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Coronary Slow Flow

"An angiographic enigma that unresolved yet"

"Henüz çözülememiş bir anjiyografik gizem"

Coronary Slow Flow (CSF) is a well known phenomenon that is defined as delayed opacification of one or more major epicardial coronary arteries during diagnostic coronary angiography in the absence of obstructive coronary artery disease. In patients with chest pain undergoing diagnostic catheterization, its prevalance among 1-7%.[1] CSF was first described by Tambe et al. in 1972 in 6 subjects presenting with chest pain.[2] In addition to angina it has been associated with others forms of myocardial ischemia, including myocardial infarction and ventricular arrhythmias.[3]

Since its first description, considerable overlap exists regarding the definition of CSF. Slow coronary artery filling could be either primary "CSF phenomenon, Syndrome Y, Idiopathic" or secondary causes. A definitive diagnosis can only be made once secondary mechanisms have been rule out (Table). In clinical practice, coronary flow assesment done by semiquantitative method "the Thrombolysis in Myocardial Infarction (TIMI) flow grade" or quantitatively " the corrected TIMI Frame Count (TFC)" method.[4] A TIMI flow grade 1, or 2 is equivalent with the presence of CSF. TIMI flow grade 0 is named as no-reflow. Quantitatively, a corrected TFC measurement >27 for all coronary arteries is considered diagnostic for CSF as described previously.[1] CSF may involve one epicardial coronary artery. In this case, left anterior descending coronary artery is the most affected vessel. But, multivessel involvement represent a more severe, diffuse disease, and perhaps could portend worse prognosis.[5]

Primary CSF	Secondary causes of CSF
Acronyms "Syndrome Y" or "Idiopathic" Normal or near-normal coronary arteries disease	Post Balloon or stent dilatation during PCI Significant obstructive coronary artery Ectatic coronary arteries Ostial significant coronary stenosis Coronary spasm Embolism Spontaneous dissection Heart Failure Valvular disease Connective tissue disorders Hematology disorders Arrhythmias (AF,VT,VF) Hypotension

Abbreviations: CSF, coronary slow flow; PCI, percutaneous coronary intervention; AF, atrial fibrillation; VT, ventricular tachycardia; VF, ventricular fibrillation

Several studies have investigated the clinical features of individuals with CSF. Distinct from Syndrome X, which is more common in women, CSF is more common in men, current smokers, obese and young patients.[1,5,6] Furthermore, Syndrome X is characterized by exercise angina, positive stress test and normal coronary arteries. But CSF patients tend to be recurrent rest or mixed pattern angina and many patients with CSF undergo their index diagnostic angiography following an acute coronary syndrome presentation and electrocardiographic changes. The reported mortality of patients with CSF is approximately <1%.[1] Eventually, recurrent angina of CSF patients lead to frequent hospital readmissions and poor quality of life.

The pathophysiologic mechanisms underlying CSF are still not well understood. Many authors state that CSF is a specific entity that should be considered as a clinical syndrome

EDITORIAL COMMENT
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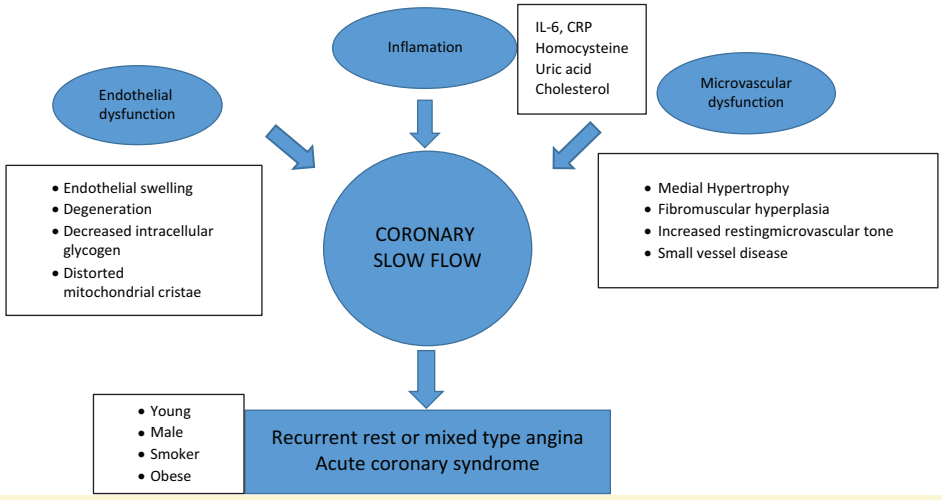

Figure 1. Adapted from Chalikias G, Tziakas D. Slow Coronary Flow: Pathophysiology, Clinical Implications, and Therapeutic Management. Angiology. 2021; 72(9): 808-818. Abbreviations. IL-6, interleukin-6. CRP, C-Reactive Protein.

rather than an only angiographic phenomenon.[5,6] There also still remain multiple questions regarding whether this pathology is limited to coronary arteries or is a manifestation of systemic vascular or endothelial disease. There are several hypotheses and theories about the mechanism for CSF (Figure). Endothelial dysfunction, increased vasomotor tone, small vessel disease, inflammatory phenomena and widespread atherosclerosis are some of the these therories.[1,6,7] Epicardial major coronary arteries in these patients are normal, but coronary arteries (conductance vessels) to regulate antegrade normal blood flow in order to adapt to increased myocardial oxygen demand are reduced. Reduced antegrad flow, endothelial dysfunction and increased microvascular resistance results myocardial ischemia; which in turn may lead to systolic and diastolic dysfunction. Its known that both systolic and diastolic functions are impaired in patients with CSF by tissue Doppler imaging.[1,6] In their study, Gulel et al. found that left ventricular deformation parameters affected by coronary slow phenomenon compared with normal subjects.[8]

Unfortunately, currently available anti-anginal agents are of limited clinical value in CSF patients. To date, no randomized controlled trial testing specific agents for patients with CSF has been conducted. Dipyridamole, nicardipine and nebivolol have some beneficial effects on CSF but nitroglycerine did not. Regarding management of CSF in the acute setting when associated with cardiopulmonary arrest, intracoronary use of adenosine or atropine appears a possible way for quick reversal of CSF.[1]

Its well known that diastolic filling and diastole duration are the main determinants of coronary blood flow. Any changes affecting these processes such as tachycardia or left ventricular hypertrophy can also change coronary flow dynamics and may result CSF. For instance; TIMI frame count is significantly higher in patients with coronary artery disease and rapid atrial fibrillation that diastolic filling period is reduced. Left ventricular diastolic function can easily and simlpy evaluate by echocardiographic method. For this purpose, Reddy et al. in 2018, proposed H_2FPEF-score, which consist of clinical and echocardiographic parameters.[9] H_2FPEF-score has a value between 0 and 9, and body mass index (BMI)>30 kg/m^2, ≥2 antihypertensive medicines, paroxysmal or persistent AF, age >60 years, and Doppler echocardiography data at rest (sPAP >35 mmHg, tissue Doppler E/é >9) are the components. Points were assigned to these 6 variables as follows; AF, 3 points; BMI, 2 points; others 1 point as described by Reddy et al.[9]

In the current issue of the journal, Türkoğlu et al. emphasized that possible relation of CSF with H_2FPEF-score.[10] They might have captured a novel and practically feasible tool to better comprehend the association of ventricular diastolic dysfunction with coronary blood flow. To the our knowledge, this is first study to investigate the association between diastolic function score index "H_2FPEF score" with CSF. In the recent study, on multivariate logistic regression analysis, male gender, current smoking, high total cholesterol level and high H_2FPEF-score (≥2) were found to be the independent predictors of CSF. They concluded that patients with high scores should be followed closely during coronary angiography for the development of CSF. But, due to retrospective nature of their study and low patient volume; large-scale, prospective, randomized controlled trials are needed to define the exact mechanisms of these relationships.

In conclusion, CSF is an important angiographic finding typically observed in patients presenting with acute coronary syndrome. This phenomenon should be considered a separate clinical entity with diverse pathogenic mechanisms and diagnostic criteria. Our current knowledge is incomplete, but further experimental investigations are nedeed to reveal the pathogenesis, diagnosis and treatment involved in CSF.

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