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ASSOCIATION BETWEEN COMMON CAROTID INTIMA-MEDIA THICKNESS (CAROTID IMT) AND CORONARY ARTERY DISEASE

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ABSTRACT: INTRODUCTION: The burden of coronary artery disease (CAD) continues to rise globally, as well as in India, recognizing sub clinical atherosclerosis is of paramount importance for prevention of CAD, stroke, and peripheral vascular disease. The early phase can be studied by two dimensional B-mode ultrasonography. This technique yields information on atherosclerotic wall changes that cannot be obtained by conventional angiography. Its non-invasive character and easy applicability make B-mode ultrasonography a powerful tool for measurement of the atherosclerotic burden. Carotid intima-media thickness (IMT) is defined as the intimal plus medial thickness as the distance between the leading edge of first echogenic line to the leading edge of second echogenic line on far wall of common carotid artery. **AIM:** To determine the association between carotid intima-media thickness and coronary artery disease. **METHODOLOGY:** A total of 180 individuals (90 patients with coronary artery disease and 90 controls coming to the department of Cardiology, were studied. All individuals were subjected to clinical examination and investigations and relevant data was collected. Ultrasound scanning of the carotid arteries was performed as per ASE (American society of echocardiography) guidelines and common carotid intima-media thickness was measured. P value less than 0.05 was considered significant. **RESULTS & CONCLUSIONS:** Mean common carotid IMT in patients with established coronary artery disease was 0.86 ± 0.17 mm and in persons without significant clinical coronary artery disease it was found to be 0.58 ± 0.08 mm. Common carotid IMT was found to be higher in diabetes, hypertension, and those with high triglycerides and low HDL. There is no correlation between common carotid IMT with history of smoking total cholesterol or LDL cholesterol levels. Cut off value of 0.8mm of common carotid intima-media thickness has a sensitivity of 58.3%, specificity of 97.77% and positive predictive value of 63.76% in differentiation of persons with significant coronary artery disease from their counterparts.

KEYWORDS: Carotid artery, intima media thickness (IMT), atherosclerosis, coronary artery disease.

INTRODUCTION: The burden of coronary artery disease (CAD) continues to rise globally, including India. In India, incidences of CAD have doubled over the last three decades. By 2015, CVD alone would amount to 1.5 million deaths, including 34% of male and 32% of female global deaths. Recognizing novel screening modalities to evaluate sub clinical atherosclerosis is of paramount importance for prevention of CAD, stroke, and peripheral vascular disease.

Atherosclerosis is a progressive systemic disease with strong interrelationship between the prevalence of disease among different vascular beds. The first clinical manifestations of cardiovascular disease often arise in a stage of well advanced atherosclerosis. The early phase can be studied by two dimensional B-mode ultrasonography in the form of increased intima-media thickness. This technique yields information on atherosclerotic wall changes that cannot be obtained by conventional angiography.

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Its non-invasive character and easy applicability a powerful tool for measurement of the atherosclerotic burden. Chambers and Norris were first to relate the severity of carotid artery stenosis with the risk of coronary artery disease. The technique was further refined by Pignoli¹ et al who defined the intimal plus medial thickness as the distance between the leading edge of first echogenic line to the leading edge of second echogenic line on far wall of common carotid artery.

The carotid arteries are most suitable for study because of their superficial location and limited movement.² The carotid artery can be followed from the clavicular level cephalic to its bifurcation and proximal 3-4 cms of internal and external carotid arteries can be studied. Good quality scans of the common carotid artery can be obtained in nearly every patient,³ whereas measurement in carotid bulb and internal carotid artery show large intra and inter observer variability.⁴

In the two dimensional image of the carotid artery, the anterior wall, lumen and the posterior wall can be distinguished. Each wall show 3 distinct zones- an echogenic zone, echo free zone and another echogenic zone. In the far wall, the interface between blood and the intima gives rise to the leading edge of the first echogenic zone. The leading edge of second echogenic zone corresponds to media- adventitial interface.

For combined IMT measurement in the far wall, there is agreement between histology and sonography and for the near wall IMT is underestimated relative to histopathology. Thus, IMT of far wall is widely used in various studies. At each longitudinal projection, 3 determinations of IMT are conducted at the site of maximum thickness and at 2 points 1 cm upstream and 1 cm downstream from the site of maximum thickness. The three values are then averaged to get IMT or alternatively the maximum IMT is used.

Measurement of common carotid IMT

Ricotta et al⁵ found an excellent correlation in the thickness of lesions obtained by ultrasonography compared to angiography. In the Rotterdam study⁶ it was shown that reliable data can be obtained in approximately 99% of all the subjects.

Several studies have suggested a close relationship between IMT and cardio-vascular risk factors, Like male sex, age, obesity, hypertension, serum cholesterol, diabetes and smoking.^{7,8,9} Median population values of IMT range between 0.4mm and 1mm and progression rates of 0.01 to 0.3 mm/year have been reported. It is well known that there are marked ethnic differences in the prevalence of CAD.^{10,11,12} Similarly carotid IMT also differs in different populations studied

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Individuals from countries with high prevalence of CAD to have greater IMT. Mohan¹³ et al found carotid IMT above 1.1 mm in 1% of non-diabetics and 20% among diabetes patients with both diabetes and microalbuminuria are 26 years more advanced in the atherosclerotic process (as assessed by IMT) than the general non diabetic population. Studies have shown that newer risk factors like CRP, Lp (a), and plasma homocysteine to be associated with increased IMT. Various studies have shown the role of carotid intima-media thickness in predicting clinical coronary events.

The Rotterdam study showed that there was a significantly higher incidence of stroke and myocardial infarction in patients who had increased IMT.

The Cardiovascular Health Study Collaborative Research Group¹⁴ have shown that the relative risk for MI or stroke for the quintile with the highest IMT as compared with the lowest quintile was 3.87. IMT is a strong independent predictor of new cardiovascular events, even after statistical adjustment for other traditional risk factors.

Changes in carotid IMT have also been adopted as a surrogate end point for determining the success of interventions that lower the level of LDL cholesterol.^{15,16}

Carotid intima-media thickness is an excellent quick, reliable and reproducible method of assessing early atherosclerosis noninvasively. Several studies have clearly indicated IMT to be a predictor of future myocardial infarction and strokes.

AIM: To determine the association between carotid intima- media thickness and coronary artery disease.

METHODOLOGY: A total of 180 individuals coming to the department of Cardiology, both as outpatients as well as inpatients were studied. Subjects were divided into 2 groups.

Group I: Individuals with significant coronary artery disease demonstrated by coronary angiography.

Group II: Individuals having normal coronary arteries in angiography.

All individuals were subjected to clinical examination and tests were done:

1. A member of the study group was considered to be diabetic if he/she was already known to be a diabetic on treatment or newly detected, based on a fasting blood glucose level of >126 mg%.
2. A member was considered to be hypertensive if he/she has established hypertension on active treatment or newly detected based on supine systolic blood pressure above 140mmHg or diastolic pressure above 90mmHg.
3. Current or past history of smoking was considered as positive history of smoking.
4. Family history was considered positive if there was a history of coronary artery disease in first generation males less than 55 years of age or in women less than 65 years age.
5. Members were considered to be obese if body mass index was above 25.
6. Waist hip ratio was measured according to the standard technique. A ratio of more than or equal to 0.85 in females and a ratio of more than or equal to 0.95 in males was taken as abnormal.
7. Dyslipidemia was considered to exist if any one of the following was present: total cholesterol>200 mg%; LDL cholesterol >130 mg%; triglyceride levels>200 mg%; HDL cholesterol level<40 mg% and total cholesterol/HDL cholesterol ratio above 5.

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Ultrasound scanning of the carotid arteries was performed in supine position with a high frequency imaging probe (7.5 MHz), at a depth of 2-3 cm. The carotid arteries were followed from the clavicular end up to their bifurcation and proximal segments of internal and external carotid artery were studied. Common carotid intima-media thickness was measured in common carotid artery, 1 cm proximal to carotid bulb at 3 different points on the far wall. The average of the maximum IMT on both sides was taken into consideration for calculating the results. Raised lesions and plaques were excluded while calculating maximum IMT.

Statistical Analysis: Statistical analysis was done using Microsoft Excel software. Chi square test and student's t test were done wherever appropriate. Correlation between carotid IMT and other variables was done using linear regression model. P value less than 0.05 was considered significant.

RESULTS: 90 pts of established coronary artery disease and 90 individuals with no significant clinical coronary artery disease taken as controls were studied.

Sl. No.	Parameter	CAD	Controls	P value
1	Age in yrs	57.8±9.94	46.2 ± 10.4	< 0.000
2	Males	67 (74.2%)	63 (70%)	NS
3	Females	23 (25.8%)	27 (30%)	NS
4	Diabetes	32 (35.8%)	9 (10%)	<0.001
5	HTN	49 (54.2%)	25 (27.8%)	<0.001
6	Smoking	49 (54.2%)	25 (27.8%)	<0.001
7	F h/o CAD	49 (54.2%)	5 (5.6%)	NS

Table 1: Baseline characters of study population

Base line characteristics of study population are summarized in table 1. When compared to controls, patients with established CAD were older, and there was high incidence of diabetes, hypertension and history of smoking in these individuals.

Anthropometric Data:

Sl. No.	Parameter	CAD	Controls	P Value
1	Weight in Kgs	58.85 ± 12.23	52.08 ± 12.76	<0.001
2	Height in cms	159.45 ± 9.48	158.6 ± 10.05	NS
3	BMI (kg/sq cm)	23.12± 4.02	20.57 ± 3.92	<0.01
4	Waist circ(cm))	88.08 ± 10.97	77.39 ± 12.43	0.0005
5	Hip circ(cm)	91.3 ± 8.96	77.39± 12.43	0.0005
6	WHR	0.96 ± 0.07	0.88 ± 0.05	0.0005

Table 2: Anthropometric data of study population

Patients with coronary artery disease have more body weight and body mass index and abnormal waist circumference and waist- hip ratio when compared to controls.

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Fasting lipid profile results of the study population were as Follows:

Sl. No.	Parameter	CAD	Controls	P value
1	Total cholesterol	187.28 ± 33.95	180.39 ± 22.45	NS
2	LDL cholesterol	116.31 ± 25.87	113.34 ± 19.34	NS
3	HDL cholesterol	36.97 ± 6.78	41.01 ± 6.12	0.01
4	Triglycerides	163.16 ± 67.08	131.37 ± 42.65	0.001
5	TC/HDL	5.69 ± 4.89	4.85 ± 5.81	NS

Table 3: Fasting lipid profile among patients & controls

No significant difference was noted in total cholesterol, LDL cholesterol levels among the two groups, whereas triglycerides levels were found to be higher and HDL cholesterol levels were found to be lower in the patients with coronary artery disease.

When the prevalence of various coronary risk factors were studied, age above 50yrs was noted in 72.5% of cases; diabetes mellitus in 35.8%; hypertension in 55.8%; smoking in 54%; obesity in 30%; abnormal waist-hip ratio in 71%; which are significantly high when compared to controls. Family history of coronary artery disease was found in 6.6% of cases and 5.5% of controls. When dyslipidemia was evaluated, 36.6% of cases had total cholesterol above 200mg%, 58% had HDL values less than 40mg% and 53% had total cholesterol to HDL ratio above 5 which are significantly different when compared to controls.

Mean common carotid IMT in patients with established coronary artery disease was 0.8632 ± 0.1742 mm and in persons without significant clinical coronary artery disease it was found to be 0.5793 ± 0.0875 mm (P value <0.001).

CAD patients	0.52 ± 1.52 mm (0.58 ± 0.08)
Controls	$0.42 - 1.02$ mm (0.86 ± 0.17)

Table 4: Mean common carotid IMT in both groups

When mean carotid IMT in established CAD patients and controls was compared in relation to coronary risk factors, the following findings were found which are summarized in.

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Parameter		CAD pts P val		Controls P val	
Age	< 50 yrs	0.89±0.18	0.00075	0.55 ± 0.075	0.0001
	>50 yrs	0.78±0.14		0.63 ± 0.09	
Type 2 DM	Absent	0.83± 0.16	0.0648 (NS)	0.57 ± 0.09	0.05
	Present	0.91± 0.19		0.64 ± 0.08	
HTN	Absent	0.83±, 0.17	0.032	0.57 ± 0.08	0.028
	Present	0.89±, 0.17		0.61 ±0.09	
Smoking	Absent	0.84± 0.15	NS	0.56 ± 0.08	0.011
	Present	0.89± 0.19		0.62 ± 0.08	
Family H/O CAD	Absent	0.78± 0.18	NS	0.58 ± 0.08	NS
	present	0.86± 0.17		0.58 ±0.09	
BMI	< 25	0.86± 0.16	NS	0.54 ±0.05	NS
	>25	0.88, 0.15		0.58± 0.06	
WHR	Low	0.84, 0.21	NS	0.59± 0.06	NS
	high	0.86, 0.16		0.59± 0.09	
W cir	Normal	0.84, 0.16	0.036	0.59± 0.05	NS
	abnormal	0.93, 0.2		0.59± 0.09	

Table 5:Carotid IMT vs Risk factors

Comparison between various study groups with respect to lipid profile Abnormalities:

Parameter		CAD pts P val		Controls P val	
T Chol	<200	0.84 ± 0.17	NS	0.57± 0.08	NS
	>200	0.87 ± 0.21		0.597± 0.086	
LDL	<130	0.85 ± 0.18	NS	0.59±0.06	NS
	>130	1.05 ± 0.45		0.59± 0.09	
HDL	< 40	0.897 ± 0.19	0.0055	0.61± 0.097	0.026
	>40	0.79 ± 0.16		0.564± 0.077	
T Chol/HDL	<5	0.81 ± 0.18	NS (0.065)	0.061± 0.08	0.061 (NS)
	>5	0.89 ± 0.18		0.063± 0.11	
TG	<200	0.84 ± 0.089	NS	0.574± 0.09	0.0051
	>200	0.88 ± 0.01		0.7±, 0.04	

Table 6: Carotid IMT vs Lipid abnormalities

When mean carotid IMT among various subgroups were compared: In patients with coronary artery disease, significantly higher values were found in patients above 50yrs of age, diabetes, hypertension, those with low HDL cholesterol levels when compared to their counterparts. In contrast no difference was noticed in patients who are smokers, with obesity and with elevated cholesterol, LDL, triglyceride levels when compared to their counter-parts.

In control subjects (without significant coronary artery disease) higher values of carotid IMT were found in persons above 50 years of age, diabetics, hypertensives, smokers, those with elevated

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triglyceride levels, and low HDL cholesterol levels when compared to their counterparts. In contrast, no significant difference was noticed among those with or without family history of coronary artery disease, obese or non-obese, or those with elevated cholesterol levels when compared to their counterparts.

Correlation of common carotid IMT with other Variables:

Sl. No.	Parameter	R value	P value
1	Sex	0.011	>0.1 (NS)
2	Age	0.53	<0.001
3	Diabetes	0.29	0.01
4	HTN	0.31	0.001
5	Smoking	0.11	>0.1 (NS)
6	Family H/O CAD	0.034	>0.1(NS)

Table 7: Correlation of carotid IMT & Risk factors

Sl. No.	Parameter	R value	P value
1	Weight	0.19	0.1-0.5 (NS)
2	Height	-0.013	>0.1 (NS)
3	BMI	0.26	0.01
4	Waist circumference	0.4	<0.001
5	WHR	0.39	<0.001
6	Total Chol	0.157	>0.1(NS)
7	TG	0.29	0.01 – 0.001
8	LDL	0.14	>0.1
9	HDL	-0.31	<0.001
10	TC/HDL	0.065	>0.1(NS)

Table 8: Correlation of carotid IMT & anthropometric data and lipid profile

When common carotid IMT is correlated with other variables, it was found to be significantly associated with age, diabetes, hypertension, body mass index, waist circumference, waist – hip ratio, serum triglyceride levels and negatively associated with HDL cholesterol level and the highest level of correlation was noticed with age, waist circumference, W/H ratio and serum HDL levels.

When carotid IMT 0.8 mm was taken as cut off point to patients with coronary artery disease, the findings were as follows:

Carotid IMT	CAD pts	Controls	Total
≥0.8 mm	53	2	55
<0.8 mm	37	88	125
	90	90	180

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Carotid IMT above 0.8 mm was found to have Sensitivity 58.8%, Specificity 97.7%, and Positive predictive value 96.36% to differentiate patients with coronary artery disease from normal persons.

DISCUSSION: In the present study, common carotid intima-media thickness (IMT) in patients with established coronary artery disease was found to be 0.86 ± 0.17 mm and in control subjects, 0.58 ± 0.09 mm. In the study by Hansa Gupta ¹⁷ et al, average common carotid intima media thickness was found to be 0.82 mm and 0.67 mm respectively.

In the British Regional Heart study¹⁸ by Shah Ebrahim et al the mean common carotid IMT in men was found to be 0.84 ± 0.21 m.m. and in women 0.75 ± 0.16 m.m. respectively.

In the Rotterdam study 0.795 ± 0.153 m.m. and in patients with myocardial infarction 0.858 ± 0.187 m.m. respectively ($p < 0.05$).

In Baldassarase D¹⁹ et al study mean carotid IMT in controls was found to be 0.94 ± 0.38 m.m. and in patients with coronary artery disease was found to be 1.08 ± 0.49 m.m. ($p < 0.05$) When carotid IMT among various subgroups was analyzed, in patients with coronary artery disease, those who are diabetic have significantly increased carotid IMT 0.91 ± 0.19 mm when compared with non-diabetics, 0.84 ± 0.16 . Similar significant difference of IMT was noticed among control group, between diabetic and non-diabetics i.e. 0.64 ± 0.08 , 0.57 ± 0.09 m.m respectively.

In Baldessarre et al series no significant difference was observed in common carotid IMT (mean) in diabetics, 1.04 ± 0.41 & non-diabetics, 1.0 ± 0.48 m.m. In contrast in Hansa et al series, significant difference was observed between diabetic & non diabetics with coronary artery disease 1.14 m.m & 0.99 m.m ($p = 0.001$), and among controls with or without diabetes, 0.84 m.m and 0.69 m.m respectively.

In present study, mean carotid IMT in hypertensives was 0.89 ± 0.17 mm and in non hypertensives, 0.83 ± 0.17 mm ($p = 0.032$). Similar significant difference was noted in control group 0.61 ± 0.09 mm and 0.57 ± 0.08 mm ($p = 0.028$). Similar results were noted in Baldessarre et al series in hypertensives and non hypertensives, 0.94 ± 0.4 m.m and 0.82 ± 0.35 m.m respectively. ($p < 0.001$).

In British Regional Heart study common carotid IMT showed strong relationship with age, systolic blood pressure and no association was noted between IMT & height, total cholesterol, HDL cholesterol, etc.

In the present study carotid IMT was significantly correlate with age ($p < 0.001$), diabetes ($p = 0.01$), hypertension ($p = 0.001$) BMI ($P = 0.01$), waist hip ratio (0.001), triglycerides ($p = 0.01-0.001$) and HDL ($p = 0.001$) levels. No significant correlation was found between IMT and smoking, height, total cholesterol level, LDL cholesterol, or TC/HDL ratio.

In the study by Baldessarre et al significant correlation was found between IMT and systolic blood pressure ($p < 0.0001$), HDL cholesterol ($p = 0.0001$), LDL ($P < 0.01$) triglycerides ($p = 0.05$). No correlation was found with BMI, total cholesterol or glycemic status.

In present study when the cut-off value of common carotid intima-media thickness was taken as 0.8 mm, patients with significant coronary artery disease were differentiated from their counterparts with a sensitivity of 58.3%, specificity of 97.77% and a positive predictive value of 96.36%. In Jhadav²⁰ et al series cut off value of 0.8 mm has a sensitivity of 30%, specificity of 88% and a positive predictive value of 70%.

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CONCLUSIONS:

1. Mean common carotid intima - media thickness (IMT) was significantly high in patients with established coronary artery disease when compared to those without clinically significant coronary artery disease.
2. Common carotid intima - media thickness was found to be higher in diabetes, hypertension and those with high triglycerides and low HDL cholesterol levels. There is no correlation between common carotid intima-media thickness with history of smoking, family history of coronary artery disease, total cholesterol or LDL cholesterol levels.
3. Cut off value of 0.8mm of common carotid intima-media thickness has a sensitivity of 58.3%, specificity of 97.77% and positive predictive value of 96.36% in differentiation of persons with significant coronary artery disease from their counterparts.

Hence measurement of common carotid intima media thickness is routinely indicated in the evaluation of patients with suspected coronary artery disease.

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