



## A Prospective Study of Prevalence of Carotid Artery Disease in Patients with Coronary Artery Disease and its Correlation with Traditional Atherosclerotic Risk Factors in Central India

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### Abstract

**Introduction:** Early atherosclerosis mainly involves carotid artery, which leads to increased carotid artery intima media thickness (CIMT). The potential value of CIMT improving the predictive capacity of traditional risk factors of CAD is an understudied and underutilized issue. Because of increasing availability of highly sensitive ultrasonography probes and for a noninvasive procedures, we can predict coronary artery disease (CAD) more precisely in patients having multiple traditional risk factors so it may reduce morbidity and mortality due to CAD and elevated CIMT can be used as surrogate marker of underlying CAD.

**Methods:** This study enrolled 250 admitted patients as a case of CAD. The patients were assessed by detailed history taking, thorough clinical examination, measurement of CIMT, blood sugar and lipid level.

**Results:** Carotid artery disease was present in 88 (35%) of 250 CAD patients. All modifiable cardiovascular risk factors were statistically significantly high in patients of CAD with carotid artery disease. In obese, diabetic, hypertensive, dyslipidemia and smoker patients, carotid artery disease was present in 55% (P = 0.00), 41% (P = 0.00), 43% (P = 0.007), 47% (P = 0.002) and 43% (P = 0.003) respectively. CAD patients who had 1 risk factor, 29% were associated with carotid artery disease. Comparison of single risk factor with patients who had no risk factor, there was non-significant correlation for carotid artery disease. CAD patients who had 2, 3, 4 and 5 risk factors, carotid artery disease was present 24 (32%) (p = 0.02), 15 (55%) (P = 0.0003), 17 (61%) (P = 0.00006) and 6 (67%) (P = 0.0008).

**Conclusion:** elevated CIMT can be used as one of the important risk factor for early diagnosis of CAD and to reduce morbidity and mortality due to CAD.

## INTRODUCTION

Ischemic heart disease and ischemic stroke are common entities that share a common pathophysiology, based on atherosclerosis. Their pathogenesis involves inflammation in the vessel wall [1]. It mainly involves

large and medium size arteries that occlusion of them may lead to reduced blood supply to the specific area causing wide spread clinical features. In the artery, atherosclerosis affect mainly tunica media, by which

tunica intima and some part of tunica media encroaching to the vessel lumen leads to stenosis of vessels lumen and occludes blood flow to the supplying area. The measurement of carotid intima media thickness (CIMT) is a well-established surrogate cardiovascular risk marker. Reports suggest that the common carotid artery and internal carotid artery have higher adjusted relative risk for coronary artery disease (CAD) and stroke predilection [2].

Since treadmill testing and trans-thoracic 2D echocardiography can have limited specificity and sensitivity in diagnosing coronary artery disease, other methods are required [3]. This applies especially to patients with atypical angina or with typical angina accompanied by a negative treadmill test (TMT) and normal 2D echocardiography, at the same time reflecting an overall need for an introduction of new complementary diagnostic instruments. The development of Doppler ultrasonography (USG) machines, advanced operating software, high resolution transducers, low cost and non-invasive procedures facilitate comprehensive analysis of the CIMT. Thickening of the intima-media is commonly recognized as the initial stage in the development of atherosclerosis. Myocardial infarction (MI) or other acute coronary syndromes are the first symptom of CAD in more than 50% of all patients with cardiovascular disease. Thus, early detection of CAD may well prove to be instrumental in introducing effective diagnosis and treatment, and may contribute to reducing morbidity and mortality, for example, through plaque stabilization and more aggressive control of atherosclerotic risk factors [4, 5]. The impact of hypertension (HTN), diabetes mellitus (DM), dyslipidemia, cigarette smoking and obesity in CIMT has already been well-established in several studies [6].

A more aggressive approach to prevention and treatment of both modifiable and emerging risk factors is warranted in the Asian Indians. Although CAD is high prevalent and highly fatal disease with no known cure, it is also highly predictable, preventable, and treatable with the existing knowledge. As per our knowledge this was the first study done in central India, in which we evaluated the carotid artery disease in CAD patients and also various cardiovascular risk factors for carotid artery disease in CAD patients.

## METHODS

A cross section observational study was carried in the Department of Medicine, M.G.M. Medical College, Indore, Madhya Pradesh, India, during period of March 2017 to February 2018. The study was approved by Ethical Committee of M.G.M. Medical College, Indore, Madhya Pradesh, India. The study was performed on 250 CAD patients admitted in Intensive Cardiac Care Unit (ICCU) and medical wards under Department of Medicine.

## Eligibility Criteria

All consecutive patients with CAD attending cardiology services in ICCU and medical wards, who provided informed valid written consent for participation.

## Exclusion Criteria

Patients not given consent, below 18 years of age, diagnosed case of chronic kidney disease and chronic liver disease have been excluded from this study.

## Criteria for diagnosis of DM

Diabetes Mellitus was defined on the basis of serum fasting glucose levels  $\geq 126$  mg/dl and/or serum post prandial 2 hour glucose level  $\geq 200$  mg/dl or HBA1c  $\geq 6.5\%$  or insulin or oral anti-diabetic drugs treatments.

## Criteria for Diagnosis of HTN

Systolic BP  $\geq 130$  mm of Hg and/or Diastolic BP  $\geq 80$  mm of Hg or on antihypertensive drugs.

## Diagnosis of Dyslipidemia

Serum high density lipoprotein level  $< 50$  mg/dl for male and  $< 40$  mg/dl for female and/or Serum Triglyceride level  $> 150$  mg/dl, and/or Serum low density lipoprotein level  $> 130$  mg/dl, and/or Lipid lowering therapy.

Criteria for diagnosis of Obesity

BMI  $\geq 25$  kg/m<sup>2</sup> was considered as obese.

## Definition of Smoker

Patient who smoke  $\geq 5$  cigarettes per day for  $\geq 1$  year.

## Diagnosis of Coronary Artery Disease

Angiographically proven CAD and/or Typical angina pain with ECG changes of myocardial infarction and more than 99th percentile elevation of upper limit of troponin I. Other angina mimickers were ruled out by appropriate clinical evaluation and diagnostic test.

## Assessment for Carotid Artery Disease

Left common carotid artery duplex color Doppler was done followed by right using highly sensitive linear probe of 7.5 to 12 MHz with ACUSON S3000 machine. The CIMT values were calculated by direct measurement of thickness between inner part of intima to outer part of media in a uniform thickness length of at least 1cm at CCA. Mean CIMT value was calculated from right and left CCA. A mean CIMT value more than 0.8mm was considered as elevated CIMT and it was considered as carotid artery disease.

## Definition of Carotid Artery Disease

Carotid artery disease was considered when CIMT value  $> 0.8$  mm.

## Statistical Analysis

The discrete data were assessed in number and percent. Chi-square test was used for determining the correlation between carotid artery disease and various atherosclerotic

risk factors. P value (2 sided) < 0.05 represents statistical significance. Mean Whitney U test was used for ordinal data. Statistical significance was assessed by Statistical Package for Social Science (SPSS) version 10.

## RESULTS

This study was conducted in 250 consecutive CAD patients attending MYH, Indore, for cardiology services. As shown in Table 1, a total of 250 patients of CAD, mean age  $59.32 \pm 12.25$  year (mean  $\pm$  SD), were enrolled in this prospective study. Carotid artery disease was present in 88 (35.2%) of 250 patients. The commonest age group of carotid artery disease (12.8%) was between 61-70 years of age. In age group 18-30, 31-40, 41-50, 51-60, 71-80 and more than 80 years, carotid artery disease was present in 0 (0%), 4 (1.6%), 10 (4%), 26 (10.4%), 12 (4.8%) and 4 (1.6%) respectively.

**Table 1.** Age Wise Distribution of Carotid Artery Disease

Age group, y	Number of patients	Carotid artery disease	
		Present	Absent
18-30	5	0 (0)	5 (2)
31-40	18	4 (1.6)	14 (5.6)
41-50	39	10 (4)	29 (11.6)
51-60	69	26 (10.4)	43 (17.2)
61-70	83	32 (12.8)	51 (20.4)
71-80	29	12 (4.8)	17 (6.8)
> 80	7	4 (1.6)	3 (1.2)
<b>Total</b>	<b>250</b>	<b>88 (35.2)</b>	<b>162 (64.8)</b>

Data are presented as No. (%)

**Table 2.** Relationship between Risk Factors and Carotid Artery Disease

Risk factor	Number of patients	Carotid artery disease		P value
		Present	Absent	
HTN	110	52 (47)	58 (53)	0.007
DM	80	33 (41)	47 (59)	0.002
Smoking	77	34 (43)	43 (57)	0.003
Dyslipidemia	84	33 (39)	51 (61)	0.002
Obesity	54	30 (55)	24 (45)	0.008

DM = Diabetes Mellitus, HTN = Hypertension

Data are presented as No. (%)

As shown in Table 2, obesity, hypertension, DM, smoking and dyslipidemia was present in 54 (21.6%), 110 (44%), 80 (32%), 77 (30.8%) and 84 (33.6%) respectively. Out of 54 obese patients, 30 (55%) patients had carotid artery disease. In our study obese patients had highest prevalence of carotid artery disease. Out of 110 hypertensive patients with CAD, 52 (47%) had carotid artery disease (P = 0.007). In DM patients

with CAD, 33 (41%) had carotid artery disease (P = 0.00). In smoker patients with CAD, 34 (43%) had carotid artery disease (P = 0.003). In dyslipidemic patients with CAD, 33 (39%) had carotid artery disease (P = 0.002). In obese patients with CAD, 30 (55%) had carotid artery disease (P = 0.00). All traditional risk factors were statistically significantly associated in patients with carotid artery disease.

As shown in Table 3, in those patients who had no risk factor, average CIMT was  $0.67 \pm 0.15$  (mean  $\pm$  SD). Patients who had systemic HTN, DM, smoking, dyslipidemia and obesity as a risk factor, their average CIMT was  $0.71 \pm 0.16$ mm,  $0.83 \pm 0.17$ mm,  $0.82 \pm 0.17$ mm,  $0.74 \pm 0.17$ mm, and  $0.74 \pm 0.16$ mm (mean  $\pm$  SD) respectively. Carotid artery disease was present more commonly in CAD patients in presence of risk factors as compare to patients without any risk factor. Maximum CIMT was present in DM patients.

**Table 3.** Mean CIMT in Patients with and without Risk Factors

Clinical characteristics	Mean CIMT in mm
No risk factor	$0.67 \pm 0.15$
HTN	$0.71 \pm 0.16$
DM	$0.83 \pm 0.17$
Smoking	$0.82 \pm 0.17$
Dyslipidemia	$0.74 \pm 0.17$
Obesity	$0.74 \pm 0.16$

CIMT = Carotid Intima Media Thickness, DM = Diabetes Mellitus, HTN = Hypertension

Data are presented as mean  $\pm$  SD

Average CIMT in CAD patients with no risk factors, was  $0.67 \pm 0.10$ mm (mean  $\pm$  SD). As shown in Table 4, Average CIMT in Patients with one, two, three, four and five or more risk factors, was  $0.71 \pm 0.2$ mm,  $0.78 \pm 0.14$ mm,  $0.83 \pm 0.12$ mm,  $0.92 \pm 0.11$ mm and  $1.10 \pm 0.10$ mm (mean  $\pm$  SD) respectively. As the number of risk factors increases mean CIMT also increases. Maximum CIMT was present in patients with five or more number of risk factors and minimum CIMT was present in patients who had no risk factors. CAD patients who had no risk factor, 5 (13%) were associated with carotid artery disease. Patients who had 1 risk factor, 25 (29%) were associated with carotid artery disease. Comparison of single risk factor with patients who had no risk factor, there was non-significant correlation for carotid artery disease (P = 0.06). As the number of risk factors increased, prevalence of carotid artery disease also increased. Most commonly carotid artery disease was present in patients who had 5 risk factors.

**Table 4.** Prevalence of carotid artery disease and Mean Carotid Intima Media Thickness according to extent of risk factors

Risk Factor	Number of patients	Carotid artery disease		P value	Mean CIMT in mm
		Yes	No		
One risk factor	85	25 (29)	60 (71)	0.06	$0.71 \pm 0.20$
Two risk factors	73	24 (32)	49 (68)	0.02	$0.78 \pm 0.14$
Three risk factors	27	15 (55)	12 (45)	0.0003	$0.83 \pm 0.12$
Four risk factors	19	12 (61)	7 (39)	0.0001	$0.92 \pm 0.11$
Five risk factors	9	6 (67)	3 (33)	0.0008	$1.10 \pm 0.10$

Data are presented as mean  $\pm$  SD or No. (%)

As shown in Table 5, patients who had single vessel disease (SVD), double vessel disease (DVD) and triple vessel disease (TVD) on coronary angiography, their average CIMT was  $0.73 \pm 0.13\text{mm}$ ,  $0.88 \pm 0.19\text{mm}$  and  $1.03 \pm 0.25\text{mm}$  (mean  $\pm$  SD) respectively. As the severity of CAD increases in is also associated with increased CIMT. There is statistically significant correlation between severity of CAD and CIMT ( $P = 0.01$ ). Maximum CIMT was present in patients with CAD-TVD.

**Table 5.** Mean CIMT according to severity of CAD

Severity of CAD	Number of patients	CIMT in mm	P value
SVD	33	$0.73 \pm 0.13$	0.01
DVD	14	$0.88 \pm 0.19$	
TVD	11	$1.03 \pm 0.25$	

CAD = Coronary Artery Disease, CIMT = Carotid Intima Media Thickness, DVD = Dual Vessel Disease, SVD = Single Vessel Disease, TVD = Triple Vessel Disease

Data are presented as mean  $\pm$  SD

## DISCUSSION

Ultrasound measurement of the carotid intima-media thickness offers the possibility of direct visualization of the presence of atherosclerotic plaque in the carotid arteries. The CIMT was measured using B mode ultrasonography and it was read by an observer blinded to the results of the coronary angiography, type of CAD, which risk factor or how many risk factors were present. B-mode color Doppler ultrasonography of the carotid arteries offers the potential for effective evaluation of early atherosclerotic changes, such as thickening of the intima-media complex and brings into focus the possibility of monitoring atherosclerotic progress in peripheral arteries [7].

In this study we found that carotid artery disease was present in 88 (35.2%) of 250 CAD patients. The commonest age group of carotid artery disease (12.8%) was between 61-70 years of age, suggest that carotid artery disease increases with older age. This is correlating with study done by Muhammad Haris et al. [8] in which they found that increasing age in years was statistically significantly correlating with carotid artery disease.

Obesity was present in 54 (27%) out of 250 CAD patients. Out of these 54 patients, 30 (55%) patients had carotid artery disease and mean CIMT was  $0.74 \pm 0.16\text{mm}$  (mean  $\pm$  SD), which was high as compare to patient without any risk factor. It was commonest risk factor found in this study. Study done by Kamran Bagheri Lankarani et al. [9], in which obesity was statistically significantly associated with elevated carotid artery disease but in our study prevalence of carotid artery disease in obese patients was less as compare to this study. In diabetic group 33 (41%) patients had carotid artery disease and mean CIMT was  $0.83 \pm$

$0.17\text{mm}$  (mean  $\pm$  SD) and highest mean CIMT was present in DM group. As compare to study done by Kamran Bagheri Lankarani et al. [9], prevalence of carotid artery disease in diabetics was higher in our study (35.8% Vs 41%). A study done by Zafar Ali Wani et al. [10], in which DM was significantly associated with carotid artery disease. In smokers, 34 (43%) patients had carotid artery disease and mean CIMT was  $0.82 \pm 0.17\text{mm}$  (mean  $\pm$  SD) and it was statistically significantly associated ( $P$  value = 0.003) with carotid artery disease and this finding was correlating with study of Kamran Bagheri Lankarani et al. [9], in which smoking was statistically significantly ( $P$  value = 0.002) correlated with carotid artery disease. Dyslipidemia was present in 92 (37%) CAD patients. Out of 92, 43 (47%) patients had carotid artery disease and it was statistically significantly associated with carotid artery disease and this finding was correlating with study of Kamran Bagheri Lankarani et al. [9]. Mean CIMT in Patients who had dyslipidemia as a risk factor, was  $0.74 \pm 0.17\text{mm}$  (mean  $\pm$  SD). 110 of 250 CAD patients included in the study were hypertensive, in which 52 (47%) patients had carotid artery disease and mean CIMT was  $0.71 \pm 0.17\text{mm}$  (mean  $\pm$  SD). Our this finding was statistically correlating ( $P$  value 0.01) with finding of Sedigheh Saedi et al. [11], but in their study, mean CIMT was more (right and left mean CIMT was  $0.86 \pm 0.29\text{mm}$  and  $0.83 \pm 0.24\text{mm}$  respectively), as compare to our study.

It is clear that prevalence of carotid artery disease is high in patients with cardiovascular risk factors as compare to those patients who had no cardiovascular risk factors. Quantitative value of CIMT also depends on number of risk factors present. Increase in the number of risk factors, is associated with significantly increased CIMT. Multiple number of risk factors has their additive effect on carotid artery disease, so as the number of risk factors increases, mean CIMT also increases. Mean CIMT value according to number of risk factors also increases with number of risk factors. In no risk factor group CIMT was minimum and maximum in five or more risk factor group. Study done by Xin Wang et al. in which mean CIMT was 0.74 mm in no risk factor group and CIMT increases with 1, 2, 3 and 4 risk factors and mean difference 0.026 mm, 0.052 mm, 0.074 mm and 0.114 mm, was present respectively but in our study mean CIMT in no risk factor group was  $0.67 \pm 0.10$  (mean  $\pm$  SD) and differences in CIMT with no risk factor group with 1, 2, 3, 4 and 5 risk factors was high as 0.04mm, 0.11mm, 0.16mm, 0.25mm and 0.43mm respectively. These findings suggest that, in our study mean CIMT values were increases more with increasing in number of risk factors as compare to above mentioned study and these findings could be due to poorly controlled risk factors.

On qualitative estimation of CIMT with number of risk factors involved, shows that increase in risk factors was

associate with increased prevalence of carotid artery disease. In patients who had no risk factors 13% were associated with carotid artery disease and patients who had five risk factors 67% patients had carotid artery disease.

Carotid intima media thickness can be used as a one of important under estimated risk factor for cardiovascular diseases. Carotid Doppler ultrasonography can be utilized as a valuable screening tool due to its several advantages, including ease of application, reproducibility, low cost and strong correlation with atherosclerosis. In conclusion, we demonstrated the usefulness of carotid intima-media thickness in predicting coronary artery disease and its severity. We can use carotid Doppler for detection of elevated CIMT and early diagnosis of CAD in patients who are having two or more cardiovascular risk factors. We can use carotid Doppler or screening of CAD patients, prior to development of myocardial infarction and reduce morbidity and mortality due to CAD.

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#### Conflict of Interest

Not declared.

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