

## Left & Right Ventricular Myocardial Performance Index and it's Relation with TIMI Frame Count in the Coronary Slow Flow Phenomenon

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Received date: January 25, 2016; Accepted date: February 25, 2016; Published date: March 10, 2016

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### Abstract

**Aim:** To investigate the left and right ventricular myocardial performance index in patients with coronary slow flow phenomenon and to determine the relationship between it and thrombolysis in myocardial infarction frame count in SCF patients

**Material and methods:** 45 patients with slow coronary flow; mean age  $51 \pm 12$  years and 20 subjects with angiographically normal coronary; mean age  $52 \pm 12$  years, were included in the study. All the subjects underwent echocardiography and tissue Doppler imaging to determine left & right ventricular diastolic functions and myocardial performance index (MPI).

**Results:** The TDE parameters obtained from the left and right ventricles showed. LV Sm, and Am, was similar in both the SCF and control groups; however, LV Em, Em/Am, IRT and MPI were significantly different in the SCF group compared to the control. RV wall Sm, and Am were similar in both the SCF and control groups however, RV Em, Em/Am, IRT and MPI were significantly different in the SCF group compared to the control. Patients had significantly higher TFC for each major epicardial coronary artery ( $P < 0.001$ ). TFC was positively correlated with the left ventricle MPI index ( $r = 0.61$ ,  $p < 0.001$ ), the right ventricle MPI index ( $r = 0.49$ ,  $p < 0.001$ ), and mitral IVRT ( $r = 0.61$ ,  $p < 0.001$ ). There was a strong inverse correlation between mean TFC and left ventricle Ea and Ea/Aa ratio ( $r = -0.70$ ,  $p < 0.001$ ;  $r = -0.45$ ,  $p = 0.001$ , respectively).

**Conclusion:** Left and right ventricular diastolic functions deteriorated in the CSF phenomenon and this deterioration was associated with increased TIMI frame count.

**Keywords:** Myocardial performance index; Coronary slow flow; TIMI frame count

### 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 [1]. 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 [2]. 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 [3,4]. Left ventricular systolic and diastolic dysfunctions have been reported in the CSF phenomenon but no study in the literature has evaluated right ventricular function in patients with CSF [5-8] 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 [9]. Previous studies showed that in arteries with slow flow, TFC is significantly increased [10-12]. The aim of the

present study was to investigate left and right ventricular functions using conventional and tissue Doppler echocardiography in patients with CSF and to determine the relationship between them and TFC.

### Patients and Methods

45 consecutive patients with CSF who had undergone diagnostic Coronary Angiography (CA) between January 2010 and January 2014 in El Minia university hospital. The control group consisted of 20 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

All patients underwent coronary angiography by the femoral approach using the standard Judkins technique in all subjects. All the cineangiograms were evaluated by an experienced cardiologist.

The diagnosis of SCF was made using the TFC method. CSF was identified using the thrombolysis in myocardial infarction (TIMI) frame count (TFC) method [4]. In brief, the first frame was accepted when there was more than 70% lumen opacification with antegrade filling. When contrast dye reached distal landmarks, the final frame was determined. The distal landmarks were the distal bifurcation of the left anterior descending artery (LAD), the distal bifurcation of the segment with the longest total distance in the left circumflex artery (LCX) and in the right coronary artery, and the first branch of the posterolateral artery. The LAD is the longest artery among the major coronary arteries. In order to obtain corrected TFC, LAD frame counts were divided by 1.7 as previously reported [13]. LAD and LCx arteries' TIMI frame counts were evaluated in the right anterior oblique projection with caudal angulation. For the right coronary artery, left anterior oblique projection with cranial angulation was used. The mean TFC was calculated for the LAD, Cx and RCA. Gibson et al. reported cutoff values for TFC (for LAD:  $36.2 \pm 2.6$ ; for Cx:  $22.2 \pm 4.1$ ; for RCA:  $20.4 \pm 3.0$ ) [13]. Any TFC values above these levels were considered CSF.

## Echocardiography

Conventional and TDE were performed for all patients using a Vivid 3 Ultrasound machine, in the left decubitus position according to the recommendations of the American Society of Echocardiography [14]. LV diameter and thicknesses were measured from the parasternal window with two-dimensional M-mode echocardiography. LV ejection fraction was measured by the modified biplane Simpson's method [15]. Doppler recordings were obtained with the pulsed sample volume placed at the tip of the mitral leaflets from the apical 4-chamber view. Peak early and late velocities, E-wave deceleration time and isovolumetric relaxation time (IRT) were measured. TDE with active TDE functions. Peak systolic myocardial velocity (Sm), peak early myocardial velocity (Em), and late myocardial velocity (Am) were measured for the lateral segment and the Em/Am ratio was calculated. The IRT was measured from the end of Sm to the beginning of Em, the isovolumetric contraction time was measured from the end of Am to the beginning of Sm, and the time period of Sm was measured as the ejection time. The MPI was calculated using the equation (isovolumetric contraction time + IRT)/ejection time [16]. The Sm, Em, and Am values obtained from the tricuspid annulus were used for the RV MPI.

## Statistical analysis

SPSS version 21 was used for the statistical analysis. All the data were expressed as mean  $\pm$  standard deviation. Categorical variables were compared via chi-square test. Normally distributed variables were compared across groups by means of Student's t test, whereas variables that were not normally distributed were compared by Mann-Whitney U test. Pearson's correlation analysis was used to evaluate relations between the variables. A P value of  $< 0.05$  was considered significant.

## Results

The clinical characteristics of 45 coronary slow flow patients and 21 normal coronary angiography individuals are presented (Table 1).

Variables	Patients	Control	P
Age (years)	56.1 $\pm$ 9.1	53.9 $\pm$ 7.9	0.34
Sex (male/female)	25/20	8-Dec	0.33
Body mass index (kg/m)	26.1 $\pm$ 1.5	25.7 $\pm$ 1.6	0.38
Family history	5	3	0.45
Smoking	15	7	0.36
Diabetes Mellitus	14	6	0.26
Dislipidemia	19	7	0.35
Systolic blood pressure	136 $\pm$ 7	140 $\pm$ 8	0.62
Diastolic blood pressure	79 $\pm$ 16	82 $\pm$ 5	0.37
Glucose (mg/dl)	91.8 $\pm$ 7	90 $\pm$ 7.6	0.49
Serum creatinine (mg/dl)	0.99 $\pm$ 0.08	0.99 $\pm$ 0.11	0.94
Hemoglobin (g/dl)	13.1 $\pm$ 0.6	12.9 $\pm$ 0.6	0.25
Total cholesterol (mg/dl)	172.8 $\pm$ 26.6	174.4 $\pm$ 27	0.83
Triglycerides (mg/dl)	165.7 $\pm$ 25	169.3 $\pm$ 20	0.58
High density lipoprotein (mg/dl)	31.5 $\pm$ 5.5	30 $\pm$ 2.2	0.25
Low density lipoprotein (mg/dl)	133 $\pm$ 29	126 $\pm$ 30	0.14
One vessel with CSF	9 (20%)	0 (0)	0.001
One vessel with CSF	16 (35.5%)	0 (0)	0.001
One vessel with CSF	20 (44.4%)	0 (0)	0.001

**Table 1:** Demographic and clinical data of both groups.

Age, sex, body mass index, diabetes mellitus, dyslipidemia, family history, and smoking status did not differ between the CSF patients and the control group. Also, there were no significant differences as regards laboratory data (Table 1) as regards conventional echocardiography parameters, there were no significant difference of LA, LVEDD, LVESD, PW, IVS, EF, and A velocity between the two groups, but the mitral E velocity, E/A ratio were higher in the control than the patients ( $p = 0.01$ ) and deceleration time of early diastolic filling was significantly higher ( $p = 0.01$ ) in the patient group (Table 2).

Variables	Patients	Controls	P
LA diameter (mm)	33.5 $\pm$ 16	33.92.1	0.52
LVEDD (mm)	47.6 $\pm$ 8.4	46.2 $\pm$ 5	0.51
LVESD (mm)	28.7 $\pm$ 1.2	30 $\pm$ 2	0.74
IVS (mm)	9.1 $\pm$ 0.4	9.2 $\pm$ 0.6	0.5
PW (mm)	8.6 $\pm$ 0.73	8.8 $\pm$ 0.41	0.45

<b>EF (%)</b>	58.5 ± 7.6	60.3 ± 5.3	0.34
<b>E, cm/s</b>	71.1 ± 6.3	97.4 ± 13.3	0.01
<b>A, cm/s</b>	68.9 ± 5.7	69.3 ± 5.1	0.81
<b>DT, ms</b>	204.2 ± 32.2	183.9 ± 28.8	0.01
<b>E/A</b>	1 ± 0.11	1.2 ± 0.2	0.01

LA: Left atrium LVEDD: Left Ventricle End Diastolic Diameter; LVESD: Left Ventricle End Systolic Diameter; IVS: Interventricular Septum; EF: Ejection Fraction; RVEDD: Right Ventricle End-Diastolic Diameter; E: Mitral E Velocity; A: Mitral A Velocity; DT: Deceleration Time.

**Table 2:** Echocardiographic parameters of CSF and the control groups.

The TDE parameters obtained from the left and right ventricles are given (Table 3). Left ventricular MPI was significantly higher in the SCF group compared to the control, also right ventricular MPI was significantly higher in the SCF group than the control.

Patients had significantly higher TFC for each major epicardial coronary artery (P < 0.001) (Table 4). TFC was positively correlated with the left ventricle MPI index (r = 0.61, p < 0.001), the right ventricle MPI index (r = 0.49, p < 0.001), and mitral IVRT (r = 0.61, p < 0.001). There was a strong inverse correlation between mean TFC and left ventricle Ea and Ea/Aa ratio (r = -0.70, p < 0.001; r = -0.45, p = 0.001, respectively) (Table 5), (Figure 1 and 2).

Variables	Patients	Controls	P
<b>Left ventricle</b>			
<b>Sm, cm/s</b>	7.9 ± 0.4	7.8 ± 0.5	0.96
<b>Em, cm/s</b>	7.3 ± 1.5	12.6 ± 2.3	0.01
<b>Am, cm/s</b>	10.8 ± 0.8	10.90.4	0.77
<b>Em/Am</b>	0.8 ± 0.1	1 ± 0.13	0.01
<b>IRT, ms</b>	100.1 ± 10.3	88 ± 11	0.01
<b>MPI</b>	0.64 ± 0.04	0.49 ± 0.05	0.01
<b>Right ventricle</b>			
<b>Sm, cm/s</b>	12.3 ± 1.9	13.1 ± 1.2	0.41
<b>Em, cm/s</b>	8.2 ± 1.02	12.6 ± 2.3	0.01
<b>Am, cm/s</b>	13.3 ± 0.8	16.1 ± 1.1	0.45
<b>IRT, ms</b>	80.5 ± 10.2	64.6 ± 14.8	0.01
<b>MPI</b>	0.51 ± 0.05	0.44 ± 0.08	0.01

E: Mitral E velocity, A: Mitral A velocity; DT: Deceleration Time; IRT: Isovolumetric Relaxation Time; MPI: Myocardial Performance Index.

**Table 3:** Tissue Doppler parameters of CSF and control groups.

Variables	Patients	Controls	P
<b>LAD</b>	35.1 ± 12.4	14.9 ± 1.3	0.001
<b>LCX</b>	38.7 ± 6.7	17.5 ± 3	0.001
<b>RCA</b>	36.3 ± 7.6	18.2 ± 2.4	0.001

<b>Mean</b>	37.6 ± 5.9	18 ± 2.8	0.001
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LAD: Left Anterior Descending Artery; LCx: Left Circumflex Artery; RCA: Right Coronary Artery.

**Table 4:** Comparison of TIMI frame count between CSF and the control groups.

## Discussion

A number of studies have been conducted to assess LV function in patients with CSF [17,18]. Some authors have reported only impaired diastolic LV function, whereas others have reported both impaired diastolic and systolic LV function in CSF patients. Several mechanisms for the pathophysiology of CSF were suggested by previous studies, such as increased small vessel resistance, endothelial dysfunction, impairment of platelet function, inflammation, and increased plasma endothelin levels. Left and right ventricular studies showed small vessel disease in patients with CSF [18,19]. Supporting this, some studies have shown that spontaneous episodes of the CSF phenomenon during angiography are associated with ST elevation in the absence of large vessel spasm [19,20]. It is well known that ischemia first impairs ventricular diastolic function [20].

Variables	cLAD-r	cLAD-p	LCX-r	LCX-p	RCA-r	RCA-p	Mean-r	Mean-p
<b>E</b>	-0.52	0.001	-0.63	0.001	-0.63	0.001	-0.7	0.001
<b>E/A</b>	-0.33	0.001	-0.51	0.001	-0.46	0.001	-0.45	0.001
<b>IRT</b>	0.45	0.001	0.61	0.001	0.6	0.001	0.61	0.001
<b>MPI</b>	0.55	0.001	0.64	0.001	0.55	0.001	0.61	0.001
<b>Right MPI</b>	0.53	0.001	0.52	0.001	0.51	0.001	0.49	0.001

cLAD: Corrected Frame Count for Left Anterior Descending Artery; LCx: Left Circumflex Artery; RCA: Right Coronary Artery; IRT: Isovolumetric Relaxation Time; MPI: Left Ventricle Myocardial Performance Index.

**Table 5:** Correlations between TIMI frame count and echocardiographic parameters.

In this study, there were significant differences between patients with CSF and control groups as regards LV, and RV MPI and diastolic functions. Bonow et al. [21] reported that the earliest indicator of myocardial ischemia is LV relaxation disorder, a parameter of diastolic function. Sezgin et al. [22] and Tan-riverdi et al. [23] also showed that there is LV relaxation disorder in SCF patients using conventional Doppler echocardiography. Despite these studies, Nurkalem et al. [24] and Baykan et al. [25] found no LV relaxation disorder in, their study on SCF patients using the same methods. In addition, TIMI frame count for coronary arteries showed a negative correlation with LV, and RV MPI. LV MPI (Tei index) is a new echocardiographic parameter which correlates with invasive measurements and is used to evaluate both systolic and diastolic functions. It can be measured from the mitral annulus with pulsed-wave TDI and is not affected by cardiac rate, blood pressure, or ventricular geometry [26]. In coronary artery disease a prolonged MPI has been shown to be an important precursor of the disease before the development of systolic dysfunction.

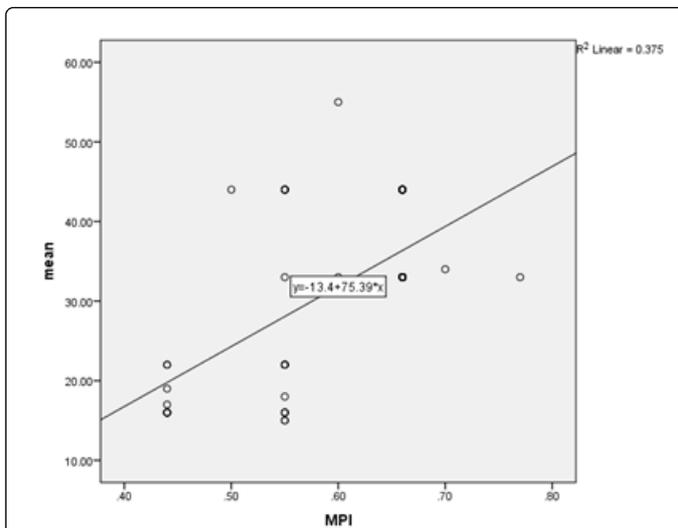


Figure 1: Correlation between mean TIMI frame count and MPI.

As a result of this study, left ventricular diastolic functions present and impaired in coronary slow flow phenomenon and this deterioration was associated with increased TIMI frame count. Further studies with larger number of patients are needed to determine the effects of left ventricular systolic and diastolic dysfunctions on mortality.

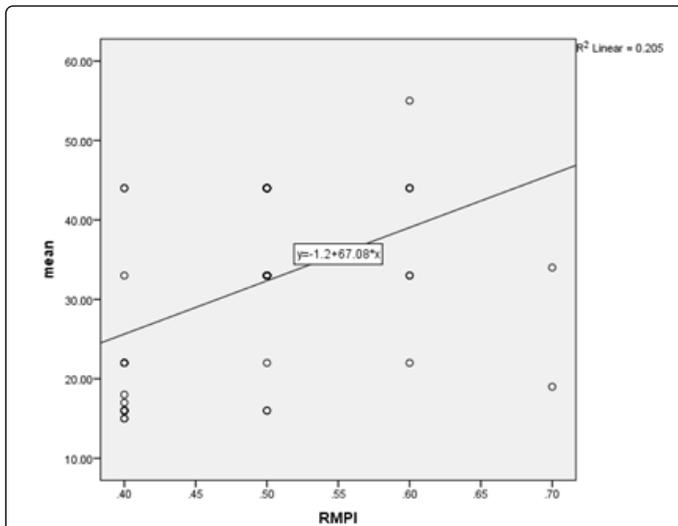


Figure 2: Correlation between mean TIMI frame count and RMPI.

## Conclusion

In conclusion, it was detected that left and right ventricular diastolic functions deteriorated in the CSF phenomenon and this deterioration was associated with increased TIMI frame count.

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