Left Ventricular Diastolic Function and Its Value in Patients with Coronary Slow Flow

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ABSTRACT

Background: Coronary slow flow (CSF) phenomenon is one of the most confusing entities of the Coronary artery disease CAD. CSF was first described as a delayed opacification of the coronary artery in the absence of significant lesion. Left ventricular (LV) functions may give insight about this important entity in patients with stable CAD. **Objectives:** Assessment of the importance of LV diastolic function in prediction of CSF phenomenon among patients with stable CAD and preserved systolic function. **Patients & methods:** The study was conducted on patients with stable CAD who are indicated for undergoing coronary angiography with exclusion of the patients with any of the following: atrial fibrillation, CABG or acute coronary syndromes. Study populations were divided according to the presence of CSF as follows: patients with CSF phenomenon (case group) and patients with normal coronary angiography (control group) . **Results :** There was significant difference between slow flow and control group regarding diastolic function. LV diastolic function was normal in 74% in control group while it was impaired in more than 95% CSF group (P<0.001). Most of patients with CSF (65.4%) had GII or III diastolic dysfunction. The grade of LV diastolic dysfunction can predict the presence of CSF in patients with stable CAD and preserved LV systolic function (74.07% specific and 95.06% sensitive). **Conclusion:** LV diastolic function assessed by conventional transthoracic echocardiography in patients with stable coronary artery disease and preserved systolic function can predict the presence of CSF in those patients.

KEYWORDS: Coronary artery disease; Coronary Slow flow; Coronary angiography; Diastolic function; Diastolic dysfunction.

DOI: 10.48047/ecb/2023.12.8.722

INTRODUCTION :

Delayed opacification of the coronaries without stenosis when contrast media is used is a characteristic of CSF. This can be identified as either an angiographic finding "phenomena" or a "syndrome" if it is accompanied by ischemic symptoms. (1). CSF commonly affects male patients and shares similar risk factors to those associated with ischemic heart diseases, including hypertension, diabetes mellitus, dyslipidemia, and smoking (2,3).

CSF can be attributed to various underlying mechanisms, including microvascular dysfunction primarily associated with endothelial dysfunction, subclinical atherosclerosis, and inflammation (2,4,5,6). The diagnostic criteria for CSF encompass a TIMI flow grade 2 or a corrected TIMI frame count exceeding 27 frames (acquired at a rate of 30 frames per second), accompanied by the absence of any significant coronary stenosis (40% or more). These criteria are deemed sufficient for diagnosing CSF in at least one epicardial vessel (7). The ischemic cascade model has shown that patients with chronic ischemia may undergo minor myocardial changes that may be clinically insignificant and difficult to detect. When patients are suspected to have early affection, changes in left ventricular relaxation pressures and volumes may occur, leading to diastolic dysfunction (8).

This study aimed to assess the value of LV diastolic function in the prediction of CSF in patients with stable coronary artery disease.

Patients & methods

Our study focuses on patients who have suspected or established diagnoses of stable coronary artery disease and are recommended for invasive coronary angiography in accordance with the latest ESC guidelines on chronic coronary syndrome (9). Specifically, we include patients in the following scenarios: when non-invasive tests yield inconclusive results or suggest a high risk of events, for evaluating options regarding revascularization; patients with certain professions (e.g., pilots) with regulatory requirements; patients unresponsive to medical therapy or experiencing anginal pain at a low level of exercise; and cases where the initial clinical evaluation indicates a high risk of events.

In order to keep the study consistent, we excluded patients who have a history of atrial fibrillation, coronary artery bypass grafting (CABG), or acute coronary syndrome (ACS).

All patients were subjected to the following:

1. Request to sign a consent form .
2. Medical history and Full clinical examination.
3. Resting electrocardiogramy (ECG).
4. Conventional Transthoracic echocardiography (TTE):

To evaluate diastolic function, we performed resting transthoracic echocardiographic studies using echocardiographic instruments (Vivid S5, Vivid S6, GE Medical Systems), following the recommendations of the American Society of Echocardiography (10). We employed various parameters, including the pulsed wave Doppler (PWD) of the mitral inflow, tissue Doppler imaging (TDI) of the mitral annulus, tricuspid regurgitation (TR) flow velocity (apical four-chamber view), and left atrial (LA) volume index (apical four-chamber view and apical two-chamber view) (11).

For patients with normal left ventricular (LV) systolic function, the following echocardiographic parameters were utilized: average E/e'>14, septal e' velocity <7 cm/s, or lateral e' velocity <10 cm/s, TR velocity >2.8 m/s, and LA volume index >34 ml/m2. Diastolic function is considered normal if less than 50% of these data points are positive, while diastolic dysfunction is indicated if less than 50% are positive. Indeterminate diastolic function is observed when exactly 50% of the data points are positive.

The PWD assessment of mitral inflow, including the estimation of E and A waves, is used to classify diastolic dysfunction if present. Grade I diastolic dysfunction is defined as E/A ≤ 0.8, provided that E ≤ 50 cm/s. Grade III diastolic dysfunction is considered if E/A ≥ 2. If E/A ≤ 0.8 but E is >50 cm/s or E/A > 0.8 but <2, further assessment is required using three criteria: average E/e' >14, TR velocity >2.8 m/s, and LA volume index >34 ml/m2.

If two or three of these criteria are present, grade II diastolic dysfunction is diagnosed. If two or three of these criteria are absent, grade I diastolic dysfunction is diagnosed. If only one of two criteria is positive and only two criteria are available for assessment, the grade of diastolic dysfunction is considered.

5- During the invasive coronary angiography: we calculated the TIMI frame count (TFC) for each artery, which is a standard part of the angiographic procedure for every patient. If a patient's TFC exceeded 2 standard deviations from the normal published range for any of the three coronary arteries, or if their TFC was greater than 27 frames (m TFC), they were classified as having coronary slow flow (CSF). **(12).**

Statistical Analysis:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0**. (**Armonk, NY: IBM Corp**).** Significance of the obtained results was judged at the 5% level. The used tests were Chi-square test, Fisher's exact correction, Student t-test, Mann Whitney test. Receiver operating characteristic curve (ROC), Spearman coefficient, and Kruskal Wallis test.

RESULTS:

Patients diagnosed with coronary slow flow (CSF) were identified using the diagnostic criteria proposed by Beltrame during invasive coronary angiography. One-hundred-sixty-two patients were recruited. The study population was then divided into two groups based on the presence of CSF, as per the aforementioned criteria.

Both groups were comparable in terms of age and sex. However, a significant difference was observed between the two groups regarding risk factors. The CSF group exhibited a higher prevalence of hypertension, diabetes mellitus, smoking, dyslipidemia, and a prior history of myocardial infarction **(Table 1)**.

Left ventricular systolic function was assessed by estimating the ejection fraction (EF) of the LV. The CSF group had a mean estimated EF of 50.79% ± 6.49%, whereas the control group had a mean EF of 59.41% ± 4.51%, indicating a significant difference (P<0.001) **(Table 2)**. Most patients in both groups had normal or preserved LV systolic function.

Table (1): Comparison between the two studied groups according to risk factors and medical history

	Slow flow (n = 81)		Control (n = 81)		χ^2	p
	No.	%	No.	%		
Smoking	57	70.4	21	25.9	32.044*	<0.001*
Hypertension	79	97.5	28	34.6	71.599*	<0.001*
Diabetes	57	70.4	26	32.1	23.743*	<0.001*
History of stroke	2	2.5	0	0.0	2.025	FEp=0.497
History of MI	66	81.5	25	30.9	42.149*	<0.001*
CHF	47	58.0	4	4.9	52.913*	<0.001*
Dyslipidemia	68	84.0	42	51.9	19.145*	<0.001*

χ^2: Chi square test, p: p value for comparing between the studied groups, *: Statistically significant at p ≤ 0.05

Table (2): Comparison between the two studied groups according to EF %.

EF %	Slow flow (n = 81)	Control (n = 81)	U	p
Min. – Max.	36.0 – 61.0	38.0 – 69.0	790.50*	<0.001*
Mean ± SD.	50.79 ± 6.49	59.41 ± 4.51		
Median (IQR)	49.0 (46.0 – 57.0)	59.0 (59.0 – 62.0)		

IQR: Inter quartile range SD: Standard deviation U: Mann Whitney test
p: p value for comparing between the studied groups *: Statistically significant at p ≤ 0.05

Diastolic function impairment was categorized into three grades based on echocardiographic variables. Left ventricular diastolic dysfunction was more prevalent in patients with CSF. The CSF group exhibited significantly greater impairment in diastolic function compared to the control group (P<0.001). While 74% of the control group had normal LV diastolic function, over 95% of patients with CSF had varying grades of impaired function, with the majority falling into Grade II or III dysfunction **(Table 3)**.

The receiver operating characteristic (ROC) curve was utilized to assess LV diastolic dysfunction as a predictor of CSF in patients with stable coronary artery disease. The curve demonstrated a specificity of 74.07% and a sensitivity of 95.06% **(Table 4)**.

Table (3): Comparison between the two studied groups according to diastolic function.

Diastolic function	Slow flow	Control	χ^2	p

	(n = 81)		(n = 81)			
	No.	**%**	**No.**	**%**		
Normal	4	4.9	60	74.1	92.428*	<0.001*
Grade I diastolic dysfunction	24	29.6	17	21.0		
Grade II diastolic dysfunction	22	27.2	1	1.2		
Grade III diastolic dysfunction	31	38.3	3	3.7		

χ^2: Chi square test FE: Fisher Exact p: p value for comparing between the studied groups
****: Statistically significant at p ≤ 0.05***

Table (4): Validity (AUC, sensitivity, specificity) for diastolic function to discriminate Slow flow (n = 81) from control (n = 81)

	AUC	p	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
Diastolic function	0.904	<0.001*	0.855 – 0.953	>0	95.06	74.07	78.6	93.7

AUC: Area Under a Curve p value: Probability value CI: Confidence Intervals NPV: Negative predictive value PPV: Positive predictive value *: Statistically significant at p ≤ 0.05, **cut off value >0 , where 0 represents normal diastolic function

DISCUSSION:

The mechanism ands presentation of coronary slow flow (CSF) are still unclear, despite the definition is clear. Our study aimed to gather more information about CSF and find a non-invasive parameter that could predict it. We found that LV diastolic function is a strong predictor for CSF in patients with stable coronary artery disease who are eligible for coronary angiography.

LV diastolic function reflects the filling of the left ventricle during diastole, which is dependent on the pressures of the LV and the pressure gradient between the LV and left atrium (LA). Impaired LV diastolic function is an indication of impaired LV relaxation due to LV stiffness, even with normal LV systolic function. Many 2D and Doppler variables are used to assess LV diastolic function (11).

Several studies have observed that LV diastolic function is altered in CSF. The impaired diastolic function reflects the severity of myocardial ischemia in these patients. Therefore, LV diastolic function may play a role in further understanding the pathogenesis of CSF and serve as a prognostic factor, especially in patients with normal LV systolic function (13). Based on our study findings, it was determined that LV diastolic function can be used as a non-invasive tool for predicting CSF in individuals with stable coronary artery disease.

Our research has identified that patients with CSF exhibit impaired diastolic function with varying degrees, even when their LV systolic function is preserved or normal. Sevimli et al., Sezgin et al., and Altunkas et al. have also come to the same conclusion in their own studies. (14, 15, 16). Tanriverdi et al showed that patients with CSF have impaired LV diastolic function, which they attributed to decreased aortic elasticity. (17). However, Baykan et al. failed to prove a difference in diastolic function among patients with CSF and other patients using conventional methods, but diastolic dysfunction was observed in these patients using tissue Doppler echocardiography (18).

However, various studies have yielded conflicting results or have not been able to conclusively identify any distinct impairment in diastolic function in individuals with CSF. Although our study did reveal a marked difference in systolic function between the CSF and control groups, with the CSF group exhibiting a lower ejection fraction (EF), all patients with CSF still maintained a preserved EF. Additionally, Wang et al. found evidence of impaired diastolic and systolic functions in patients with CSF (19), which is in agreement with the results of another study by Suner et al. (20). A case-control study by Seyyed-Mohammadzad et al. demonstrated that patients with CSF tend to exhibit LV systolic dysfunction (21). They added that there is no difference in diastolic function between CSF patients and the control group. Fallah et al. concluded that diastolic function is normal in CSF patients, but there might be a subtle increase in LV filling pressures (22).

The different results regarding diastolic dysfunction in CSF patients across studies may be attributed to the stage at which diastolic function was assessed in the different studies. Diastolic function has been found to improve over time in patients with CSF presenting with non-ST-segment elevation myocardial infarction (NSTEMI) (23).

CONCLUSION:

Conventional transthoracic echocardiography can assess LV diastolic function in patients with suspected or established stable coronary artery disease, and predict the presence of CSF in such patients.

There is no conflict of interest.
The authors received no funding concerning this manuscript.

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