Predictors of Slow Flow Phenomena without Epicardial Coronary Obstruction In Patients with Acute Coronary Syndrome

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Abstract:

Acute thrombosis on top of an atherosclerotic coronary plaque rupture is the initial cause of acute coronary syndrome (ACS), a collection of clinical symptoms. Our understanding of ACS has evolved over the past ten years due to new research. Plaque erosion and calcified nodules are now considered alternative definitions of ACS, rather than just lipid deposition. Additionally, the idea of a superimposed thrombus with necessary lethal consequences has been replaced with the idea of healed plaques and thrombus contributing to plaque progression. Complete occlusion of the coronary thrombus is often detected in ST-segment elevation myocardial infarction (STEMI); alternatively, non-occlusive coronary thrombus is seen in unstable angina or non-ST-elevation myocardial infarction (UA/NSTEMI). Thrombus on preexisting plaque, progressive mechanical obstruction, Prinzmetal's angina or coronary spasm-induced dynamic obstruction, infection or inflammation, and secondary unstable angina brought on by an imbalance in the global oxygen supply and demand of the heart. In the absence of obstructive coronary artery disease, slow coronary flow (SCF) phenomenon is a coronary microvascular disease that is identified by delayed dyeopacification in the coronary arteries during an angiography. According to reports, patients who get a diagnostic coronary angiography because they may have coronary artery disease had a 1-7% incidence of SCF.The delayed distal artery opacification that characterizes the coronary slow flow phenomenon (CSFP) on angiography is a clinical entity that occurs when there is no significant epicardial coronary stenosis. The widespread application of ECG indicators in a variety of therapeutic settings could be impacted by P-wave inscriptions.Reviewing the coronary flow phenomena in patients with acute coronary syndrome is the goal of the current investigation.

Keywords: ACS, Flow Phenomena, Epicardial Coronary Obstruction.

Introduction:

In the absence of substantial obstructive lesions, coronary slow-flow phenomenon (CSFP) is a clinical syndrome marked by delayed or sluggish blood flow through the coronary arteries. Acute myocardial infarction, sudden cardiac death, angina pectoris, and other clinical symptoms are linked to this occurrence, which is noteworthy while being extremely uncommon (1).

Finding the CSFP predictors in coronary artery patients has drawn increasing attention in recent years as a means of improving the condition's diagnosis and treatment plans. Numerous clinical, angiographic, laboratory, and demographic characteristics that may be connected to CSFP have been the subject of numerous research.

Together with pertinent references, Li et al. give a succinct summary of some of the major CSFP predictors that have been found in the literature. To determine which patients are most likely to develop CSFP, a number of predictors have been proposed. Imaging, laboratory, and clinical data are among these predictors. Age, male gender, smoking, hypertension, diabetes, and dyslipidemia are clinical predictors. Elevated levels of homocysteine, uric acid, and C-reactive protein are laboratory predictors. The degree of atherosclerosis and the existence of coronary calcification are two imaging predictors (2).

Age: Research has shown that among patients with coronary artery disease, being older is a strong predictor of CSFP. For instance, Xu et al. discovered that patients with CSFP were considerably older than those without CSFP (mean age 63.4 vs. 58.4 years) in a research involving 268 patients with suspected coronary artery disease (3).

Hypertension: Several studies have found that hypertension is a predictor of CSFP. For instance, Ji et al. found that hypertension was an independent predictor of CSFP (4) in a research involving 413 patients with acute coronary syndrome.

Diabetes mellitus: Several research have suggested that diabetes mellitus is a risk factor for CSFP. For instance, Gupta et al. discovered that patients with CSFP had a greater frequency of diabetes mellitus than those without CSFP (41.7% vs. 16.1%) in a research involving 116 patients with angiographically normal coronary arteries(5).

Inflammatory indicators: A number of research have looked into the relationship between CSFP and several markers of inflammation, including interleukin-6 (IL-6) and C-reactive protein (CRP). Ercan et al., for instance, discovered that CRP and IL-6 levels were considerably greater in individuals with CSFP than in those without CSFP in a research including 80 patients with suspected coronary artery disease. A number of other predictors of CSFP have been found in addition to conventional risk factors and microvascular dysfunction. These include the occurrence of obstructive sleep apnea, systemic lupus erythematosus (SLE), and higher levels of inflammatory markers such as high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6)(6).

Endothelial dysfunction: The pathophysiology of CSFP has also been

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linked to endothelial dysfunction, which is characterized by decreased vasodilation and elevated oxidative stress. Elawady et al. (7) found that endothelial dysfunction, as measured by flow-mediated dilation of the brachial artery, was considerably more severe in individuals with CSFP compared to those without CSFP in a study involving 54 patients. Lastly, thrombus or plaque rupture may potentially contribute to the development of CSFP. These elements may result in microvascular blockage, which would cause the coronary arteries' blood flow to be delayed or sluggish.

Being at risk for coronary artery disease (CAD) with conventional risk factors such smoking, diabetes, hypertension, and hyperlipidemia is one of the most significant predictors of CSFP. According to multiple studies, individuals with CSFP had higher rates of these risk factors than patients without the illness, indicating that these factors may contribute to the development of CSFP (8).

The existence of microvascular dysfunction, which can be determined by assessing coronary flow reserve (CFR) with a variety of methods such positron emission tomography or Doppler flow wire, is another predictor of CSFP. According to multiple investigations, patients with CSFP had lower CFRs than those without the illness, indicating that a possible contributing element to the pathophysiology of this disorder could be compromised microvascular function(9).

Female gender is one of the most reliable predictors of CSFP, as evidenced by the fact that CSFP patients are more likely to be female than controls in a number of studies, including a recent meta-analysis by Cutri et al. (10). Age, body mass index (BMI), and lower socioeconomic class (SES) are other demographic characteristics that have been linked to CSFP.

The association between CSFP and conventional cardiovascular risk factors, like smoking, diabetes, dyslipidemia, and hypertension, has also been established, albeit the exact relationship and research population will determine how strong the evidence is. Furthermore, a number of other risk factors have been suggested, including lipoprotein-associated phospholipase A2 (Lp-PLA2), serum uric acid, and homocysteine, which may be indicative of underlying inflammation and endothelial dysfunction (2).

It has been demonstrated that certain imaging results, particularly those pertaining to microvascular dysfunction, such as reduced index of microcirculatory resistance (IMR), aberrant coronary flow velocity patterns, and impaired coronary flow reserve (CFR), are highly predictive of coronary syndrome-like symptoms. CSFP has also been linked to endothelial dysfunction, as shown by brachial artery flow-mediated dilation (FMD), which may be a sign of a systemic vasculopathy affecting the peripheral and coronary vasculature (11).

Moreover, predictors of CSFP have also been found using imaging modalities as optical coherence tomography (OCT) and intravascular ultrasound (IVUS). According to IVUS research, CSFP is linked to higher remodeling index, plaque eccentricity, and plaque burden. Predictors such elevated lipid

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content, plaque rupture, and microvascular blockage have also been found in OCT studies. In a 2019 study by Wang et al. that was published in the Journal of Investigative Medicine, the scientists assessed 117 individuals with CAD and discovered that a low hemoglobin level and a high platelet-to-lymphocyte ratio were independent predictors of CSFP. Additionally, compared to patients without CSFP, the authors observed that individuals with CSFP had greater levels of fibrinogen and D-dimer, which are indicators of blood coagulation and fibrinolysis (12).

According to a study by Arbel et al., smoking is the factor that most accurately predicts the occurrence of SCF. After doing a multivariable analysis, they proposed male sex, a higher BMI, and a low HDL-c level as independent predictors of the SCF phenomenon. They also showed that male sex was the most powerful independent predictor of this phenomena. Additionally, according to their research, male sex and BMI may be indicators of the SCF phenomenon (13).

Other hypothesized causes linked to the SCF phenomenon include endothelial dysfunction, inflammation, elevated uric acid levels, circumstances related to changes in platelet characteristics, and changes in blood rheological properties. The study conducted by Akpinar et al. could not find any correlation between platelet or white blood cell counts and SCF. After examining the connection between SCF and whole blood cell counts, Akpinar et al. proposed red cell distribution width and platelet count

as separate indicators of this phenomena(14).

Uric acid levels and SCF were found to be significantly correlated by Naing et al. (15). These findings also suggested that serum uric acid levels might be used independently as a predictor of SCF.

References:

1. **Beltrame, J. F., Tavella, R., Jones, D., & Zeitz, C. (2021).** Management of ischaemia with non-obstructive coronary arteries (INOCA). BMJ, 375.

2. **Li, J., Wang, Y., Zhao, C., et al., (2020).** Incremental value of three-dimensional echocardiography for evaluating left atrial function in patients with coronary slow flow phenomenon: A case control study. Cardiovascular Ultrasound, 18(1), 1–10.

3. **Xu Y, Meng HL, Su YM, Chen C, Huang YH, Li XF, Fan MK, Yan YJ, Wu J, Jiang MH, Pan M (2015):** Serum YKL-40 is increased in patients with slow coronary flow. Coron Artery Dis; 26(2):121–5.

4. **Ji Q, Zeng Q, Huang Y, Shi Y, Lin Y, Lu Z, Meng K, Wu B, Yu K, Chai M, Liu Y. (2014):** Elevated plasma IL-37, IL-18, and IL-18BP concentrations in patients with acute coronary syndrome. Mediators of inflammation; 2014.

5. **Gupta, M. D., Akkarappatty, C., Girish, M. P., Kumar, R., Rain, M., Tyagi, S., & Pasha, M. A. Q. (2014).** Association between the Glu298Asp and 4b/4a polymorphisms of endothelial nitric oxide synthase and coronary slow flow in the North Indian population.

Coronary artery disease, 25(3), 192-197.

6. **Ercan TE, Ercan G, Severge B, Arpaozu M, Karasu G (2008):** Mycoplasma pneumoniae infection and obsessive-compulsive disease: a case report. J Child Neurol 23:338–340.

7. **Elawady, M., Moustafa, T. M., Safwat, M., & Amin, B. N. (2022).** Overview of Coronary Flow Phenomenon in Patients with Acute Coronary Syndrome. NeuroQuantology, 20(12), 2121.

8. **Ooi, E. L. (2022).** lschaemia With No Obstructive Coronary Artery Disease (INOCA): Insights Into Assessment and Obstructive Sleep Apnoea Association (Doctoral dissertation).

9. **Ding, Y. D., Pei, Y. Q., Wang, R., et al., (2020).** Increased plasma lipoproteinassociated phospholipase A2 levels are associated with coronary slow flow. Disease, 472–476. https://doi.org/10.1097/MCA.0000000000000855

10. **Cutri, N. (2011).** Clinical studies of patients with acute coronary syndromes in the absence of obstructive coronary artery disease (Doctoral dissertation).

11. **Alvarez, C., & Siu, H. (2018).** Coronary slow-flow phenomenon as an underrecognized and treatable source of chest pain: case series and literature review. *Journal of investigative medicine high impact case reports*, 6, 2324709618789194.

12. **Wang, Yong, Mou-jie Liu, Hui-min Yang, Chun-yan Ma, Peng-yu Jia, Da-lin Jia, and Ai-jie Hou. (2018):** "Association between increased serum alkaline phosphatase and the coronary slow flow phenomenon." BMC cardiovascular disorders 18, no. 1: 1-6.

13. **Arbel, Y., Rind, E., Banai, S.,et al., (2012).** Prevalence and predictors of slow flow in angiographically normal coronary arteries. Clinical Association, 9(5).

14. **Akpinar, I., Sayin, M. R., Gursoy, Y. C., et al., (2014).** Plateletcrit and red cell distribution width are independent predictors of the slow coronary flow phenomenon. Journal of Cardiology, 63(2), 112–118.

15. **Naing, Z., & Qiu, C. G. (2013).** Dawn of the most influential mechanism from the nightmare of slow coronary flow phenomenon: a randomized controlled study.

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