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A Comparative Study of Coronary Sinus Flow by Transthoracic Echocardiography in ST-segment Elevation Myocardial Infarction with Significant Coronary Stenosis And Normal Persons

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***Abstract:* Aim:** *The study aimed to assess the coronary sinus flow by transthoracic echocardiography (TTE) in ST-segment elevation myocardial infarction patients undergoing coronary angiography and comparing with the coronary sinus flow in the normal population without having coronary artery disease risk factors.*

Methods: *This was a retrospective, single centered, case-control study conducted in patients presenting to a tertiary care center in India from June 2015 to December 2016. Fifty patients with ST-segment elevation myocardial infarction (STEMI) were included as cases and 50 normal population without heart disease and cardiovascular risk factors were included as controls. Coronary sinus blood flow, coronary sinus diameter (CSD), left ventricular ejection fraction (LVEF), coronary sinus velocity time integral (CSVTI) were obtained by TTE in all participants.*

Results: *Coronary sinus flow was 8.9 in cases and 13.9 in controls, depicting statistically significant difference (p<0.001). The CSD and CSVTI were also statistically lower in cases than in controls (<0.001). By ROC analysis, the best cut off value of 11.7 CSF was found to be 90% sensitive and 80% specific in discriminating cases from controls.*

Conclusion: *The measurement of blood flow in the coronary sinus by transthoracic echocardiography is a valuable parameter for the diagnosis of significant coronary stenosis in STEMI patients.*

Keywords: *Coronary sinus; echocardiography; ST-segment elevation myocardial infarction*

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I. Introduction

Coronary heart diseases (CHD) have emerged as a major health burden worldwide with atherosclerosis being the prominent cause of death(1,2). Three-fourths of deaths due to CHD occur in the low and middle-income countries including India (3). As prevention is better than cure, its early and apt diagnosis is important in risk stratification and for guiding further management.

Previously, invasive diagnostic approaches were found to be used extensively, but the advancement in technology has now allowed non-invasive techniques to compete with the direct methods of diagnostics of coronary vascular pathology.

Due to the presence of an atherosclerotic plaque or in myocardial infarction, the coronary flow reserve (CFR) gets limited, which can be assessed by measuring coronary sinus flow using echocardiography. The coronary sinus flow tends to be an indirect factor for evaluating the prognosis of MI with time. Earlier, transesophageal echocardiography (TEE) was mostly used for measurements of CFR in the proximal significant left descending artery (LAD) stenosis(4, 5). However, TEE fails to measure the mid and distal segments of the coronary tree due to its non-visualization. Moreover, literature state, transthoracic echocardiographic (TTE) assessment of CFR in the distal LAD and right coronary artery (RCA) is significantly correlated with the results obtained with intracoronary Doppler wire for the LAD and RCA stenosis(6, 7). Thus, this study aimed to assess the coronary sinus flow by TTE in ST-segment elevation myocardial infarction patients undergoing coronary angiography and comparing with the coronary sinus flow in the normal population without having coronary artery disease risk factors.

II. Methods

Study design and population:

This is a single centered, case-control study conducted in patients presenting to a tertiary care center in India from June 2015 to December 2016. Fifty patients with ST-segment elevation myocardial infarction (STEMI) (thrombolysed or not thrombolysed) diagnosed by symptoms, ECG changes or echocardiographic evidence of regional wall motion abnormality were included as cases and 50 normal population without heart disease and cardiovascular risk factors were included as controls. Patients with poor echo window, hemodynamic instability, mitral or tricuspid valve regurgitation of a grade more than 2+, patients who are contraindicated for coronary angiography, persons with cardiac risk factors or previous CVS disorders were excluded from the study. Informed consent was taken from every participant.

Coronary sinus blood flow (CSBF), coronary sinus diameter (CSD), left ventricular ejection fraction (LVEF), coronary sinus velocity time integral (CSVTI) were obtained by transthoracic echocardiography (TTE) in all participants. Coronary angiogram was done and studied using computerized quantitative angiography in STEMI patients.

Measurement of coronary sinus flow:

The echocardiographic study was performed with all participants in the left lateral decubitus position and with electrocardiography recorded simultaneously. The echocardiographic data were acquired with a PHILIPS IE33, echocardiographic machine and transthoracic probe First, the standard parasternal long-axis view was obtained. An M-mode tracing was recorded for the subsequent measurements: left ventricular end-diastolic diameter and left ventricular end-systolic diameter. Then LVEF was calculated. Second, the parasternal right ventricular inflow tract view was obtained. The transducer was manipulated to visualize the mouth of the coronary sinus. To avoid the influence of atrial contraction, the coronary sinus diameter was measured at a 1-cm distance from the mouth just before the P wave on electrocardiography using adjusted. A pulsed-wave sample volume (3 mm) was placed at a 1-cm distance from the mouth and then rotated a small amount (Doppler angle between the ultrasound beam and vessels <30°) to obtain the optimum Doppler flow signals, and spectral recordings of the flow were made.

Analysis of coronary sinus blood flow:

The antegrade phase of flow in the coronary sinus moving into the right atrium was analyzed. The peak velocities (centimeters per second), peak pressure gradient (millimeters of mercury), mean velocities (centimeters per second), mean pressure gradient (millimeters of mercury), and velocity-time integral (centimeters) were determined through digitized Doppler spectral envelopes. The blood flow per stroke (milliliters per stroke) and the blood flow per minute (milliliters per minute) in the coronary sinus were calculated according to the following formulas: **blood flow per stroke = π × D2/4 × velocity time integral; and blood flow per minute = π × D2/4 × velocity-time integral × heart rate,** where π is the ratio of the circumference of a circle to its diameter, and D is the coronary sinus diameter.

Coronary angiography:

Coronary angiography was done with SIEMENS catheterization laboratory system with analysis. Coronary angiography was performed via radial or femoral approach suitable to the patient under local anesthesia. Then quantitative angiography was performed in multiple projections to visualize the artery with stenosis and lesion characteristics were studied. Minimum lumen diameter, reference diameter and % of stenosis are calculated using computerized quantitative angiography analysis. More than 50% of stenosis was considered significant stenosis.

Statistical analysis:

Continuous variables were expressed as mean ± SD values and categorical as counts and percentages. Appropriate statistical tests (student's t-test, Chi-square test, Pearson's correlation, receiver operating characteristic (ROC) analysis) were used to compare the efficacy of the CSF by TTE in the diagnosis of significant coronary artery stenosis using coronary angiography as standard. P-value was used to determine the level of significance; p-value <0.05 was considered as statistically significant. All data were analyzed using the Statistical Package for Social Sciences program (SPSS, version 17; Chicago, IL, USA).

III Results

The mean age of cases was **48.64 ± 10.53** years when compared to mean age in controls **47.72 ± 9.37** years, it was observed that majority of patients were in the age group of 40 – 49 followed by 50 – 59 yrs. The proportion of males was higher in both cases and controls. Ejection fraction was significantly lowered in cases as compared to the control group. Coronary sinus flow was **8.9 in cases and 13.9 in controls,** depicting statistically significant difference **(p<0.001).** The CSD and CSVTI were also statistically lower in cases than in controls (<0.001). Baseline demographics are detailed in **Table 1.**

The CSVTI, CSF and CSF/min were compared among gender, diabetic vs. non-diabetic, hypertensive vs. non-hypertensive, smoker vs. non-smoker, hyperlipidaemic vs. non-hyperlipidaemic (**Table 2).** Of which, study parameters were statistically lowered only in smokers as compared to non-smokers (p <0.05).

There was a ***significant negative correlation between CSF and stenosis of LAD and LCX and a significant positive correlation between CSF and stenosis of RCA (p<0.05)***. It was observed that the values of CSVTI, CSF, and CSF/min decreased with an increase in the number of vessels involved. Moreover, on applying correlation, it was observed that there was a negative correlation between CSF and no. of vessels involved (p = 0.000). The BMI and CSF were found to be poorly correlated and the percentage stenosis was found to be significantly related inversely (p = 0.004) (**Table 3**).

The area under the curve provides unbiased estimates of sensitivity and specificity; it is a comprehensive representation of pure accuracy i.e. discriminating ability over the entire range of tests. To assess the maximum sensitivity, the specificity of CSF in identifying abnormality, the best cut off value is calculated using ROC analysis (**Figure 1**). Best cut off values is established by selecting a point closer to the top left-hand curve that provides greatest sum of sensitivity and specificity. **The best cut off value of 11.7 CSF was found to be 90% sensitive and 80% specific in discriminating cases from controls** (**Table 4**).

IV Discussion

In the recent era, non-invasive diagnostic modalities have bloomed up to provide equivalent information as that of invasive measures. Since a few years, the coronary sinus blood flow has been used to diagnose severe coronary artery stenosis by TEE or TTE especially in LAD lesions or in a situation such as alteration of circulation. The TEE is a semi-invasive procedure, which evaluates CSF with good reproducibility, and allows the monitoring of flow before and after the administration of a vasodilator drug. However, vasodilators are not safe every time. At times in patients with CAD, these can result in angina pectoris and even more serious results(8). Thus the increased focus was made on TTE. Detection and reproducibility of the coronary sinus with transthoracic Doppler echocardiography as evaluated by Liu Z B et al. (9). Coronary sinus flow by TTE was first tested by Zheng XZ et al. in hypertensive patients(10).

This study was performed to evaluate coronary sinus flow by TTE. A total of 50 subjects diagnosed with STEMI and undergoing angiography were selected as cases and 50 subjects with no cardiac disease and without cardiac risk factors were selected as controls. The average CSF/min was determined to be 110.5 ± 15.5 in normal subjects and 68.06 ± 22.9 mL/min in patients with CAD. The diagnostic sensitivity, specificity, and best cut-off value of the coronary sinus flow for predicting significant coronary artery stenosis were 90%, 80%, and 11.7 respectively.

Zheng XZ et al. (11) evaluated the coronary sinus flow (mL/minute) by TTE in 78 patients, to distinguish between normal subjects and patients with significant (> 50%) coronary artery disease (CAD). The percentage of stenosis >70% was best detected by coronary sinus flow <198 mL/minute (sensitivity, 81.35%; specificity, 70.37%; positive predictive value, 63.63%; negative predictive value, 86.36% and accuracy, 75%; P < 0.001). He concluded that the coronary sinus flow per minute was an accurate parameter for the assessment of significant stenosis of the coronary artery.

Toufan M, et al. (12) measured the coronary sinus blood flow (CSBF) and CSVTI via TTE in patients with acute myocardial infarction in association with the LVEF, and wall motion scoring index. The CSBF in the AMI group was 287.8±128 ml/min and in the control group was 415±127 ml/min (p=0.001). Also, CSVTI was significantly lower in the AMI group than the control group (11.16±2.85 and 17.56±2.72 mm, p=0.003). There was a significant correlation between CSBF and LVEF (r=0.52, p=0.01), WMSI (r=-0.77, p=0.0001) and CSBF and in-hospital mortality (r=0.58 p=0.03), also between CSVTI and LVEF (r=0.85, p=0.0001). Meenakshi et al, (13) used TTE for assessing CSBF in 232 patients with CAD of various categories including patients with ACS, patients with AMI undergoing thrombolysis, symptomatic patients with CAD with a previous MI admitted for diagnostic CAG and patients with AWMI awaiting elective PTCA with bare-metal stenting and compared them with controls. In the CAG group, the correlation between CSBF and lesion severity was assessed while in the thrombolysis and PTCA groups, CSBF levels before and after treatment were evaluated. The control group had CSD of 8.73 ± 2.08 mm and mean CSBF of 441 ±172 mL/min. Both the diameter and mean CSBF levels were reduced in patients with CAD. In the AMI group, patients with anterior wall myocardial infarction showed a greater percentage increase in CSBF after thrombolysis than patients with inferior wall myocardial infarction.

Study Limitations

The poses some limitations such as small sample size, echocardiographer was not blinded, coronary sinus flow is not correlated with LV mass, interobserver and intraobserver variability not studied.

V. Conclusion

In light of the results, it can be concluded that the measurement of blood flow in the coronary sinus by transthoracic echocardiography is a valuable parameter for the diagnosis of significant coronary stenosis in STEMI patients. However, estimating coronary sinus flow by TTE to discriminate CAD patients from normal persons require further studies with large sample size.

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Tables

Table 1: Baseline demographics of cases and controls

Variable	Cases (N = 50)	Controls (N = 50)	Chi square	p value
Age (Mean ± SD, years)	48.64 ± 10.53	47.72 ± 9.37	7.10	0.13
20-29, n (%)	1 (2%)	2 (4%)		
30-39, n (%)	7 (14%)	10 (20%)		
40-49, n (%)	16 (32%)	18 (36%)		
50-59, n (%)	12 (24%)	16 (32%)		
60-69, n (%)	14 (28%)	4 (8%)		
Male, n (%)	33 (66%)	30 (60%)	0.386	0.534
BMI (Mean ± SD, Kg/m^2)	25.02 ± 2.67	24.45 ± 2.9	1.008*	0.316
Smoking, n (%)	27 (54%)	0 (0%)	36.98	<0.001
Alcohol, n (%)	28 (56%)	0 (0%)	38.89	<0.001
Hyperlipidaemia, n (%)	7 (14%)	0 (0%)	7.5	0.006
Ejection fraction (Mean ± SD, %)	38.44 ± 5.79	60.46 ± 3.09	23.7	<0.001
Coronary sinus flow (Mean ± SD)	8.9 ± 3.22	13.9 ± 1.77	9.6	<0.001
Coronary sinus diameter (Mean ± SD, mm)	0.64 ± 0.082	0.72 ± 0.065	5.46	<0.001
Coronary sinus velocity time integral (Mean ± SD)	13.46 ± 3.41	19.29 ± 1.62	10.902	<0.001
Heart rate (Mean ± SD, per minute)	78.5 ± 9.58	79.44 ± 6.2	0.579	0.564
Coronary sinus flow per minute (Mean ± SD)	68.06 ± 22.90	110.35 ± 15.5	10.79	<0.001

SD- Standard deviation, BMI – body mass index

Table 2: Comparison of study parameters among different variables

	Variables		**T value**	**P value**
	Male	**Female**		
CSVTI (Mean ± SD)	13.01 ± 3.46	15.25 ± 2.68	1.9	0.063
CSF (Mean ± SD)	8.55 ± 3.43	10.33 ± 1.72	1.57	0.121
CSF/min (Mean ± SD)	66.19 ± 24.96	75.60 ± 9.18	1.16	0.249
	Diabetic	**Non-diabetic**		
CSVTI (Mean ± SD)	13.25 ± 3.66	13.72 ± 3.13	0.486	0.629
CSF (Mean ± SD)	8.45 ± 3.28	9.48 ± 3.12	1.12	0.267
CSF/min (Mean ± SD)	65.38 ± 24.16	71.48 ± 21.30	0.932	0.356
	Hypertensive	**Non-hypertensive**		
CSVTI (Mean ± SD)	13.92 ± 3.31	12.68 ± 3.53	1.28	0.206
CSF (Mean ± SD)	9.40 ± 3.19	8.01 ± 3.17	1.48	0.145
CSF/min (Mean ± SD)	73.09 ± 23.09	59.13 ± 20.24	2.1	0.037
	Smoker	**Non-smoker**		
CSVTI (Mean ± SD)	11.83 ± 2.87	15.37 ± 3.04	4.228	<0.001
CSF (Mean ± SD)	7.31 ± 2.80	10.78 ± 2.66	4.46	<0.001
CSF/min (Mean ± SD)	58.33 ± 21.36	79.50 ± 19.45	3.64	0.001
	Hyperlipidaemic	**Non-hyperlipidaemic**		
CSVTI (Mean ± SD)	15.57 ± 4.16	13.12 ± 3.21	1.8	0.07
CSF (Mean ± SD)	11.23 ± 4.28	8.53 ± 2.91	2.13	0.38
CSF/min (Mean ± SD)	81.13 ± 26.57	65.94 ± 21.89	1.65	0.105

- CS VTI - Coronary sinus velocity time integral,CSF – coronary sinus flow, CSF/min – CSF per min,SD- standard deviation

Table 3: Correlation of coronary sinus flow with different variables

Variable	R value	P value
LAD	-0.877	0.0001
LCX	-0.402	0.004
RCA	0.396	0.004
No. of vessels	-0.583	0.0001
Percentage of stenosis	-0.402	0.004
BMI	-0.261	0.067

Table 4: ROC analysis for coronary sinus flow

Area under curve	0.902
P-value	<0.001
95% confidence interval	0.839 – 0.964
Best cut-off value	11.7
Sensitivity	90%
Specificity	80%

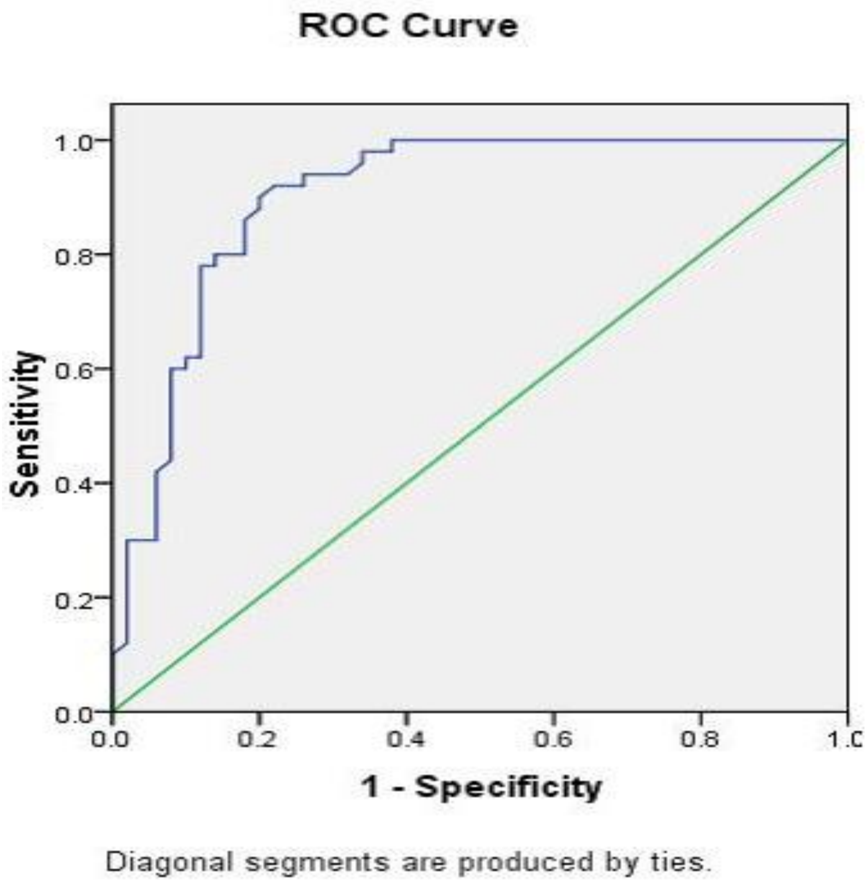

Figure 1: ROC curve for coronary sinus flow

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