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STUDY ON THE FACTORS INVOLVED IN THE DEVELOPMENT OF CORONARY COLLATERALS IN HYPERTENSIVE AND NON-HYPERTENSIVE PATIENTS OF CORONARY ARTERY DISEASE

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ABSTRACT

Background: Coronary artery disease (CAD) results from the narrowing of coronary arteries that leads to inadequate blood supply to the heart muscles, resulting in Acute Coronary Syndrome (ACS). The coronary collaterals which develop will be an alternative source of blood flow in CAD. Myocardial ischemia stimulates the development of coronary collaterals by releasing various angiogenic growth factors, like the Vascular Endothelial Growth Factor (VEGF). Serum VEGF will serve as an important biomarker in CAD; thus, it can predict coronary collateral development. **Aim:** To study the factors affecting the development of coronary collaterals in hypertensive and non-hypertensive patients with CAD. **Methods:** The study includes 100 patients who have done coronary angiography, with an average age of 60±15. Consent was obtained from all patients, and 2 ml of blood was collected. The serum VEGF concentration and cystatin-C were quantified. Coronary Angiograms, along with other reports, were collected and analyzed. CAD was diagnosed for those with ≥ 70% stenosis inany one of the major coronary artery. Coronary collateral gradings was performed as per Rentrop Scoring system. The serum VEGF and cystatin-C levels were correlated with the collateral scores and other cardiovascular risk factors. **Results:** A significant correlation was found between the collateral scores and serum VEGF level in hypertensive patients only. No significant correlation was found between VEGF level, collateral scores and cardiovascular risk factors. **Conclusions:** Cardiovascular risk factors in turn increase the serum VEGF level, which results in collateral development. Age and sex did not show show any significant association especially old age and females, with serum VEGF levels.

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INTRODUCTION

Coronary artery disease (CAD) is reported to be one of the leading causes of death. CAD has increased during the last four decades [1]. CAD is one of the major causes of death in developing countries like India, accounting for nearly one-third of all deaths [1]. Coronary collateral formation is an alternative conduit for blood flow in CAD [2]. Coronary angiography is the standard method for identifying coronary collaterals [3]. Collaterals connect the epicardial coronary arteries and represent the alternate source of blood to the myocardium in the occlusion of main coronary blood vessels [4]. Collaterals visible in angiograms are anatomically and functionally well-developed [5]. Various studies show that well-developed coronary collaterals reduce mortality [6]. Right and Left Coronary arteries mainly supply blood to the heart. For decades, Coronary arteries were considered end arteries [7]. Recent investigations done on autopsy specimens showed that anastomosis occurs between the branches of coronary arteries both at epicardial and myocardial levels [8]. The functional values of this anastomosis vary but become more effective in progressive pathological conditions when the original artery is affected by occlusive CAD [9]. Collaterals are the alternate blood supply route to the heart during the resting level. They cannot increase blood flow sufficiently in situations of increased myocardial O2 demand. Still, more recent studies in animal models and humans have demonstrated that collaterals can provide sufficient flow during exertion or stress [10]. A coronary angiogram is considered the golden standard for the diagnosis of CAD. Coronary collaterals are traced out using Coronary Angiography [11]. Various studies showed that patients with collateral formation have less mortality when compared to patients without its development [12,13]. Coronary collaterals are crucial for prognostic significance in CAD. This understanding is pivotal for formulating and implementing future therapeutic strategies to treat Coronary Artery Disease effectively.

Myocardial Ischemia causes stimulus to induce coronary collateral development, possibly through various signaling processes [2]. VEGF-A is one of the main growth factors in angiogenesis and arteriogenesis during CAD [14]. Studies show that serum VEGF-A levels are higher in patients with more collaterals and lower in patients with fewer or poor collaterals [15]. Various risk factors are associated with CAD, including gender, age, increased cholesterol level, and blood pressure [16]. This work aims to study the factors affecting the development of coronary collaterals in hypertensive and non-hypertensive patients with CAD and investigate Coronary Artery Morphology's impact on coronary collateral development in patients diagnosed with significant obstructive coronary artery diseases.

MATERIALS AND METHODS

The present study is an observational, Analytical, Cross-sectional study. The sample size was calculated using previous studies of Coronary artery dominance-dependent collateral development in the human heart, with 80% power and 95% confidence**.** The study samples include 100 patients who underwent angiography for two years with symptoms suggestive of coronary artery disease from VIMS Hospital, Salem. Ethical approval for the study was obtained from the Institutional Ethical Committee of Vinayaka Mission's Kirupananda Variyar Medical College & Hospitals, Salem Reference no-VMKVMC&H/IEC/19/44. The study was registered in the Clinical Trial Registry of India reference-REF/2020/09/036448.

Coronary Angiography was performed via percutaneous transfemoral and radial approach, injecting radio-opaque contrast into coronary blood vessels, and the image was taken using x-ray fluoroscopy. These images were recorded in digital media and stored in the cardiac catheterization laboratories. After obtaining their consent, a coronary Angiogram of 100 patients, mean age 60±15 with occlusion ≥ 70%, was selected for the analysis. To avoid confounding data, patients with a history of coronary bypass grafting, PCI, and pulmonary heart disease are excluded from this study. 2ml of blood was withdrawn from the patient (before administration of Nitro-glycerine before angiography), and clinical data and angiograms were collected after getting consent from the patients.

Clinical parameters-Cardiovascular risk Factors

Hypertension was defined as systolic BP ≥140mm of Hg and diastolic BP ≥90 mm of Hg [17]. Hyperlipidaemia was diagnosed according to the guidelines of the National Cholesterol Education Programme (NCEP) [18].

Vascular Endothelial Growth Factors

The VEGF concentration was quantified via the ELISA method using the ELISA kit (Elab sciences) with a Sensitivity of 18.75pg/ml and a Detection Range of 31.25-2000pg/ml. The kit recognizes Human VEGF-A with a Coefficient of verification

<10% in repeatability. The blood samples collected for VEGF analysis are allowed to clot at room temperature and centrifuged for 15 min at 100Xg at 2-8°C, and the supernatant is collected for the assay. This ELISA kit applies to the sandwich-ELISA principle. After adding antibodies specific for Human VEGF A and HRP. The optical density was measured using spectrophotometry, and OD was noted. The Concentration of VEGF –A is calculated. Two consecutive values are taken, and the average value is considered true. The VEGF–A level was compared with the collateral score of CAD patients with cardiovascular risk factors like age, gender, hyperlipidemia, and hypertension.

Coronary angiography and collateral scoring

Coronary angiography was done through the femoral and radial approaches. The angiograms were examined in different planes, and data was documented after a double-blinding procedure by two Interventional cardiologists. 50 eligible patients had significant coronary artery disease in any major coronary artery. Collateral grading uses the Rentrop Scoring system, which involves a four-point scale.

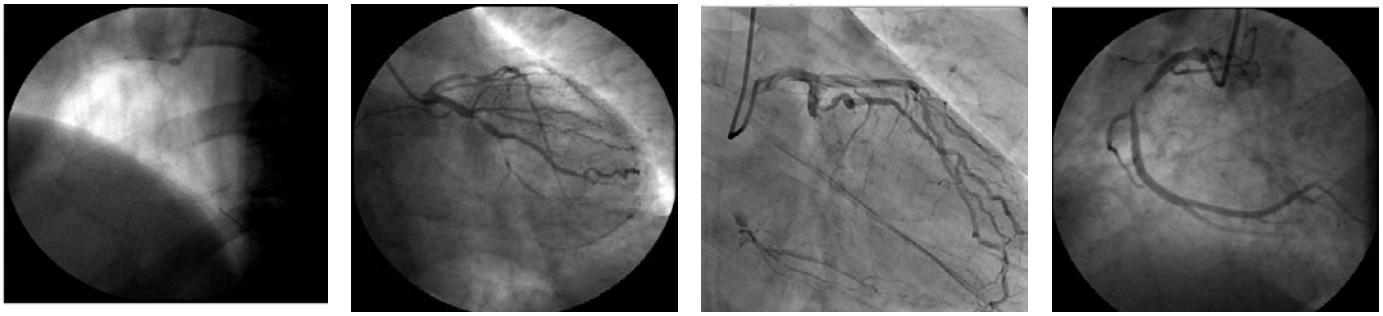
- 0 - absence of visible collaterals,
- 1 - presence of thread-like, poorly opacified collaterals.
- 2 - moderate opacification of collateral channels,
- 3 - denotes high opacification of collateral channels.

Collaterals graded as 0-1 are categorized as having a low collateral score, while those graded as 2-3 are classified as having a high collateral score [18].

Coronary artery Morphology and collateral scoring

A total of 100 angiograms was received from the VIMS, Hospital Salem, for 2 years from 2019 to 2021 after detailed evaluation by interventional cardiologists grouped based on the artery affected. The affected artery blocks of the major artery were divided into 3 proximal, mid & distal segments. The proximal segment of the right coronary artery (RCA) extends from the ostium of the coronary artery to half the distance to the acute branch; the mid-segment extends up to an acute angle of the heart, and the distal segment from the distal end of the mid-segment to the origin of the posterior descending branch. The Left Anterior Descending (LAD) artery is anatomically divided into three segments: Proximal, Mid, and Distal. The Proximal segment spans from the ostium of the LAD to the origin of the first septal branch. The Midsegment extends from the origin of the first septal branch to the origin of the third septal branch, while the Distal segment ranges from the origin of the third septal branch to the apex of the left ventricle. Regarding the Left Circumflex artery, its Proximal segment stretches from the ostium to the origin of the first marginal branch. The Midsegment lies between the origins of the two marginal branches, and the Distal segment extends up to the posterior interventricular groove (Figure 1).

The coronary dominance of either side of the circulation is determined by which artery provides the posterior interventricular artery supplying the diaphragmatic surface. In codominance, branches of both coronary arteries reach the crux of the heart and give rise to the posterior interventricular branch in the posterior interventricular groove. Multivessel disease was determined by the number of significantly diseased coronary arteries. 1VD vessel disease is the presence of significant disease in any of the major arteries. 2VD is considered if any two major arteries have significant disease, and 3VD is considered if any three have significant disease.



Angiogram with grade 0 collateral score	Angiogram with grade 1 collateral score	Angiogram with grade 2 collateral score	Angiogram with grade 3 collateral score

Figure 1: Angiogram with a 4-point scale (Rentrop scoring system)

Statistical Analysis

The differences between groups are analyzed using the Chi-square test and the students' unpaired t-test. P-value<0.05 was taken as significant. The SPSS 20 was used for statistical analysis.

RESULTS

The collected data were analyzed. The p-value of 0.05 is considered a significant level.

Table 1: Age of the study population

	Frequency	Percent
21 - 30 yrs	5	5.0
31 - 40 yrs	15	15.0
41 - 50 yrs	21	21.0
51 - 60 yrs	22	22.0
61 - 70 yrs	29	29.0
Above 70 yrs	8	8.0
Total	100	100.0

The above table shows the distribution of the study population's age, with 29% between 61 and 70 years.

Table 2: Sex of study population

	Frequency	Percent
Female	45	45.0
Male	55	55.0
Total	100	100.0

Table 3: Crosstab - Age * Groups

			Groups		Total
			Cases	Controls	
Age (years)	21 - 30	Count	0	5	5
		%	0	10	5
	31 - 40	Count	1	14	15
		%	2	28	15
	41 - 50	Count	10	11	21
		%	20	22	21
	51 - 60	Count	15	7	22
		%	30	14	22
	61 - 70	Count	19	10	29
		%	38	20	29
	Above 70	Count	5	3	8
		%	10	6	8
Total		Count	50	50	100
		%	100	100	100

Table 3 shows the distribution of age and sex of the study population.

Table 4: Chi-Square Analysis of Age

	Value	df	p-value
Pearson Chi-Square	22.516[a]	5	0.0004

*p - Value, ** Highly Significant at p < 0.01*
p - Value, # No Significant at p > 0.050

Table 5: Crosstab - Sex * Groups

			Groups		Total
			Cases	Controls	
Sex	Female	Count	23	22	45
		%	46.0%	44.0%	45.0%
	Male	Count	27	28	55
		%	54.0%	56.0%	55.0%
Total		Count	50	50	100
		%	100.0%	100.0%	100.0%

Table 6: Chi-Square Analysis of Sex

	Value	df	p-value
Pearson Chi-Square	0.040[a]	1	0.841

*p - Value, ** Highly Significant at p < 0.01*
p - Value, # No Significant at p > 0.050

Table 4 shows the significance of age, whereas table 6 shows the non-significance of sex among the study population

Table 7: CrosstabCystatin C mg/l * Groups

			Groups		Total
			Cases	Controls	
Cystatin C mg/l	1	Count	16	12	28
		%	32.0	24.0	28.0
	2	Count	22	26	48
		%	44.0	52.0	48.0
	3	Count	12	12	24
		%	24.0	24.0	24.0
Total		Count	50	50	100
		%	100	100	100

Table 8:Chi-Square of Cystatin C

	Value	df	p-value
Pearson Chi-Square	0.905[a]	2	0.636

*p - Value, ** Highly Significant at p < 0.01*
p - Value, # No Significant at p > 0.050

Tables 7 & 8 show the non-significance of Cystatin C when analyzed by Pearson Chi-Square. Tables 9 and 10 show that Serum VEGF level was high in patients with Excellent coronary collateral scores but no statistical significance was noted between the grade of collaterals and serum VEGF level

Table 9: Parameters - Group Statistics

Groups		N	Mean	SD
Age	Cases	50	60.14	10.04
	Controls	50	49.80	15.37
Triglycerides mg/dl	Cases	50	103.66	40.33
	Controls	50	187.42	176.05
Cholesterol mg/dl	Cases	50	137.14	62.17
	Controls	50	147.92	51.39
HDL Cholesterol mg/dl	Cases	50	48.38	15.47
	Controls	50	64.67	23.81
LDL Cholesterol mg/dl	Cases	50	80.04	19.77
	Controls	50	77.52	32.08
Cystatin C mg/l	Cases	50	1.92	0.75
	Controls	50	2.00	0.70
VEGF	Cases	50	0.77	0.48
	Controls	50	0.69	0.45

Table 10: Parameters - Independent Samples Test

	Levene's Test for Equality of Variances		t-test for Equality of Means						
	F	Sig.	t	df	p-value	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
								Lower	Upper
Age*	12.56	0.001	3.98	84	0.0001	10.34	2.5958	5.178	15.502
Triglycerides* mg/dl	6.23	0.01	-3.28	54	0.002	-83.76	25.5427	-134.97	-32.56
Cholesterol* mg/dl	0.531	0.47	-.945	98	0.347	-10.78	11.4064	-33.42	11.86
HDL Cholesterol* mg/dl	6.68	0.01	-4.06	84	0.0001	-16.29	4.0155	-24.28	-8.31
LDL Cholesterol* mg/dl	15.73	0.01	.47	82	0.64	2.52	5.3287	-8.08	13.12
Cystatin C* mg/l	1.27	0.26	-.55	98	0.58	-.08	.1452	-.37	.21
VEGF	0.48	0.49	.91	98	0.37	.084	.092289	-.099	.268

**Equal variances not assumed; p - Value, ** Highly Significant at p < 0.01; p - Value, # No Significant at p > 0.050*

Table 11: Baseline characteristic of patients with low and high coronary collateralization

Level of lesion	Control		Case	
	Low collateralization	High collateralization	Low collateralization	High collateralization
Proximal100%	30 (60%)	20 (40%)	40 (80%)	10 (20%)
95-99%	8 (16%)	5 (10%)	10 (20%)	2 (4%)
70-95%	10 (20%)	6 (12%)	8 (16%)	2 (4%)
Middle100%	20 (40%)	18 (36%)	30 (60%)	10 (20%)
95-99%	18 (36%)	5 (10%)	14 (28%)	1 (2%)
70-95%	10 (20%)	18 (36%)	13 (26%)	15 (30%)
Distal100%	30 (60%)	20 (40%)	20 (40%)	20 (40%)
95-99%	0 (0%)	4 (8%)	0 (0%)	3 (6%)
70-95%	0 (0%)	8 (16%)	6 (12%)	4 (8%)
Proximal 100%	34 (68%)	6 (12%)	38 (76%)	7 (14%)
95- 99%	20 (40%)	4 (8%)	24 (48%)	5 (10%)
70-95%	10 (20%)	5 (10%)	15 (30%)	13 26%)
Middle 100%	20 (40%)	8 (16%)	20 (40%)	10 (20%)
95-99%	10 (20%)	12 (24%)	27 (54%)	12 (24%)
70-95%	8 (16%)	4 (8%)	19 (38%)	9 (18%)
Distal 100%	18 (36%)	8 (16%)	38 (76%)	7 (14%)

Level of lesion	Control		Case	
	Low collateralization	High collateralization	Low collateralization	High collateralization
95-99%	0 (0%)	5 (10%)	5 (10%)	3 (6%)
70-95%	0 (0%)	6 (12%)	2 (4%)	4 (8%)
Proximal 100%	30 (60%)	4 (8%)	20 (40%)	10 (20%)
95- 99%	0 (0%)	8 (16%)	8 (16%)	2 (4%)
70-95%	0 (0%)	3 (6%)	1 (2%)	5 (10%)
Middle 100%	18 (36%)	10 (20%)	25 (50%)	10 (20%)
95-99%	5 (10%)	8 (16%)	8 (16%)	4 (8%)
70-95%	0 (0%)	6 (12%)	1 (2%)	6 (12%)
Distal 100%	32 (64%)	5 (10%)	38 (76%)	5 (10%)
95-99%	3 (6%)	2 (4%)	3 (6%)	3 (6%)
70-95%	2 (4%)	0 (0%)	2 (4%)	4 (8%)

Table 12: Coronary Dominance

Coronary Dominance	Control		Cases	
	Low collateralization	High collateralization	Low collateralization	High collateralization
Right coronary	14 (28%)	16 (32%)	32 (64%)	8 (16%)
Left coronary	21 (42%)	6 (12%)	23 (46%)	7 (14%)
Co-dominance	10 (20%)	8 (16%)	12 (24%)	3 (6%)
One vessel disease	32 (64%)	14 (28%)	25 (50%)	8 (16%)
Two vessel diseases	21 (42%)	6 (12%)	22 (44%)	6 (12%)
Three Vessel Disease	34 (68%)	8 (16%)	23 (46%)	18 (36%)

Table 13: Baseline characteristic of patients with low and high coronary collateralization according to sex

Case			Control	
	Low collateralization	High collateralization	Low collateralization	High collateralization
Male	24	3	16	12
Female	13	10	12	10

Tables 11, 12 & 13 show the baseline characteristics of patients with low and high coronary collateralization

DISCUSSION

Coronary collaterals are an alternative source of blood supply to the heart in case of Occlusive CAD [19]. Collateral formation occurs around 12 weeks after occlusion in patients with chronic occlusion [20]. In patients with Acute Coronary occlusion, the time frame for collateral formation is too short [21]. Collateraldecreasesthe risk for infarction prevents cardiogenic shock, mainly in patients where the risk increases with an increase in the number of Cardiovascular risk factors [22].

Age

Previous studies show that the development of coronary collaterals was found to be excellent in patients >60 compared to patients ≤60 years of age [23]. The prevalence of well-developed collaterals in the younger age group when compared to the old age group (≤60 years) was reported by Pohl et al. [24], which is similar to the above findings. Nakae et al. suggested in their studies that collateral pathways develop more efficiently in young aged patients [25], which is supported by the studies made by Balci [26], suggesting that the total number of collateral pathways decreases with aging in older patients. According to other data, High-grade collaterals were significantly higher in middle-aged individuals compared to the elderly [27]. Sun et al. suggested that collateral development is less in patients older than >60 years. In the present study no significant association was found with the age and level of collateral development,

which supports the studies done by Fujita [28] that collateral development is not related to age. Furthermore, van der However et al. in their study, divided the patients into two groups (≤64 years and ≥65 years) and found no association between higher age and the development of poor collaterals [29].

Gender

Studies by Ajayi et al. suggested that in the collateral development, there was no significant association between the coronary collaterals and gender [23]. Fujita [28] and Sun et al. [18]. suggested in his study that there is a significant difference in collateral development in males compared to females, and fewer collaterals are developed in females compared to males, but still, some studies show that collateralization is more in females with multi-vessel disease [30]. In this study, no significant difference is noted in the prevalence of collaterals between males and females. Therefore, there is no association between gender and level of collateral development.

Morphological features

a) Artery affected

In the study conducted by Ajayi et al. [23] and Elsman et al. [31]. showed that in patients with occlusion of RCA, there was a good response to the development of coronary collaterals, similar to that of a study by Zhen Sun et al. [18]. The collateral formation on the left coronary artery is attributed to the larger size of the left artery than the right one. The degree of coronary collateral formation primarily hinges on the extent of atherosclerosis, and a comparison of collateral formation is typically conducted across three major arteries at the same occlusion level. Approximately 50% of cases involve infarction due to LADS occlusion, while 30% involve the RAC, and 20% involve the LCA [32]. However, no significant disparity is observed in collateral formation levels among the three major coronary arteries with identical occlusion levels.

b) Level of lesion

Moreover, the level of lesion plays a substantial role in collateral development. The formation of collaterals in the occluded artery correlates with the donor artery's distribution extent and the occlusion's chronicity. Larger collateral channels tend to form in cases of complete thrombolytic occlusion. The pressure differentials between the proximal and distal segments of the occluded artery induce significant stress, prompting increased collateral formation levels [33].

An increase in flow rate and shear stress in the existing collateral arteries cause endothelial activation and an increase in monocyte adhesion and their transformation into the macrophages, which cause morphological changes and remodeling [34]. Piek et al. [35] suggested in their studies that the proximal location of the lesions is an important predictor of collateral development. Ajayi et al. [36]. Supported this by explanation, as proximal location results in an increase in shear stress and lowers the threshold for the formation of myocardial ischemia, it stimulates the collateral formation. In this study, a significant change in the collateral formation is based on the level of occlusion. This study noted a significant effect on the level of occlusion and collateral formation. The present study also shows a significant association between the proximal location of the lesions in LAD and LCA, possibly due to the larger size of the artery, and no significant association was seen in the Right coronary artery.

c) Coronary dominance

The dominance is set according to the coronary artery that supplies the posterior interventricular artery. The most common is right dominance, and left dominance is seen only in a few cases. The two arteries are codominant in nearly 10% and 15% of cases [37]. Few studies have been conducted on the effect of coronary dominance and collateral development. Studies were done by Ajayi et al. [23]. This shows the prevalence of excellent collaterals in patients with a right coronary arterial dominant pattern rather than a left coronary dominant pattern. This study noted no significant association between coronary dominance and collateral formation.

d) Level of disease

The process of angiogenesis is mediated by an increase in the shear stress. If the hemodynamically relevant stenosis is found between the two arteries, a pressure gradient is created, which causes collateral formation. A study done on 21 patients with multivessel disease by Zhi Liu et al. [38] found a close relationship between the severity of the disease and collateral grade. In multivessel disease, it was found that the level of ischemia that the organ sensitizes is much higher in Multivessel disease compared to two-vessel and 1-vessel disease. The low collaterization was noticed in patients with single-vessel disease. In this study, it is noticed that the chi-square p-value is <0.001, which is considered a significant value to find an association between the level of disease and grade of collateral formation

The study was conducted to know the effect of cardiovascular risk factors like age, Gender, Diabetes mellites, Hypertension, and Hyperlipidaemia on collateral score and serum VEGF-A level in patients with Acute coronary syndrome. In the above study, an increase in the level of serum VEGF-A was noted in patients with good collateral scores, but a statistically significant association was not found between the serum VEGF level and collateral score. Zhen found that collateral formation is less in females and reduces with increasing age [23]. But in the above study no significant association was found between age and gender on collateral score with serum VEGF-A level.

Glycated hemoglobin results from the one-way-enzymatic chemical binding of glucose to the protein chain of Haemoglobin in Erythrocytes. It reflects the average plasma glucose concentration and serves as a marker for between 4 weeks and 3 months in 97% of patients with dyslipidemia. A high glucose level causes endothelial dysfunction, which is important for coronary collateral formation [18]. The Fluid shear stress is sensed by the endothelium, which responds to the changes in the expression of Vascular Endothelial growth factors that cause arterial remodeling. Angiogenesis, defined as true capillary formation from pre-existing ones, can only partly contribute to enhanced tissue perfusion. Functional collateral vessels are formed from pre-existing ones by a process best described by Arteriogenesis [39, 40]. VEGF induces migration and proliferation of endothelial cells (ECs) and is considered a unique angiogenic growth factor [41]. Even though VEGF acts as a specific mitogen that induces monocyte activation and migration, studies show a biologically relevant concentration increase in serum VEGF-A during Myocardial Ischemia capable of stimulating the proliferation of Endothelial cells. It was found that VEGF-A serum level is enhanced in a situation where collateral formation is induced. Time course elevation in serum VEGF-A after myocardial infarction shows that it has a major role in activating collateral formation [42]. In this study, it is observed that hypertension correlates negatively with the development of collaterals and the level of serum VEGF-A, and a significant association was found between the serum VEGF level and coronary collateral formation. Hence, Diabetes can be considered an independent predictor of poorly developed collateral circulation [43]. Contrary to the above findings, some studies show little difference in collateral formation between diabetic and non-diabetic patients [44]. Wang et al. found that elevated diastolic blood pressure is related to high coronary collateralization by altering blood flow velocity in diastole and tangential fluid shear stress on the endothelial surface [45]. The present study found a significant association between the serum VEGF-A level and collateral score in patients with hypertension. It was found that collateral score and Serum VEGF-A level are higher in patients with hypertension, contrary to de Marchi [46 - 51] et al., who suggested better collateral formation in the absence of arterial hypertension. No significant association was found in the above study between the Serum VEGF level and collateral score in patients with dyslipidemia.

CONCLUSION

Collaterals decrease the risk of infarction and prevent cardiogenic shock in patients with Acute myocardial infarction. Increasing the serum VEGF - A causes improvement in the formation of collaterals. A vast difference was noted in the development of coronary collaterals in hypertensive and non-hypertensive patients. Impaired VEGF-A causes monocyte migration, which is disturbed in hypertension and has low collateralization. However, hypertension causes an increase in serum VEGF-A level by increasing the fluid shear stress, which in turn increases the remodeling pressure and collateralization level. The above findings can be considered a prognostic determinant of vascular outcome and risk stratification in revascularization treatment and considered during effective methods of understanding and employing therapeutic strategies for preventing the events in patients suffering from CAD with advanced coronary atherosclerosis. A significant association was recorded between the proximal level of occlusion in the left anterior descending and left circumflex artery and the grades of collateral formation. The level of disease has a positive synergistic effect on collateral development. However, there is not much difference in the development of collaterals based on the artery affected and coronary dominance. These findings can be considered as the prognostic determinants of vascular outcome and considered during effective methods of understanding and employing therapeutic strategies for preventing the events in patients suffering from CAD.

Limitations of the study:

A few parameters of the study were not statistically significant, as the difference based on the location of the blockage (left vs right coronary artery), the trend suggests better outcomes in the left. If a larger sample size was taken and analyzed, it might reveal a statistically significant difference. Future studies can be

done to investigate the underlying mechanisms behind better collateral development with proximal blockages.

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FINANCIAL ASSISTANCE
Nil

CONFLICT OF INTEREST
The authors declare no conflict of interest

AUTHOR CONTRIBUTION
Senthil Kumar B conceptualized the whole study and design and also contributed to data collection. Sheeja Balakrishnan analysed and interpreted the results. Sheeja Balakrishnan and G. Yuvabalakumaran contributed to preparing the first draft of the manuscript. Senthil Kumar B, Kouser Banu Khaleeluddin, and K. Ezhil Vendhan checked the manuscript. did the corrections in the final draft. All the above authors reviewed the results and approved the final version of the manuscript.

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