Left ventricular function in patients with coronary slow flow

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Abstract: Background: The coronary slow flow (SCF) phenomenon has direct clinical implications, as it has been linked to clinical manifestations of myocardial ischemia, life-threatening arrhythmias, sudden cardiac death and recurrent acute coronary syndromes. Several hypothesis of its mechanism including a form of early phase of atherosclerosis, microvessel dysfunction, imbalance between vasoconstrictor and vasodilatory factors and platelet function disorder were proposed. How and to what extent do these etiological factors affect left ventricular (LV) function. **Aim**: To evaluate LV systolic and diastolic function in SCF patients. **Material and methods**: 100 patients with angiographically diagnosed CSFP but with otherwise normal epicardial coronary arteries and 50 subjects with angiographically normal coronary arteries constituted the control group were included in the study. All the subjects underwent echocardiography and tissue Doppler imaging to determine left ventricular systolic and diastolic functions. **Results**: As regard systolic function measured by modified Simpson's method, ejection fraction was similar in both the SCF and control groups (*62.2 ± 5.1* vs *64.4 ± 4.6*, p=<0.22. As regard diasystolic function, Conventional echocardiography showed significantly lower maximal velocity of early diastolic filling (E) and ratio of maximal early to late diastolic filling (E/A) (in the patient group(54.6 ±6.9 cm/s vs 74.5 ± 12.5 cm/s, p<0.001 and 1.1±0.25 vs 1.44±0.17, p<0.001 respectively). Maximal velocity of atrial diastolic filling (A) and deceleration time of early diastolic filling (DT) were similar. Among tissue Doppler parameters, E' was significantly lower in the patient group(8.6 ± 1.6 cm/s vs 14.9 ± 2.8 cm/s, p < 0.001), E/e' was significantly higher in the patient group (6.4 ± 0.78 vs 5.03 ± 0.83, p < 0.001). **Conclusion**: Coronary slow flow phenomenon is associated with left ventricular diastolic dysfunction, requiring a close follow-up in this patient group.

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1. Introduction

In some patients with chest pain who are scheduled for selective coronary angiography, slow contrast agent passage is observed through the epicardial coronary arteries in the absence of stenosis. This phenomenon has been designated the slow coronary flow (SCF) phenomenon **(Yilmaz et al, 2010).** Slow coronary flow (SCF) phenomenon is an angiographic finding characterized by delayed opacification of the distal vasculature despite the presence of angiographically normal or near normal coronary arteries. Several follow-up studies revealed that most of the patients with SCF experience recurrent chest pain requiring readmission for acute exacerbations. Moreover, they also demonstrate electrocardiographic and/or scintigraphic evidence of ischemia**. (Beltrame et al, 2013).** The exact etiology and pathogenesis of SCF is still unknown. Functional and morphological abnormalities in the microvasculature, endothelial dysfunction, raised inflammatory markers, occult atherosclerosis, and anatomical factors of epicardial arteries have all been implicated in the pathogenesis of CSF. Based on these findings, it is hypothesized that SCF may be a form of at least an early phase of atherosclerosis that involves both small vessels and epicardial coronary arteries **(Cin et al, 2003)**. Also coronary flow reserve is impaired in patients with SCF **(Erdogan et al, 2007).** The effect and reflection of microvascular and endothelial dysfunction in SCF patients on left ventricular (LV) systolic and diastolic functions are still not well clarified (***Baykan et al, 2009).*** Myocardial velocity determined by tissue Doppler imaging is a new technique that has been used recently to analyze left ventricular function. The development of tissue Doppler imaging opens up the possibility of also assessing left ventricular function **(*Yolande, 2010*)**. The Thrombolysis in Myocardial Infarction TIMI frame count (TFC) method is an objective method for evaluating coronary blood flow. This

method measures the number of frames over which the contrast flows from the injection site to a predefined distal point. Previous studies showed that in arteries with slow flow, TFC is significantly increased **(*Gibson and Zorkun, 2005*).**

2. Material and methods

100 consecutive patients with CSF who had undergone diagnostic Coronary Angiography (CA) during the period from May 2015 to May 2016 in the National Heart Institute. The control group consisted of 50 consecutive patients with normal coronary arteries who had undergone CA during the same period. Indications of CA were determined with positive results of myocardial ischemia in noninvasive tests and typical angina pectoris. All patients were assessed for demographic features, cardiovascular risk factors, laboratory parameters, and medications. The local ethics committee approved the study protocol and written informed consent was obtained. The exclusion criteria were as follows: previous history of myocardial infarction, congestive heart failure, coronary ectasia, patients with valvular heart disease, prosthetic valves, pulmonary, hepatic, renal disease, malignancy, diabetes mellitus, hypertension, left bundle branch block, and a rhythm other than sinus.

Coronary angiography and analysis of TIMI frame count:

All the images were evaluated by an experienced cardiologist. Coronary angiography was performed by the femoral approach using the standard Judkins technique. Coronary arteries on the left and right oblique planes, and cranial and caudal angles were demonstrated. The diagnosis of coronary slow flow was made using the TIMI frame count (TFC) method. The cutoff values for TFC were taken (for LAD: 36.2±2.6; for Cx: 22.2±4.1; for RCA: 20.4±3.0). Any TFC above these levels was considered coronary slow flow ***(Gibson and Zorkun, 2005)***.

Echocardiography:

The examination was performed at rest using echo machines (Siemens/Acuson SC2000, GE/vivde 7 and Philips) using a 3 MHz transducer was performed within 24 hours after discharge from catheterization laboratory. Echocardiographic images were obtained in the left lateral position. and performed according to the guidelines of the American Society of Echocardiography 2016 **(Nagueh et al., 2016)**. Two-dimensional echocardiography and the modified Simpson's rule were used to determine ejection fraction (EF), left ventricular end-diastolic and end-systolic diameters. The following parameters were calculated: maximal velocity of early diastolic filling (E), deceleration time (DT) of (E), maximal velocity of atrial diastolic filling (A), the ratio of maximal early to late diastolic filling (E/A). Tissue Doppler imaging was performed using the same echocardiographic unit with the tissue Doppler mode of the device. In the apical four-chamber view, early diastolic (e') was measured from the lateral corner of the mitral annulus, then the ratio of E/e' was calculated.

3. Results

The study included 150 patients with chronic stable angina; they are classified into two groups: Patients with primary coronary slow flow (PCSF) group = 100 patients, patients with normal coronary flow (Control) group = 50 patients.

Table (5): Demographic data and risk factors:.

	PCSF group No = 100	Control group No = 50	P value
Age			
Mean ± SD	54.4 ± 6.97	52.8 ± 7.4	0.38
Gender:			
Male	67 (67%)	38 (76%)	0.257
femal	33(33%)	12(24%)	
Family history of CAD	29 (29%)	12 (24%)	0. 517
DM	100(100%)	50(50%)	……
Hypertension	38 (38%)	23 (46%)	0.347
Smoking	72(72%)	18 (40%)	< 0.001
Dyslipidemia	56 (56%)	13 (26%)	0.001
Prior CAD	0 (0%)	0 (0%)	----

CAD: Coronary artery diseases; DM: Diabetes Mellitus

Conventional echocardiographic data:

Table (6): parameters of the LV volume and EF in both groups.

	CSFP n=100	**control n=50**	**p value**
LVESD (cm	3.26±0.59	3.14±0.53	0.64
LVEDD (cm)	5.15±0.5	5.02±0.52	0.3
EF (modified Simpson) (%)	62.2±5.1	64.4±4.6	0.22
LVEDV (mL/m2)	101.7±30.2	100.2±26.2	0.84
LVESV (mL/m2)	45.7±16.2	42.2±13.2	0.39

Table (7): Pulsed wave Doppler data in both groups.

	CSFP n=100	control n=50	p value
E wave (cm)	54.5 ± 6.9	74.5 ±12.5	<0.001
A wave (cm)	50.5 ±10.3	51.6± 9.0	0.318
E/A	1.1± 0.25	1.44±0.17	<0.001
DT(msec)	216.3 ± 42.9	220±21.	0.72
IVRT	100.2 ±14.2	92.6±16.4	0.19

Table (8): Tissue Doppler data in both groups.

	CSFP n=100	control n=50	p value
e' (cm/s)	8.6 ± 1.67	14.9 ± 2.78	<0.001
E/e'	6.4 ± 0.78	5.03 ± 0.83	<0.001

4. Discussion

In our study, there was no statistical difference between the two groups regarding the gender and the age, This was in agreement with ***(Ari et al, 2010)*** where they found patients with PCSF were more males, this might be contributed to the nature of the population studied with certain differences between the Japanese people and the Egyptians. Regarding smoking, in our study PCSF phenomenon was more common in smoker with highly statistically significant difference, this was in agreement with **(*Beltrame J et al, 2013)*** and disagrees with ***(Gunes et al, 2009)*** this might be because all of those studies were conducted in Turkey which previously was a country with the highest smoking rates in the world till 2009 ***(McGongal, 2009)*** and marked increase in smoking rates in Egypt in last years ***(Yolande, 2010)*** according to Egypt Global Adult Tobacco Survey that was conducted in 2012.

Echocardiographic Data of both groups:

In our study, diastolic functions of the left ventricle were significantly impaired in patients with coronary slow flow compared to the control group. Although no statistical differences with respect to systolic functions. In addition,. A large number of studies have demonstrated that CSFP is associated with myocardial ischemia, the earliest indicator of it is LV relaxation disorder, a parameter of diastolic function (***Yılmaz et al, 2013).***

Regarding diastolic functions, in our study there was statistically significant difference between the control and PCSF groups detected by conventional PW Doppler echocardiography. This was in agreement with **(Tanriverdi et al, 2010).** Despite these studies, **(Nurkalem et al, 2009**) found no LV relaxation disorder in SCF patients using conventional PW Doppler echocardiography also, this might be because conventional Doppler is affected by preload and heart rate (**Ozdemir et al, 2007).**

Unlike this, myocardial velocities obtained using tissue Doppler echocardiography (TDE) are considered to be new parameters to evaluate LV functions not affected by change in load and heart rate and thus yield more accurate results **(Ozdemir et al, 2003).**

In the present study, there is significant difference in left ventricular diastolic parameters in both groups using TDE. The E/e' values were significantly higher in the CSF group. This is in agreement with **(*Wang et al,2015)*** who used both conventional and TDE methods to evaluate the diastolic function of SCF patients. The conventional method showed non significant difference between diastolic functions of the two groups; however, using the TDE method revealed that, e' velocity, of SCF patients was significantly lower than in the control group and E/e' ratio was higher in the SCF patients.

Regarding systolic function, our study used conventional echocardiography and showed no differences between both groups.

This agree with a lare number of studies like ***(Yılmaz et al, 2013)*** when they used conventional

echocardiography for assessement of systolic function of the left ventrlicle.

When used more sensitive methods for for assessement of systolic function of the left ventrlicle as myocardial performance index, the mitral annular systolic velocity using TDE ***(Yılmaz et al, 2013)*** and 2-D speckle tracking echocardiography ***(Wang et al, 2015*)** showed in addition to affection diastolic function there is also impairement of systolic function of the left ventricle in the SCF patients.

Conclusion

Coronary slow flow phenomenon is associated with left ventricular diastolic dysfunction, requiring a close follow-up.

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