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Original Research Article

Assessment of coronary slow flow and its implications

Rajeev Ranjan, Santanu Das, M. Azizul Haque, Pritam Kumar Chatterjee*

Department of Cardiology, Kolkata National Medical College, Kolkata, West Bengal, India

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***Correspondence:**
Dr. Pritam Kumar Chatterjee,
E-mail: pchatterjee2@gmail.com

ABSTRACT

Background: CAG is seen as the gold standard for the diagnosis of epicardial coronary artery disease. The clinical significance of coronary microvascular dysfunction has not been given much attention as epicardial coronary artery disease. Coronary slow flow phenomenon is another independent entity which is less studied and treatment plan and prognosis are not yet established. The objective of this study was to provide better understanding about the presence and pathophysiologic significance of coronary slow flow phenomena in patients undergoing coronary angiography (CAG) for various indications by corrected TIMI frame count (CFTC) in vessels without any flow limiting disease.
Methods: We measured CTFC in patients enrolled for CAG. We compared CTFC among different presentations and in different arteries. We also compared coronary slow flow phenomenon to normal flow in coronaries and its correlation to risk factors
Results: We found that coronary flow was significantly slower in non-infarct related arteries (NIRA) in the setting of ST segment elevation myocardial infraction (STEMI) and non-ST segment elevation myocardial infraction (NSTEMI) with no obstructive epicardial lesion as compared to coronary flow in absence of acute myocardial infraction (AMI). Significant slow flow was present in NIRA in STEMI compared to NSTEMI. Similarly slow flow was noted in unstable angina compared to chronic stable angina patients. Predominantly involved vessel was left anterior descending artery (LAD).
Conclusions: Coronary flow was slower in NIRA in the setting of STEMI and NSTEMI with no obstructive epicardial lesion as compared to coronary flow in absence of AMI.

Keywords: Coronary slow flow, NIRA, NSTEMI, STEMI

INTRODUCTION

Coronary angiography, seen as the gold standard for the diagnosis of coronary artery disease, can often be the ultimate test in the chest pain diagnostic algorithm. Even at the end of this diagnostic road, a diagnosis of 'normal coronary arteries' based on the absence of epicardial coronary stenosis may not convey the entire story in terms of the patient's condition or prognosis.

The coronary slow flow (CSF) is an angiographic phenomenon, characterized by slow filling of coronary arteries with dye during coronary angiography in the absence of significant epicardial coronary artery stenosis. This condition, which may affect one or all coronaries, was originally described by Tambe et al in 1972.[1] Although it is well-known to interventional cardiologists for approximately four decades, the aetiology, treatment plan and prognosis are not yet established. Rather than representing a simple angiographic curiosity, CSFP 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 .[2-4]

Incidence of coronary slow-flow is reported to be 1-7% of all coronary angiograms. This clinical entity, which can present identically to most acute coronary syndromes,

may account for up to 4% of unstable angina admissions.[3] The clinical course can be quite challenging to physicians and debilitating to patients, with recurrence of chest pain occurring in up to 80% and hospital readmission in almost 20% of cases in less than a 2-year follow-up period.

We will be trying to elicit its correlation with different risk factors and co morbid conditions along with different presenting features. We will like find out the clinical characteristics, causative mechanisms, clinical implications which might help in therapy and prognostication and to establish it as an entity as a whole, which can be idiopathic (primary) or secondary.

Aims and objectives

The aim of the study was to provide better understanding about the presence and pathophysiologic significance of coronary slow flow. To assess the coronary slow flow phenomena in patients undergoing coronary angiography for various indications by corrected TIMI frame count (CFTC) in vessels without any flow limiting disease. To study the correlation between coronary slow flow and various risk factors for CAD.

METHODS

It was a hospital based cross-sectional, observational, study conducted in Calcutta National Medical College, Kolkata. Subjects who fulfilled the predetermined inclusion criteria were be studied. This study took place for a period of one year (January 2019 to January 2020).

Sample size

Sample consists of all-inclusive cases that are to undergo coronary angiography in the department of cardiology in our institute from January 2019 to January 2020 for screening of coronary slow flow. Total number of patients were 350.

Sample design

Consecutive patients fulfilling inclusion criteria were included. We performed corrected TIMI frame count among patients undergoing coronary angiography in our catheterization laboratory. Before catheterization a protocol based clinical examination was used to assess demographic profile, cardiac history, atherogenic risk factors, feature of extra coronary vascular disease and co-morbidities.

Ethical approval was obtained from the hospital committee.

Inclusion criteria

Patients who need to undergo coronary angiography for evaluation of various presentations in the department of cardiology. Written informed consent will be taken from all patients.

Exclusion criteria

Known or suspected acute or chronic renal failure and history of contrast nephropathy. Electrolyte imbalance, patient with severe anaemia. Haemodynamically unstable. Patient with bypass graft lesion. Refusal to give informed consent

Parameters to be studied and study tools

Age and sex distribution of study population; major risk factors of atherosclerosis namely, smoking, diabetes, hypertension, dyslipidaemia, family history of premature coronary artery disease; clinical features suggesting acute coronary syndrome; routine blood examination like haemoglobin, ESR, total WBC count, differential WBC count, platelet count; blood biochemistry like fasting and post prandial blood sugar, urea, creatinine, sodium, potassium, lipid profile; electrocardiography; tread mill test; echocardiography coronary angiography- corrected TIMI frame count or flow velocity were parameters studied.

RESULTS

We studied the status of coronary microcirculation in patients presenting at Calcutta National Medical College, Kolkata with ischemic heart disease. We divided the patient population into different groups according to the presentation such as chronic stable angina, unstable angina, STEMI and NSTEMI. Corrected TIMI frame count of the coronary arteries undergoing coronary angiogram was studied. Among patient population we studied, 68 patients presented with CSA, 52 patients presented with UA, 185 patients presented with STEMI, 45 patients presented with NSTEMI. Demographic data are presented in Tables 1 and 2.

Table 1: Gender distribution among different presentation.

Sex	Diagnosis				Total	P value	Significance
	CSA	NSTEMI	STEMI	UA			
Male	48 (70.59)	26 (57.78)	143 (77.3)	42 (80.77)	259 (74)		
Female	20 (29.41)	19 (42.22)	42 (22.7)	10 (19.23)	91 (26)	0.031	Significant
Total	68 (100)	45 (100)	185 (100)	52 (100)	350 (100)		

Table 2: Distribution of risk factors in patient population.

Risk factors	No. of patients with risk factors
Diabetes	159
Hypertension	212
Smoking	186
Dyslipidemia	238

Male patients dominated the study population among all types of presentations. There was significant difference in the mean CTFC among the male and female patients noted. We studied the distribution of 4 major risk factors on our study population. Of the risk factors studied, dyslipidemia was the most common risk factor followed by hypertension and smoking and diabetes in that order. There was a strong correlation between number of risk factors and mean CTFC with correlation coefficient of 0.98 and p<0.001. Dyslipidaemia and diabetes showed statistically significant difference with mean CTFC. There was no significant difference between smoker and non-smoker mean CTFC in different presentations.

We compared mean CTFC in patients and found that the coronary flow was significantly slower in non-infracted arteries in the setting of STEMI and NSTEMI despite no obstructive epicardial coronary artery lesion as compared to patients with chronic stable angina and unstable angina. Among the non-infarct related arteries without any obstructive lesion in STEMI and NSTEMI significant slow flow was noted in STEMI compare to NSTEMI group of patients. The mean CTFC in our study group was lower than that found by Gibson et al who measured CTFC (30.9±15.0 frames) on NIRAs 90 minutes after thrombolysis.[5] Likewise significant slow flow was found in patients with unstable angina compared to chronic stable angina. This may be due to time delay for angiography after symptom onset in our study population. These findings suggest presence of microvascular dysfunction independent of epicardial events. Similarly, CTFC in infarct related arteries in STEMI group showed slow flow compared to NSTEMI.

In our study population normal looking epicardial coronary arteries was present in 95 patients which is 27% of the study population. These include patients with completely normal coronary arteries, some with recanalized vessels, and those with microvascular diseases. Out of all normal coronaries 18 patients were found to have coronary slow flow in at least one major epicardial coronary artery and otherwise normal arteries formed the study group. These were compared with normal angiography group of patients with normal coronary flow. Mehta et al reported that slow flow is more common in female patients.[6] All the females were pre-menopausal. Nilavan et al studied coronary slow flow phenomenon in Madras medical college, Chennai.[7] CSFP was more common in males with smoking (p value <0.05). This association was similar to the study conducted by Beltrame et al in an Australian population.[8] LAD was the most commonly affected artery (69%). 48% of patients with CSFP presented with CSA and remaining 52% with ACS similar to Iranian population study. In another study in north India at GIPMER New Delhi in 2017, they found mean age 53±10 years and 92.5% were males.[9] BMI and smoking were significantly higher in cases than controls (p<0.05).[9] The mean CTFC in slow flow phenomenon (CSFP) group was significantly higher with a significant statistical difference from that of normal angiography with normal flow group of patients. Distribution of slow flow patients among UA was highest, followed by NSTEMI and STEMI respectively showing a statistically significant difference. Almost all of them presented with angina symptoms. Among these patients smoking was most prevalent risk factors followed by dyslipidaemia and then hypertension and diabetes (Table 3). Among all the risk factors slow flow was significantly correlated with smoking only. Left anterior descending artery was the commonest involved artery.[10]

Table 3: CTFC in patients with different risk factors.

Risk factors	CSA	UA	STEMI NIRA	NSTEMI NIRA	Overall
DM	24.92	24.28	27.81	26.57	25.89
HTN	23.53	24.03	27.53	26.80	25.47
Smoking	22.94	24.74	26.88	26.50	26.01
Dyslipidemia	23.34	25.10	28.07	26.42	25.73

DISCUSSION

The presence and significance of microvascular dysfunction in ischemic heart disease is a subject of intense investigation. We studied the status of coronary microvascular function in patients presented with ischemic heart disease with different presentations such as CSA, UA, STEMI, NSTEMI patients using corrected TIMI FRAME count method. We found that coronary flow was significantly slower in non-infarct related arteries in the setting of STEMI and NSTEMI despite no obvious epicardial obstructive coronary lesion as compared to coronary flow in absence of acute AMI (p<0.001).[11,12] CFTC in females was more than that of males but was not statistically significant (p<0.10). Significant slow flow was present in NIRA in STEMI compared to NSTEMI. Similarly slow flow was noted in unstable angina compared to chronic stable angina patients. The correlation between various risk factors and mean CTFC was studied and found to be significantly associated. Slower flow in non-infarct related arteries without any flow limiting obstruction implies presence of primary microvascular dysfunction independent of

epicardial stenosis. Microvascular dysfunction was directly related to number of atherosclerotic risk factors which suggests it might precede thrombotic occlusion and accounts for persistent chest pain. Diabetes, smoking, dyslipidaemia predicts higher CTFC. Marks et al followed patient with chest pain and normal coronary angiogram over a period of 8.5 years and found three-fold higher mortality for those with abnormal coronary flow reserve (20% versus 7%; p=0.016).[13] Yilmaz et al performed a similar retrospective analysis in a Turkish population and identified the features of metabolic syndrome as the major co morbidities associated with CSFP.[14] Nicotine and sex were not found to be associated with this condition.

Similarly, we found coronary slow flow phenomenon in absence of obstructive epicardial lesion with male patients dominating the group. They presented mainly as CSA and unstable angina. CTFC in these patients was significantly higher than those with normal coronary flow suggesting microvascular dysfunction. Among the various risk factors smoking found to be strongly correlated. Predominantly involved vessel was LAD. Future studies need to be done on large population likewise in other ethnic groups residing in different parts of India to study in detail the various specific biomarkers contributing to CSF phenomenon in Indian patients which might provide new insight into the Pathophysiology of this intriguing entity that might be of diagnostic and/or therapeutic use.

It has been found that slower flow throughout all three arteries in STEMI is associated with a higher risk of adverse outcomes, poorer wall motion in remote territories, poorer tissue perfusion on digital subtraction angiography and a greater magnitude of ST depression in remote territories such as the anterior precordium in inferior MI.[5,15,16] Poorer flow in nonculprit arteries may be the result of more extensive necrosis in shared microvasculature, or a result of vasoconstriction mediated through either a local neurohumoral or paracrine mechanism. Indeed, Gregorini et al have demonstrated that the CTFC and fractional wall shortening is improved in both the culprit and nonculprit arteries after administration of α-blockers, indicating that "α-adrenergic storm" may play a role.[17]

This study has a limitation that it was done on a limited number of patients.

CONCLUSION

We found that coronary flow was significantly slower in non-infarct related arteries in the setting of STEMI and NSTEMI with no obstructive epicardial lesion as compared to coronary flow in absence of acute AMI (p<0.001). CFTC in females was more than that of males but was not statistically significant (p<0.10). Significant slow flow was present in NIRA in STEMI compared to NSTEMI. Similarly slow flow was noted in unstable angina compared to chronic stable angina patients. Predominantly involved vessel was LAD.

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