ISSN: 0976-3031

Available Online at http://www.recentscientific.com

CODEN: IJRSFP (USA)

International Journal of Recent Scientific Research
Vol. 10, Issue, 07(B), pp. 33448-33452, July, 2019

International Journal of Recent Scientific Research

DOI: 10.24327/IJRSR

Research Article

CHARACTERISTICS OF PATIENTS WITH CORONARY SLOW FLOW PHENOMENON; AN EXPERIENCE FROM SRI LANKA

Bandara H.G.W.A.P.L., Jegavanthan A., Kogulan T., Karunaratne R.M.S.P., Hewaratne U.I., Kodithuwakku N.W., Kularatne A., Jayawickreme S.R., Dolapihilla S.N.B., Weerakoon W.M.G., Mayurathan G and Rathnayake T

Cardiology Unit, Teaching Hospital Kandy, Sri Lanka

DOI: http://dx.doi.org/10.24327/ijrsr.2019.1007.3673

ARTICLE INFO

Article History:
Received 6th April, 2019
Received in revised form 15th May, 2019
Accepted 12th June, 2019
Published online 28th July, 2019

Key Words:

Coronary slow flow, TIMI frame count, Coronary angiography, Coronary microcirculation

ABSTRACT

Background: Phenomenon of Coronary Slow Flow (CSF) is a rare clinical entity leading to angina, ischemic electrocardiographic changes and abnormal cardiac scintigraphy while having normal appearance of coronary arteries.

Objective: The study was aimed to explore the clinical and angiographic characteristics of this peculiar condition among our Sri Lankan patients.

Methodology: A retrospective cross sectional study was conducted at teaching hospital Kandy, Sri Lanka. All consecutive patients scheduled for coronary angiography between 2014 and 2016 were included. CSF was diagnosed based on the Thrombolysis In Myocardial Infarction (TIMI) frame count (TFC) of coronary flow. Coronary arteries without plaque burden and a TFC > 27 of flow rate was defined as having CSF phenomenon. Angiograms were reviewed by two examiners individually. The clinical details were obtained by interviewer administered questionnaire. A comparison was made with age and gender matched control group, who had normal coronaries.

Results: The mean age of the sample was 52.18 ± 8.99 years and 65.50% (n=25) were males. Out of the sample, 15.00% (n=6) had diabetes, 32.50% (n=13) had hypertension and 32.50% (n=13) had dyslipidaemia as risk factors. Out of that 67.50% (n=27) had acute coronary syndromes and 50.00% (n=20) presented with recurrent atypical chest pains. In the sample 50.00% (n=50) had positive, 37.50% (n=15) had negative and 12.50% (n=5) had inconclusive stress test by Bruce protocol. Out of the sample, 57.50% (n=23) had ejection fraction ≥55% and 62.50% (n=25) hadn't have wall motion abnormalities

Prevalence of CSF in triple vessels was 35.00% (n=14). There were 45.00% (n=18) had slow flow involving two vessels being Left Anterior Descending (LAD) & Right Coronary Artery was the commonest combination. Single vessel involvement was 20.00% (n=8) and LAD was the commonest artery involved. There was no statistical significance of age (p=0.74), gender (p=0.52), prevalence of hypertension (p=0.91), diabetes mellitus (p=0.83), dyslipidaemia (p=0.24) among patients with CSF compared to controls.

Conclusion: CSF phenomenon is an infrequent finding in patients with angina but commonly precipitates to recurrent episodes of chest pains. These patients often have positive stress tests and occasional to have wall motion abnormalities in echocardiography. Micro-vascular metabolism and altered coronary haemodynamics should be further exploded in this clinical entity in future studies.

Copyright © Bandara H.G.W.A.P.L *et al,* 2019, this is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

The phenomenon of Coronary Slow Flow (CSF) is an angiographic clinical verity, which is characterized by late opacification of the distal segments of the coronary artery without having a significant stenosis [1]. This is often an uncommon angiographic observation, with an observed incidence ranging 1%-7% of patients undergoing diagnostic angiography to evaluate Ischemic Heart Disease (IHD) [2, 3].

Though this phenomena is recognized by the cardiologists for nearly four decades, the exact vascular hemodynamic mechanisms are yet to be understood. There are several theories that had step forward to explain the pathophysiology of CSF, including dysfunction of small vessels [4], diffuse

Corresponding author:* **Bandara H.G.W.A.P.L
Department of Gyneco-Obstetrics of the University of Uele in Isiro (D R Congo)

atherosclerosis [5], vascular inflammation [6], endothelial dysfunction [7], and platelet aggregation dysfunctions [8]. Interestingly, this cohort of patients has a variety of symptoms profile, as it has been connected to the manifestations of myocardial ischemia, various cardiac arrhythmias, repeated Acute Coronary Syndromes (ACS) and even sudden cardiac death [9, 10, 11, 12].

Although the pathophysiology remains uncertain, it is important to identify the main risk factors, behavior of the disease and the patient's therapeutic response to treat them adequately with optimal medical management. However, the gravity of this condition is generally underestimate as a result of the relative rarity, yet unknown explanation of the mechanism of this angiographic appearance and variable response to treatment options. Here, we have aimed in our study to explore the clinical and angiographic characteristics of this peculiar condition among Sri Lankan patients.

METHODOLOGY

Study design and setting

The study was conducted at cardiology unit, teaching (General) hospital Kandy, Sri Lanka as a retrospective cross-sectional study.

Inclusion criteria

All coronary angiograms of the patients who were evaluated for IHD during 2014 to 2016 were included for the study. Among them, the patients who had no coronary plaque disease and having delayed coronary flow rate were selected for the study. All of them were reviewed by the cardiology team to obtain the clinical and echocardiographic details. Information related to the presence of vascular risk factors, history of angina, past history of ACS and details of previous hospitalizations were recorded.

A control group was selected, which was consisted of age matched equal number of patients who were evaluated for IHD and subsequently found to have no coronary plaque disease and having normal coronary flow rates.

Exclusion criteria

Patients who had more than mild valvular heart disease, any form of cardiomyopathy, pulmonary arterial hypertension, ongoing cardiac rhythm disorders, known hematological disorders, patients with renal or hepatic disease and patients with coronary ectasia were excluded from the study. Addition to that acutely ill patients who were having cardiogenic shock and patients who had vaso-vagal episodes during the angiography also were excluded.

Angiographic evaluation and definition of Coronary Slow Flow

The standard Judkins technique for left heart catheterization and standard angiographic views using right and left, caudal, and cranial angulations were used for angiographic recordings. Those angiograms were reassessed, and Thrombolysis in Myocardial Infarction (TIMI) frame counts were determined for each individual coronary artery by two investigators independently, and the average value was obtained. Images were acquired at 15 frames/s, and all the final TIMI frame counts for each individual coronary artery was multiplied by 2 to equalize the standard frame rate of 30 frames/s as for the definition of coronary slow flow. TIMI frame count was calculated from the beginning of the vessel opacification to the most distal reference point of the respective vessels. The TIMI frame counts in the Left Anterior Descending (LAD) artery were divided by a constant of 1.7 to correct for the increased length, and to formulate a corrected value for LAD. Based on Gibson's study, a frame count > 27 was defined as having slow flow for an individual vessel [13].

Ethical clearance

This study proposal was approved by local ethical review committee of teaching hospital Kandy, Sri Lanka and informed consent was obtained from the participants authorizing the use of their information for analysis and publication.

Statistical analysis

Quantitative data was expressed as mean with Standard Deviation (SD). The statistical significance of continuous variables among subgroups were evaluated by Student t-test and variation of categorical variables were evaluated by Chi-square test. Qualitative data was expressed as percentages. The Statistical Package for Social Sciences version 17 (SPSS) was used for all calculations. Differences were considered statistically significant when the p value was < 0.05.

RESULTS

The demographic characteristics and vascular risk factors

There were 40 patients in the study sample. The mean age of the patients was 52.18 ± 8.99 years and 62.50% (n=25) were males. The mean age of symptoms origin was 48.36±9.49yeras. There were 15.00% (n=6) of diabetics, 32.50% (n=13) of hypertensives and 32.50% (n=13) had dyslipidemia. There were 67.50% (n=27) of patients presented with acute Myocardial Infarctions (MI). However, 50.00% (n=20) presented with recurrent atypical chest pains. Altogether, 85% of patients got chest pain at least once per month within their past one year period. In the sample, 50.00% (n=20) had positive, 37.50% (n=15) had negative and 12.50% (n=5) had inconclusive exercise stress test by Bruce protocol. Interestingly, 57.50% (n=23) had ejection fraction ≥55% and 62.50% (n=25) hadn't have any regional wall motion abnormalities. The baseline characteristics of the study sample are demonstrated in *table 01*.

Table 1 Baseline characteristics and vascular risk factors of the study sample

Variable	**Results**
Age (mean ± SD)	52.18±8.99 years
Gender	
Male	62.50% (n=25)
Female	37.50% (n=15)
Co-morbidities	
Diabetes	15.00% (n=06)
Hypertension	32.50% (n=13)
Dyslipidemia	32.50% (n=13)
Smoking*	32.50% (n=40)
TIMI Frame Count	
LAD	43.98±16.05
LCX	35.59±16.05
RCA	36.59±16.92

SD= Standard Deviation , LAD= Left Anterior Descending, LCX= Left Circumflex, RCA= Right Coronary Artery, Smoking*= Current and ex-smokers

Vascular territories affecting slow flow phenomenon

The Left Anterior Descending (LAD) artery was involved in 85.00% (n=34) of cases, whereas Right Coronary Artery (RCA) and Left Circumflex (LCX) artery were involved in 65.00% (n=26) and 52.50% (n=21) of cases respectively (Figure-01).

Prevalence of CSF in triple vessels was 35.00%. (n=14). There were 45.00% (n=18) had slow flow involving two vessels being LAD & RCA was the commonest combination. Single vessel involvement was 20.00% (n=8) and among that LAD was the commonest artery involved (75.00%).

There were 32.50% (n=13) had concomitant slow flow in LAD and LCX, while 45.00% (n=18) had simultaneous slow flow in LAD and RCA. Similarly, 22.50% (n=09) had concurrent slow flow in LCX and RCA. Isolated LAD coronary slow flow involvement was observed in only 17.50% (n=07) patients.

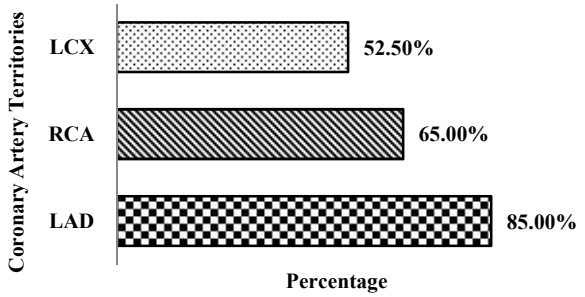

Figure 1 The distribution of coronary slow flow among coronary territories

Comparison of vascular risk factors with controls

The incidence of vascular risk factors and the common hematological parameters of patients with CSF compared with the control group. However, there was no statistical significance of age (p=0.74), gender (p=0.52), prevalence of hypertension (p=0.91), diabetes mellitus (p=0.83), dyslipidaemia (p=0.24), mean haemoglobin concentration (p=0.79), mean white blood cell count (p=0.43) or mean platelet count (p=0.76) among patients with CSF compared to controls *Table 2*.

Table 2 The comparison of vascular risk factors between the patients with CSF and the control group.

Variable	CSF Group	Control group	P value
Age	52.18±8.99	52.25±7.56	0.74
Gender (Male%)	62.50%	60.45%	0.52
Hypertension	32.50%	35.67%	0.91
Diabetics	15.00%	19.42%	0.83
Dyslipidemia	32.50%	30.41%	0.24
Hb (g/dL)	13.56±1.34	14.26±2.13	0.79
WBC count	15.63±2.56	14.23±1.52	0.43
Mean platelet Count	256.32±61.27	275.04±60.84	0.76

SD= Standard Deviation Hb= Hemoglobin Concentration, WBC= White blood cell

DISCUSSION

The phenomenon of coronary slow flow is believed to be as a result of microvascular dysfunction and it is probably linked to an initial process of atherosclerosis [14,15]. The reported prevalence of CSF phenomenon differs among multiple studies. *Hawkins et al*. reported a prevalence of 5.5% among patients referred for coronary angiography based on TIMI frame count definition [2]. In another two individual studies, the prevalence of CSF phenomenon was estimated to 1% among patients who underwent coronary angiography, based on the same TIMI frame count definition [16,17]. However, *Diver et al*. was able to estimate that nearly 5% of patients presenting with ACS exhibit the evidence of CSF without obstructive coronary artery disease [18].

Considering the coronary circulation, the optimal flow dynamics is maintained with the integrity of "conductance vessels", and the "resistive vessels" (so called "small vessels" of less than 400 μm of diameter), which mainly control the myocardial blood flow in the absence of any significant stenosis of the epicardial coronaries [19,20].

Interestingly, the microvasclar dysfunction has been characteristically described in the pathophysiology of CSF phenomenon since its first description [21]. In parallel to these findings, *Mangieri et al*. [16] found some anatomical changes such as thickening of vessel walls with luminal size reduction in endomyocardial biopsies. Subsequently, *Beltrame et al*. [22] described that elevated resting coronary microvascular tone is associated with CSF phenomena. Based on these data, it is believed to be that the CSF happens as a combination of both structural and functional anomalies of both macro and micro circulation of the coronary arteries.

A growing body of evidence has proposed that the normal endothelial functions are need to maintain the optimal vascular tone, platelet activity, leukocyte adhesion and vascular smooth muscle proliferation. It has been reported that the alteration of above physiological processes as a result of endothelial dysfunction also implicated in the etiology of CSF phenomenon [23].

Typically these patients present with rest pain rather than with exertional angina in most of the time according to many observations. They may have resting Electrocardiographic (ECG) abnormalities yet normal stress ECGs and imaging[24]. Similarly, in our study nearly half of them had atypical chest pains. However, many had positive exercise ECGs contrast to some previous studies. Unfortunately, as a result of their ambiguous presentation, some may have subjected for even repapered cardiac catherazation yielding frustration to both patient and the physician.

The frequencies of vascular territorial involvement in CSF phenomenon in this study showed some deviation to those observed in previous studies. *Hawkins et al*. had found that LAD, LCX, and RCA were involved in 67%, 69%, and 58% respectively [2]. However, in our study, LAD was most frequently involved as for 97% of time. The exact reason for this observation is unclear and need further studies to evaluate this observation among our patients. Interestingly, there were 35% patients had multi-vessel involvement in our series.

Fineschi et al. [25] and *Hawkins et al*. [2] had found that patients with CSF and patients with coronary arteries having normal flow rates had no difference of the incidence of traditional atherosclerotic risk factors. Similarly, our study also indicates that patients with CSF phenomena is not differ from their vascular risk factors to patients with normal epicardial coronary flow pattern.

Various studies have highlighted the independent predictors of CSF phenomenon. *Hawkins et al*. suggested male sex, a higher body mass index, and a reduced high density lipoprotein-cholesterol level as independent predictors of this condition [2]. *Arbel et al.* had shown that the smoking was the robust predictor of the SCF phenomenon [26]. However, these discrepancies may be related to racial differences or unknown other confounding factors among patients with CSF syndrome. Endothelial dysfunction and vascular inflammation, which are subsequently related to alteration of the properties of platelet, and other hematological parameters also known to be proposed as risk factors associated with the CSF phenomenon [14,17,18] However, in our study, we found no association between white blood cell or platelet counts in patients with CSF compared to controls. Nevertheless, *Akpinar et al*. explored the connection between whole blood cell counts and CSF and proposed that the red cell distribution width and platelet count as independent predictors of this phenomenon [27].

In case of the management, there are no evidence based strong therapeutic measures or pharmacological approaches to treat this condition. As a novel therapeutic strategy, coronary interventions also failed to make much hope in treating this situation. However, dipyridamole and mibefradil, which both influence the functional obstruction in small arteries, was able to restore the TIMI frame count but nitroglycerine, failed to achive this results [28]. Importantly, there are some evidence that statins appear beneficial for patients with CSF, expectedly as a result of their anti-inflammatory properties [29]. More recently, some of the researches have established that nebivolol can both improve the symptoms as well as the endothelial function improving the quality of life in these patients with CSF phenomenon [30].

CONCLUSION

CSF phenomenon is an infrequent finding in patients with angina. Multi-vessel involvement is seen more frequently and the often involved vessel being LAD. These patients often have positive stress test and occasional to have wall motion abnormalities in echocardiography.

Our current understanding regarding the pathophysiology and coronary flow dynamics of patients with CSF is incomplete. However, physicians should have a high degree of clinical awareness of this condition and its clinical significance. The presence of significant deviations in SCF predictors among various studies may implicates the presence of unknown confounders, which should be addressed in future large scale prospective studies with a focus of achieving a potential promising therapeutic approach.

Limitation of the study

We would like to emphasize some of the limitation of our study. First, it included non-randomized small number of subjects due to rarity of the disease, so the observed results may have encountered selection bias.

Second, the current study only considered the fact that the presence or absence of CSF phenomenon as a categorical variable. However, an evaluation focusing the degree of coronary slow flow into clinical outcome also would be beneficial to evaluate in future studies. Third, the patients' medication and the therapeutic response were not followed up as this was a retrospective study. Hence, further large scale studies are required to elaborate the relationship of coronary flow dynamics, endothelial and microcirculatory dysfunctions and clinical outcome of these patients.

Acknowledgement

We would extremely thank our patients at cardiology unit Kandy, and the staff of the cardiology unit, for their contribution towards the success of this study.

Funding: None

Conflict of interest

The authors declare that they have no conflict of interest.

Reference

1. Beltrame JF. Chest pain and normal angiography. In: Braunwald Heart Disease (e-Edition). Braunwald E (Ed.), Elsevier, PA, USA, 1329 (2006).
2. Hawkins BM, Stavrakis S, Rousan TA, Abu-Fadel M, Schechter E. Coronary slow flow--prevalence and clinical correlations. Circ J. 2012;76(4):936-42.
3. Chaudhry MA, Smith M, Hanna EB, Lazzara R. Diverse spectrum of presentation of coronary slow flow phenomenon: a concise review of the literature. Cardiol Res Pract. 2012;2012:383181.
4. Mosseri M, Yarom R, Gotsman MS, Hasin Y. Histologic evidence for small-vessel coronary artery disease in patients with angina pectoris and patent large coronary arteries. Circulation 1986; 74: 964-972.
5. Pekdemir H, Cin VG, Cicek D, Camsari A, Akkus N, Doven O, Parmaksiz HT. Slow coronary flow may be a sign of diffuse atherosclerosis. Contribution of FFR and IVUS. Acta Cardiol 2004; 59: 127-133.
6. Turhan H, Saydam GS, Erbay AR, Ayaz S, Yasar AS, Aksoy Y, Basar N, Yetkin E. Increased plasma soluble adhesion molecules: ICAM-1, VCAM-1, and E-selectin levels in patients with slow coronary flow. Int J Cardiol 2006; 108: 224-230.
7. Damaske A, Muxel S, Fasola F, Radmacher MC, Schaefer S, Jabs A, Orphal D, Wild P, Parker JD, Fineschi M, Munzel T, Forconi S, Gori T. Peripheral hemorheological and vascular correlates of coronary blood flow. Clin Hemorheol Microcirc 2011; 49: 261-269.
8. Gokce M, Kaplan S, Tekelioglu Y, Erdogan T, Kucukosmanoglu M. Platelet function disorder in patients with coronary slow flow. Clin Cardiol 2005; 28: 145-148.
9. Cutri N, Zeitz C, Kucia AM, *et al*. ST/T wave changes during acute coronary syndrome presentation in patients with the coronary slow flow phenomenon. Int J Cardiol 2011;146:457-8.
10. Horjeti B, Goda A. Acute ischemia manifestation in a patient with coronary slow flow phenomenon. J Electrocardiol 2011.
11. Wozakowska-Kaplon B, Niedziela J, Krzyzak P, *et al*. Clinical manifestations of slow coronary flow from acute coronary syndrome to serious arrhythmias. Cardiol J 2009;16:462-8.
12. Saya S, Hennebry TA, Lozano P, *et al*. Coronary slow flow phenomenon and risk for sudden cardiac death due

to ventricular arrhythmias: a case report and review of literature. Clin Cardiol 2008;31:352-5.
13. Gibson CM, Cannon CP, Daley WL, Dodge JJ, Alexander BJ, Marble SJ, *et al*. TIMI frame count: a quantitative method of assessing coronary artery flow. Circulation. 1996;93(5):879-88.
14. Li JJ, Xu B, Li ZC, Qian J, Wei BQ. Is slow coronary flow associated with inflammation? Med Hypotheses. 2006;66(3):504-8.
15. Lanza GA, Crea F. Primary coronary microvascular dysfunction: clinical presentation, pathophysiology, and management. Circulation. 2010;121(21):2317-25.
16. Mangieri E, Macchiarelli G, Ciavolella M, Barilla F, Avella A, Martinotti A, *et al*. Slow coronary flow: clinical and histopathological features in patients with otherwise normal epicardial coronary arteries. Cathet Cardiovasc Diagn. 1996;37(4):375-81.
17. Beltrame JF, Limaye SB, Horowitz JD. The coronary slow flow phenomenon--a new coronary microvascular disorder. Cardiology. 2002;97(4):197-202.
18. Diver DJ, Bier JD, Ferreira PE, Sharaf BL, McCabe C, Thompson B, *et al*. Clinical and arteriographic characterization of patients with unstable angina without critical coronary arterial narrowing (from the TIMI-IIIA Trial). *Am J Cardiol.* 1994;74(6):531-7.
19. Daimon M, Watanabe H, Yamagishi H, *et al*. Physiologic assessment of coronary artery stenosis by coronary flow reserve measurements with transthoracic Doppler echocardiography: comparison with exercise thallium-201 single piston emission computed tomography. J Am Coll Cardiol 2001;37:1310-5.
20. Hozumi T, Yoshida K, Ogata Y, Noninvasive assessment of significant left anterior descending coronary artery stenosis by coronary flow velocity reserve with transthoracic color Doppler echocardiography. Circulation 1998;97:1557-62.
21. Tambe AA, Demany MA, Zimmerman HA, *et al*. Angina pectoris and slow flow velocity of dye in coronary arteries- -a new angiographic finding. Am Heart J 1972;84:66-71.
22. Beltrame JF, Limaye SB, Wuttke RD, *et al*. Coronary hemodynamic and metabolic studies of the coronary slow flow phenomenon. Am Heart J 2003;146:84-90.
23. Sezgin AT, Sigirci A, Barutcu I, *et al*. Vascular endothelial function in patients with slow coronary flow. Coron Artery Dis 2003;14:155-61.
24. Beltrame JF, Ganz P. Evaluating patients with persistent chest pain and no obstructive coronary artery disease. JAMA 302 (6), 622-624 (2009).
25. Fineschi M, Gori T. Coronary slow flow: description of a new "cardiac Y" syndrome. *Int J Cardiol*. 2009;137(3):308-10
26. Arbel Y, Rind E, Banai S, Halkin A, Berliner S, Herz I, *et al*. Prevalence and predictors of slow flow in angiographically normal coronary arteries. Clin Hemorheol Microcirc. 2012;52(1):5-14.
27. Akpinar I, Sayin MR, Gursoy YC, Aktop Z, Karabag T, Kucuk E, *et al*. Plateletcrit and red cell distribution width are independent predictors of the slow coronary flow phenomenon. *J Cardiol.* 2014;63(2):112-8.
28. Kurtoglu N, Akcay A, Dindar I. Usefulness of oral dipyridamole therapy for angiographic slow coronary artery flow. Am J Cardio 2001;87:777-9.
29. Beltrame JF, Turner SP, Leslie SL, *et al*. The angiographic and clinical benefits of mibefradil in the coronary slow flow phenomenon. J Am Coll Cardiol 2004;44:57-62.
30. Gunes Y, Tuncer M, Guntekin U, *et al*. Regional functions of the left ventricle in patients with coronary slow flow and the effects of nebivolol. Ther Adv Cardiovasc Dis 2009;3:441-6.

How to cite this article:

Bandara H.G.W.A.P.L *et al*., 2019 Characteristics of Patients With Coronary Slow Flow Phenomenon; An Experience From Sri Lanka. *Int J Recent Sci Res.* 10(07), pp. 33448-33452. DOI: http://dx.doi.org/10.24327/ijrsr.2019.1007.3673

****