diabetes mellitus, hyperlipidemia, and family history of heart disease had no significant difference between patients with and without CSFP.

Conclusion: Coronary slow flow phenomenon is not an uncommon finding during diagnostic coronary angiography. The observed associations with modifiable risk factors, particularly smoking and hypertension, suggest that attention to risk factor modification may be beneficial in patients with CSFP and should be considered in clinical practice.

Keywords: Coronary Angiography; Ischemic Heart Disease; Microvascular Dysfunction; Risk Factors.

1. Background

The coronary slow flow phenomenon (CSFP), often overlooked as a cause of chest pain, is defined by delayed coronary opacification observed during diagnostic angiography, occurring without obstructive epicardial coronary stenosis or other conditions that typically hinder coronary flow (1, 2). Initially described in 1972, CSFP may be more prevalent than commonly recognized. CSFP has been identified in as many as 7% of patients undergoing diagnostic angiography and may represent up to 4% of admissions for unstable angina (3). Patients with CSFP primarily exhibit recurrent chest pain, which is often not linked to physical exertion and frequently results in repeated hospitalizations (4, 5).

Different studies have examined the clinical characteristics of individuals with CSFP, with somewhat contradicting results. A study in Australia (4) identified male sex and nicotine use as significant associated factors (4). This

study showed that patients with CSFP exhibited a significantly younger age profile. On the other hand, a Turkish study showed no association between nicotine use and this condition (6). Notably, the cardiovascular risk burden among the population under study is significant.

2. Objective

This study was conducted to assess the prevalence of CSFP in our population and find the clinical features associated with CSFP.

3. Methods

The present research was a cross-sectional study conducted between 2019 and 2020 in the Department of Cardiology, Ghaem Hospital, Mashhad, Iran. The included subjects were patients who had undergone diagnostic angiography due to clinical suspicion of cardiovascular disease. The sampling method used in this study was consecutive sampling. The patients were educated on the details and purposes of the study and had the right to leave the study at any time. Furthermore, written informed consent was obtained from all patients. The present study was approved by the Ethics Committee of Islamic Azad University of Mashhad (ethics code: IR.IAU.MSHD.REC.1401.057).

Study design

The inclusion criteria in this study were (i) a history of angiography, and (ii) 40-75 years of age. Patients with a past medical history of myocardial infarction, heart failure, left ventricle ejection fraction < 40%, a history of heart valvular disease, impaired renal function (eGFR < 90 mL/min), impaired liver function (AST and ALT serum levels > 3 times the standard limit), any active acute or chronic infectious disease, any hematological disorders, hypothyroidism or hyperthyroidism, coronary anomalies, coronary ectasia (dilation of a coronary artery > 1.5 times the adjacent segment, as the standard caliber), and CSFP in a coronary artery with > 50% stenosis were excluded from the study. The total number of evaluated patients was 1112, of whom 166 patients were included in the study, with 84 in the CSFP and 82 in the normal coronary angiography group (as controls). A data collection form was used to record the demographic (age and sex) and medical profiles of the included patients. Hyperlipidemia was defined as an LDL > 100 mg/dL or a history of controlled hyperlipidemia via lifestyle modification or medical therapy. Hypertension was defined as a systolic blood pressure > 140 mmHg or a diastolic blood pressure > 90 mmHg, or a history of controlled hypertension.

Measurements

Blood pressure was measured using a sphygmomanometer on the right arm following a ten-minute rest, with two consecutive readings taken at five-minute intervals. The final blood pressure value was recorded as the average of these measurements. Diabetes and dyslipidemia were evaluated through laboratory tests, with diabetes defined as a fasting blood glucose level exceeding 125 mg/dL or a condition managed through dietary modifications or pharmacotherapy. A fellowship-trained interventional cardiologist performed coronary angiography in accordance with the American Heart Association guidelines. The presence of CSFP was determined based on a corrected TIMI frame count exceeding 27 frames per second in any of the major coronary arteries, in the absence of significant stenosis (> 50%) (7).

Statistics

SPSS version 26 was used for the statistical analyses in this study. Continuous variables were reported using mean and SD, and categorical variables were reported using frequency (%). Depending on the normality of the variables, unpaired t-test or Mann-

Whitney U tests, or Mann-Whitney U or Kruskal-Wallis tests were used for comparing the continuous variables. Furthermore, the chi-square was used to compare the categorical variables. Logistic regression was performed to find the risk factors for developing CSFP. Statistical significance was considered at the p-value < 0.05.

4. Results

Baseline Clinical Characteristics

A total of 166 patients were included in the study, with a mean age of 55.65 ± 9.44 years. The majority of the participants were female (57.2%), while males comprised 42.8% of the population. Among the study population, 23.5% had diabetes, 54.5% had hypertension, and 12% had hyperlipidemia. Smoking and opioid use were reported by 28.3% and 19.3% of participants, respectively. A positive family history of cardiovascular disease (CVD) was present in only 1.2% of cases (Table 1).

Table 1. The clinical features of subjects at baseline

Age (mean ± SD)		**55.65±9.44**
Sex (n, %)	**Male**	**71 (42.8)**
	Female	**95 (57.2)**
Diabetes (n, %)	**Yes**	**39 (23.5)**
	No	**127 (76.5)**
Hypertension (n, %)	**Yes**	**90 (54.5)**
	No	**75 (45.5)**
Hyperlipidemia (n, %)	**Yes**	**20 (12)**
	No	**146 (88)**
Smoking (n, %)	**Yes**	**47 (28.3)**
	No	**129 (71.7)**
Opioids (n, %)	**Yes**	**32 (19.3)**
	No	**134 (80.7)**
CVD family history (n, %)	**Yes**	**2 (1.2)**
	No	**164 (98.8)**
CSFP (n, %)	**Yes**	**84 (50.6)**
	No	**82 (49.4)**

Comparison of Clinical Features between Patients with Normal Angiography and CSFP

The prevalence of CSFP among the patients during the study period was 7.5%. Patients with CSFP had a higher proportion of males (53.6% vs. 31.7%, p = 0.004) compared to those with normal angiography findings. The prevalence of diabetes (20.2% vs. 26.8%, p = 0.32) and hyperlipidemia (10.7% vs. 13.4%, p = 0.7) was comparable between the two groups. Hypertension was more frequent in the CSFP group (61.4% vs. 47.6%), but this difference did not reach statistical significance (p = 0.07) (Table 2).

Notably, smoking was significantly more common among patients with CSFP (40.5% vs. 15.9%, p < 0.001). Similarly, opioid use was higher in the CSFP group (23.8% vs. 14.6%, p < 0.001). There was no difference in the prevalence of a family history of CVD between the two groups (p > 0.9) (Table 2).

Table 2. Comparison of clinical features between patients with a normal angiography and CSFP

		Normal angiography	CSFP	p-value
Age (mean ± SD)		55.11±9.95	56.20±8.95	0.4
Sex (n, %)	Male	26 (31.7)	45 (53.6)	0.004
	Female	56 (68.3)	39 (46.4)	
Diabetes (n, %)	Yes	22 (26.8)	17 (20.2)	0.32
	No	60 (73.2)	67 (79.8)	
Hypertension (n, %)	Yes	39 (47.6)	51 (61.4)	0.07
	No	43 (52.4)	32 (38.6)	
Hyperlipidemia (n, %)	Yes	11 (13.4)	9 (10.7)	0.7
	No	71 (86.6)	75 (89.3)	
Smoking (n, %)	Yes	13 (15.9)	34 (40.5)	<0.001
	No	69 (84.1)	50 (59.5)	
Opioids (n, %)	Yes	12 (14.6)	20 (23.8)	<0.001
	No	70 (85.4)	64 (76.2)	
CVD family history (n, %)	Yes	1 (1.2)	1 (1.2)	>0.9
	No	81 (98.8)	83 (98.8)	

Multivariate Logistic Regression Analysis

In the multivariate logistic regression model (Figure 1), female sex was independently associated with a lower likelihood of CSFP (OR = 0.364, 95% CI: 0.173–0.764, p = 0.008). Hypertension emerged as a significant risk factor for CSFP, with an odds ratio of 3.392 (95% CI: 1.511–7.615, p = 0.003). Similarly, smoking was a strong independent predictor of CSFP (OR = 3.583, 95% CI: 1.450–8.859, p = 0.006). Other factors, including age (p = 0.932), diabetes (p = 0.11), hyperlipidemia (p = 0.947), opioid use (p = 0.801), and family history of CVD (p = 0.785), were not significantly associated with CSFP in the adjusted model.

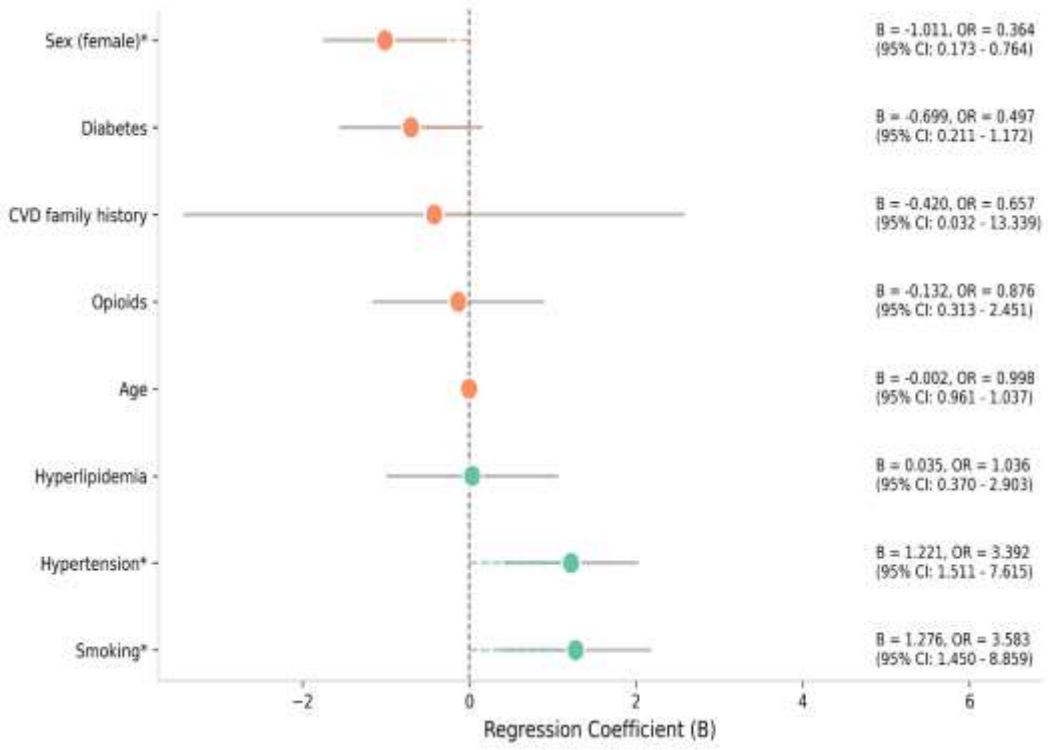

Figure1. The Lollipop plot for Multivariate logistic regression analysis. The variables with a p-value < 0.05 are marked by *.

5. Discussion

The present study showed that the prevalence of CSFP among the patients during the study period was 7.5%. Furthermore, this study revealed that male sex, smoking, opioid use, and hypertension were more prevalent among patients with CSFP. It should be noted that although opioid use was more common among patients with CSFP, it did not emerge as an independent predictor after adjustment for confounding variables. The association between hypertension and CSFP was not significant in univariate analysis but became significant after adjustment. The present study was one of the largest studies on CSFP patients in Iran (8, 9).

Although the exact pathophysiology of CSFP is not fully understood, proposed mechanisms include endothelial dysfunction, early-stage atherosclerosis, and metabolic or inflammatory disorders, which may contribute to impaired coronary microvascular function (8, 11).

This study showed a relatively high prevalence of CSFP among the studied population. Another study reported a prevalence of 1% among patients with acute coronary syndrome (4). Other studies had a prevalence of 4-5.5% (5, 10). The discrepancy between the prevalence of CSFP in different populations could be explained by the difference in the study design. Furthermore, some genetic predispositions have been shown to be responsible for a higher prevalence of CSFP in some populations (11, 12).

Several studies have assessed the risk factors associated with CSFP. Multivariate analyses showed only male sex and body mass index as independent predictors of the occurrence of CSFP (4, 6). Our findings supported the impact of male sex, while introducing other factors, including hypertension and smoking. The study by Ozen et al. also showed the importance of hypertension as a predictor of CSFP, possibly due to the systemic vascular disturbance in this condition. Ultimately, they suggested that such patients be closely followed up for risks associated with CSFP (13). Also, the study by Tanriverdi et al. supports the findings of the present study regarding the role of smoking. They concluded that the oxidative stress induced by smoking leads to decreased coronary blood flow (14).

However, the present study did not identify other cardiovascular risk factors as predictors of CSFP. It may be due to the elevated frequency of cardiovascular risk factors in our cohort, relative to prior investigations. Also, this could be explained by the fact that CSFP is a heterogeneous phenomenon, linked to several comorbidities, and that any combination of them may result in diminished flow.

Despite its large study sample, the present study had some limitations. First, the observational nature of the study limits robust conclusions. Second, studies related to opium use are challenging, given the stigma and perception of it as an illegal act. Also, it should be mentioned that a universal definition of CSFP is lacking (15).

6. Conclusion

This study found a notable prevalence of CSFP among the patients undergoing angiography, highlighting its clinical relevance and the need for further investigation into its risk factors. The observed associations with modifiable risk factors, particularly smoking and hypertension, suggest that attention to risk factor modification may be beneficial in patients with CSFP and should be considered in clinical practice.

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