

# A Study on Usefulness of Flow Mediated Vasodilatation of Brachial Artery in Assessing the Severity of Coronary Artery Disease and its Correlation with Coronary Angiogram

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## ABSTRACT

**Introduction:** The endothelium is a special tissue that releases numerous substance that moderates tone of the vascular bed, growth of cells, platelet and WBC interactions. Significantly, the evolution of atherosclerosis occurs much early in life, and endothelial dysfunction accelerates atherosclerosis and occurs much before the development of morphological changes in the vascular bed. Hence; the present study was undertaken for assessing the usefulness of flow mediated vasodilatation of brachial artery in assessing the severity of coronary artery disease and its correlation with coronary angiogram.

**Material and methods:** A total of 75 subjects were enrolled. Group A included 18 subjects with non-critical CAD, Group B included 33 subjects with SVD, Group C included 8 subjects with DVD and Group D included 16 subjects with TVD. Complete demographic and clinical details were obtained. All patients who have been diagnosed having coronary artery disease which includes chronic stable angina, ST elevation MI, non ST elevation MI, unstable angina within the last 1month and have undergone CAG. Patients were subjected to symptom analysis, clinical examination, laboratory investigations and flow mediated vasodilation studies of brachial artery. All the results were analysed by SPSS software.

**Results:** By conventional criteria the association between the study groups and smoking is considered to be not statistically significant since  $p > 0.05$ . There was meaningfully real increase in severity of CAD as duration of smoking increases in our study subjects. By conventional criteria the association between the study groups and alcoholism is considered to be not statistically significant since  $p > 0.05$ . The diabetic status in non-critical CAD group is meaningfully less than DVD group by 1.15 times with a mean difference of 8 percentage points. By conventional criteria the association between the study groups and brachial artery resting diameter status is considered to be not statistically significant since  $p > 0.05$ . There was meaningfully real increase in severity of CAD as Increase in FMD % decreases in our study subjects.

**Conclusion:** Apart from assessing the traditional cardiovascular risk factors, it is also important to assess the endothelial function of the patient by methods like FMD.

**Keywords:** Flow mediated vasodilatation, Coronary artery

responds to various internal and external stimuli via complicated receptors in cell membrane and mechanisms of signal transduction, leading to the formation and discharge of various vascular active hormones and factors. The ability of blood vessels to react to physical and biochemical stimuli in the blood flow and circulation in response to changes in the local surroundings. Various blood vessels react to an amplification in flow or more accurately stress, by dilation. This process is defined as flow mediated vasodilatation. A primary mediator of FMD is nitric oxide derived from endothelium. This property of endothelium could be used for risk evaluation.<sup>1-3</sup>

Usually, loss of nitric oxide (NO) bio function denotes a widely dysfunctional phenotype across endothelial properties. Hence, the evaluation of its vasodilating property as a result of NO and various other molecules could offer knowledge on the reliability and utility of the endothelium. Surprisingly, cardiovascular risk factors are related with dysfunction of endothelium and risk factor alteration leads to enhancement in vascular function. Endothelial dysfunction has been found out in the coronary epicardial and resistance vessels and in the arteries of periphery, so endothelial dysfunction could be considered as a systemic condition.<sup>4,5</sup> Significantly, the evolution of atherosclerosis occurs much early in life, and endothelial dysfunction accelerates atherosclerosis and occurs much before the development of morphological changes in the vascular bed.<sup>6-9</sup> Hence; the present study was undertaken for assessing the usefulness of flow mediated vasodilatation of brachial artery in assessing the severity of coronary artery disease and its correlation with coronary angiogram.

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## INTRODUCTION

The endothelium is a special tissue that releases numerous substance that moderates tone of the vascular bed, growth of cells, platelet and WBC interactions. The endothelium

## MATERIAL AND METHODS

The present study was conducted in the department of cardiology, cardiology OPD, medical wards and IMCU at Stanley medical college and hospital, Chennai. A total of 75 patient's data was enrolled in the present study and were divided into different study groups as shown in Table 1. Group A included 18 subjects with non-critical CAD, Group B included 33 subjects with SVD, Group C included 8 subjects with DVD and Group D included 16 subjects with TVD. Patients diagnosed with coronary artery disease within 1 month and have undergone coronary angiogram from the period January 2014 to September 2014 in ICCU/ cardiology wards were included in the study. Patients were subjected to symptom analysis, clinical examination, laboratory investigations and flow mediated vasodilation studies of brachial artery. The final analysis was made at the end of the study to achieve the fore mentioned goals using appropriate statistical methods.

### Inclusion Criteria

All patients who have been diagnosed having coronary artery disease which includes chronic stable angina, ST elevation MI, non ST elevation MI, unstable angina

Treatment Groups	Name of Group	Number of Subjects
Group A	Non Critical CAD	18
Group B	SVD	33
Group C	DVD	8
Group D	TVD	16

**Table-1:** Group wise distribution

within the last 1month and have undergone CAG.

All patients who have undergone primary/ facilitated PCI within the above mentioned time.

Patients between 20 and 60 years of age.

### Exclusion Criteria

Patients with any form of connective tissue disorder, chronic kidney disease, Chronic liver disease

Any patient < 20 and > 60 yrs of age.

All the results were recorded in Microsoft excel sheet and were analysed by SPSS software. Chi- square test, ANOVA and student t test were used for assessment of level of significance.

## RESULTS

By conventional criteria the association between the study groups and smoking is considered to be not statistically significant since  $p > 0.05$ . By conventional criteria the association between the study groups and duration of smoking levels among study subjects is considered to be statistically significant since  $p < 0.05$ . The average duration of smoking in non-critical CAD group is meaningfully less than SVD group by 1.92 times with a mean difference of 1.85 years. The average duration of smoking in non-critical CAD group is meaningfully less than DVD group by 2.16 times with a mean difference of 2.33 years. The average duration of smoking in non-critical CAD group is meaningfully less than TVD group by 11.75 times with a mean difference of 21.50 years. There is meaningfully real increase in severity of CAD as duration of smoking increases in our study subjects. By conventional criteria the association between the study

Smoking	Non Critical CAD	%	SVD	%	DVD	%	TVD	%
Smoking -	14	77.78	18	54.55	2	25.00	2	12.50
Smoking +	4	22.22	15	45.45	6	75.00	14	87.50
Total	18	100	33	100	8	100	16	100
chi-square statistic	6.89							
degrees of freedom	3							
P value Chi Squared Test	0.142							

**Table-2:** Smoking

Alcoholism	Non Critical CAD	%	SVD	%	DVD	%	TVD	%
Alcoholism -	17	94	23	70	7	88	16	100
Alcoholism +	1	6	10	30	1	13	0	0
Total	18	100	33	100	8	100	16	100
chi-square statistic	10.1							
degrees of freedom	3							
P value Chi Squared Test	0.308							

**Table-3:** Alcohol habit

Hypertension	Non Critical CAD	%	SVD	%	DVD	%	TVD	%
Normal	7	39	23	70	6	75	11	69
Hypertensive	11	61	10	30	2	25	5	31
Total	18	100	33	100	8	100	16	100
chi-square statistic	9.25							
degrees of freedom	3							
P value Chi Squared Test	0.055							

**Table-4:** Hypertension

groups and alcoholism is considered to be not statistically significant since  $p > 0.05$ . By conventional criteria the association between the study groups and duration of alcohol intake is considered to be not statistically significant since

Diabetes	Non Critical CAD	%	SVD	%	DVD	%	TVD	%
Normal	10	56	15	45	3	38	4	25
Diabetic	8	44	18	55	5	63	12	75
Total	18	100	33	100	8	100	16	100
chi-square statistic		14.5						
degrees of freedom		3						
P value		0.006						

**Table-5: Diabetes**

LDL	Non Critical CAD	%	SVD	%	DVD	%	TVD	%
≤ 90 mg/dl	10	56	9	27	2	25	6	38
91 to 100 mg/dl	5	28	6	18	4	50	5	31
101 to 110 mg/dl	3	17	16	48	2	25	5	31
> 110 mg/dl	0	0	2	6	0	0	0	0
Total	18	100	33	100	8	100	16	100
P value ANOVA		0.02561195						

**Table-6: LDL correlation**

HDL	Non Critical CAD	%	SVD	%	DVD	%	TVD	%
≤ 40 mg/dl	7	39	15	45	6	75	4	25
41 to 50 mg/dl	10	56	18	55	2	25	12	75
51 to 60 mg/dl	1	6	0	0	0	0	0	0
> 110 mg/dl	0	0	0	0	0	0	0	0
Total	18	100	33	100	8	100	16	100
P value ANOVA		0.554489079						

**Table-7: HDL correlation**

LVEF(%)	Non Critical CAD	%	SVD	%	DVD	%	TVD	%
≤ 40%	0	0	0	0	0	0	5	50
41 to 50%	0	0	0	0	29	88	5	50
51 to 60%	10	63	8	100	4	12	0	0
> 60%	6	38	0	0	0	0	0	0
Total	16	100	8	100	33	100	10	100
P value ANOVA		0.0000						

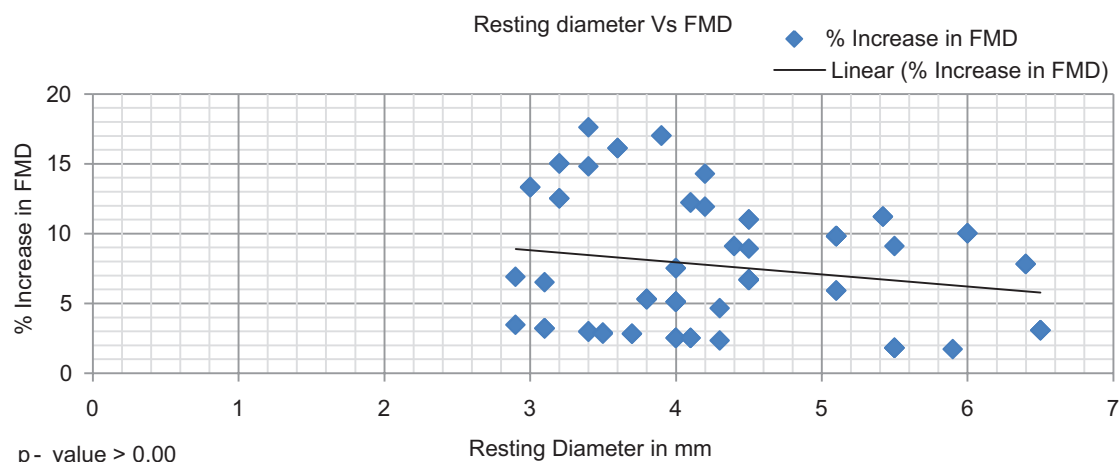
**Table-8: LVEF correlation**

Brachial artery resting diameter	Non Critical CAD	%	SVD	%	DVD	%	TVD	%
≤ 4 mm	14	78	9	27	5	63	9	56
4 to 5 mm	1	6	12	36	3	38	1	6
5 to 6 mm	2	11	11	33	0	0	3	19
> 6 mm	1	6	1	3	0	0	3	19
Total	18	100	33	100	8	100	16	100
P value ANOVA		0.092547156						

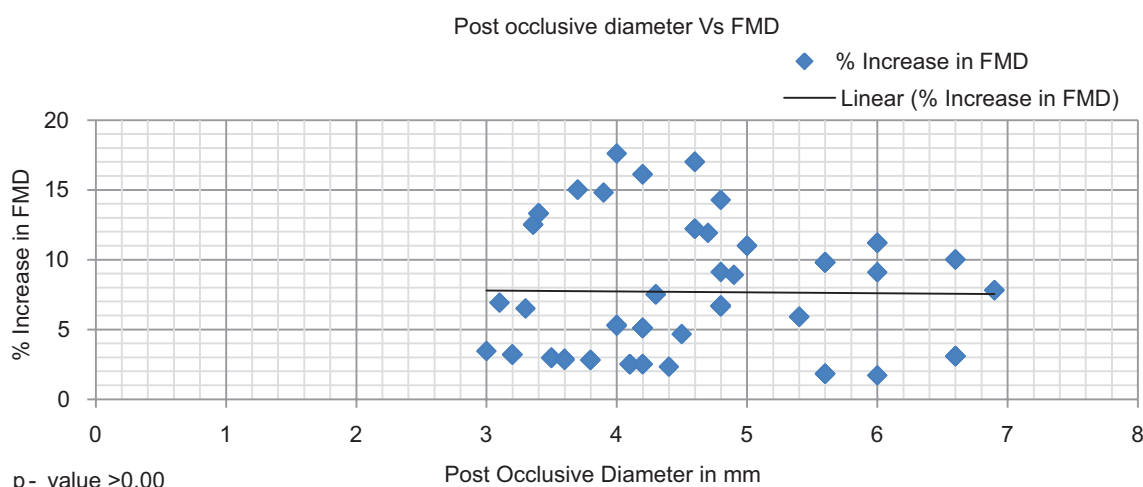
**Table-9: Brachial artery resting diameter correlation**

Post occlusive diameter	Non Critical CAD	%	SVD	%	DVD	%	TVD	%
≤ 4 mm	8	44	5	15	5	63	6	38
4 to 5 mm	7	39	16	48	3	38	4	25
5 to 6 mm	2	11	9	27	0	0	3	19
> 6 mm	1	6	3	9	0	0	3	19
Total	18	100	33	100	8	100	16	100
P value ANOVA		0.54579025						

**Table-10: Post occlusive diameter**



**Graph-1:** Resting diameter



**Graph-2:** Post occlusive diameter

$p > 0.05$ . By conventional criteria the association between the study groups and hypertension status is considered to be not statistically significant since  $p > 0.05$ . By conventional criteria the association between the study groups and diabetes status levels among study subjects is considered to be statistically significant since  $p < 0.05$ . The diabetic status in non-critical CAD group is meaningfully less than SVD group by 1.22 times with a mean difference of 10 percentage points. The diabetic status in non-critical CAD group is meaningfully less than DVD group by 1.15 times with a mean difference of 8 percentage points. The diabetic status in non-critical CAD group is meaningfully less than TVD group by 1.2 times with a mean difference of 13 percentage points. This difference is true and significant and has not occurred by chance. Meaningfully real increase in severity of CAD in relation to diabetic status in our study subjects. By conventional criteria the association between the study groups and duration of diabetes among study subjects is considered to be statistically significant since  $p < 0.05$ . By conventional criteria the association between the study groups and LDL levels among study subjects is considered to be statistically significant since  $p < 0.05$ . By conventional criteria the association between the study groups and HDL status is considered to be not statistically significant since

$p > 0.05$ . By conventional criteria the association between the study groups and LVEF% among study subjects is considered to be statistically significant since  $p < 0.05$ . There is meaningfully real increase in severity of CAD as LVEF% decreases in our study subjects. By conventional criteria the association between the study groups and brachial artery resting diameter status is considered to be not statistically significant since  $p > 0.05$ . By conventional criteria the association between the study groups and post occlusive diameter status is considered to be not statistically significant since  $p > 0.05$ . There is a negative correlation between resting diameter and FMD. This is indicated by the Pearson's R Correlation value of  $-0.1869$  with a  $p$ -value of  $0.0000$ . This means as resting diameter increases the percentage increase in FMD decreases in our study subjects. There is a positive correlation between post occlusion diameter and FMD. This is indicated by the Pearson's R Correlation value of  $-0.0148$  with a  $p$ -value of  $0.0000$ . This means as post occlusion diameter increases the percentage increase in FMD increases in our study subjects. By conventional criteria the association between the study groups and Gensini scores among study subjects is considered to be statistically significant since  $p < 0.05$ . There is meaningfully real increase in severity of CAD as Increase in FMD % decreases in our study subjects.

## DISCUSSION

Variations in myocardial blood flow could be utilised as a stand-in factor for micro vascularity. Coronary blood flow reserve is calculated by using the numerator as maximal coronary blood flow during maximal coronary hyperaemia divided by the resting coronary blood flow. This optimal flow response process is both endothelium- and non-endothelium-dependent, and a coronary blood flow reserve capacity ratio  $<2.0$  is taken as not normal. The quantification of microvascular function which is dependent on endothelium, the percentage rise in coronary blood flow in reaction to vasodilators (acetylcholine) administered at rising titre is monitored. Numerous ways to quantify microvascular function have been used, example with proximal injection of contrast the amount of cineangiographic frames that will take to fill a distal most vessel is measured.<sup>8-13</sup>

In the present study, the diabetic status in non-critical CAD group is meaningfully less than SVD group by 1.22 times with a mean difference of 10 percentage points. The diabetic status in non-critical CAD group is meaningfully less than DVD group by 1.15 times with a mean difference of 8 percentage points. The diabetic status in non-critical CAD group is meaningfully less than TVD group by 1.2 times with a mean difference of 13 percentage points. Sancheti S et al studied whether endothelial dysfunction determined by FMD of brachial artery predicts the presence or absence of coronary artery disease and its correlation with the severity of coronary artery disease. One hundred six patients admitted between May 2014 and April 2015 who were posted for coronary angiography diagnosed to have chronic stable angina on clinical basis and/or by exercise stress test, for evaluation of coronary artery disease were submitted to standard clinical evaluation, calculation of percentage FMD by Angiodefender device. There was no correlation between number of risk factors and percentage of FMD. Significantly higher proportion of cases with less FMD had higher prevalence of coronary artery disease and vice-versa. Significantly higher proportion of cases with positive stress test had less percentage of FMD and vice-versa. Significantly higher proportion of cases with less percentage of FMD and positive stress test had higher prevalence of obstructive coronary artery disease and vice-versa. Specificity was 100% when percentage of FMD was  $\leq 10$ . FMD an inexpensive and non-invasive test provides information regarding extent and severity of coronary artery disease.<sup>14</sup>

In the present study, by conventional criteria the association between the study groups and LDL levels among study subjects is considered to be statistically significant since  $p < 0.05$ . By conventional criteria the association between the study groups and HDL status is considered to be not statistically significant since  $p > 0.05$ . By conventional criteria the association between the study groups and LVEF% among study subjects is considered to be statistically significant since  $p < 0.05$ . This means as resting diameter increases the percentage increase in FMD decreases in our study subjects. There is a positive correlation between post occlusion

diameter and FMD. This is indicated by the Pearson's R Correlation value of  $-0.0148$  with a p-value of 0.0000. There is meaningfully real increase in severity of CAD as Increase in FMD % decreases in our study subjects. Tandon S et al assessed endothelial function by brachial artery flow mediated vasodilatation and its association with coronary artery disease. Two hundred and forty-one individuals comprising of 101 patients with CAD (angiographically proven, or with history of documented myocardial infarction) and 140 individuals without CAD were included in the study. All subjects underwent clinical evaluation, fasting lipid profile, treadmill test and FMD assessment. Selected individuals underwent coronary angiography too. Brachial artery diameter and Doppler indices (systolic and diastolic velocity time integrals) were recorded using high resolution ultrasonography at baseline, immediately after and at one minute after release of cuff (occlusion time 5 minutes). FMD was calculated as percentage increase in brachial artery diameter at one minute. FMD index was calculated as the ratio of FMD and percentage increase in flow during reactive hyperaemia. Mean FMD was significantly higher in non-CAD group ( $8.71 \pm 4.77\%$ ) than in CAD group ( $3.77 \pm 2.03\%$ ;  $p < 0.0001$ ). The FMD index was also significantly higher in the non-CAD group (0.031) than in CAD group (0.021;  $p = 0.0117$ ). On multiple regression analysis, FMD index was found to be significantly associated with presence of CAD ( $p = 0.0015$ ), independent of conventional cardiovascular risk factors. Endothelial function as assessed by FMD is significantly depressed in patients with established CAD and this association is independent of presence of conventional cardiovascular risk factors.<sup>15</sup>

## CONCLUSION

Apart from assessing the traditional cardiovascular risk factors, it is also important to assess the endothelial function of the patient by methods like FMD. It is very clear the physiological alteration (endothelial dysfunction) in the body due to atherosclerosis, diabetes and other risk factors occur much before the structurally evident changes like plaques. FMD could be used as a tool to determine the endothelial function of the patients very early in the course natural history of CAD.

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