Extra Cranial Carotid Doppler Study For Atherosclerosis A Marker of Coronary Artery Disease.

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ABSTRACT:

Introduction :
There is increasing evidence day by day that coronary artery disease and carotid atherosclerosis are related. Extracranial Carotid arteries are easily accessible and the Doppler study of these vessels being a noninvasive, easily reproducible and relatively inexpensive, could be of great assistance in predicting and monitoring the coronary artery disease.

Aims And Objectives:
To study 1) extracranial carotid artery intima media thickness, degree of luminal stenosis and of atherosclerotic plaque by Doppler ultrasonography 2) association of conventional cardiovascular risk factors with carotid Doppler abnormalities in cases of coronary artery disease(CAD).

Materials and methods: Study design: case control study study setting: Indira Gandhi government medical College Nagpur outcome measures : carotid intima media thickness, plaque and carotid stenosis.

Inclusion criteria: angiographically proved cases of coronary artery disease.

Exclusion criteria: Acute cerebrovascular accident, acute myocardial infarction, hepatic and renal failure and cases with neck pathologies. 52 cases with angiographically proven significant CAD and 26 controls without CAD (angiographically normal) were enrolled. They were evaluated for conventional cardiovascular risk factors and subjected to Extra Cranial Carotid Doppler assessment by B mode ultrasonography. IMT >0.8mm was considered as significant.

Results: CIMT > 0.8mm was present in 42 (80.7%) cases compared to 9 (34.6%) controls (P =<0.05) Carotid plaque was present in 34(65.38%) compared to 6 (23%) controls.15.3% cases were having significant carotid luminal stenosis(>50%) and 1.9% critical stenosis(>70%).

In univariate analysis, age, male gender, Hypertension, dyslipidemia, DM, smoking were found to be independently associated with CIMT& except age, male gender & smoking rest of the risk factors were also associated with carotid artery luminal stenosis.

In multivariate analysis LDL-Cholesterol, BMI, DM showed positive correlation and HDL-cholesterol showed negative correlation with to carotid Doppler abnormality. Cases with more than two risk factors were having mean IMT 1.1±0.2mm compared to 0.77+0.2mm controls p value (0.009). CIMT and luminal stenosis increased as the number of involved coronary vessels increased .

Conclusion: Significantly increased CIMT is an independent risk factor for coronary artery disease. Degree of carotid stenosis is positively associated with number of coronary arteries involved. Increased CIMT is associated with increasing number of risk factors in cases of angiographically proved coronary artery disease. Extracranial carotid artery luminal stenosis and IMT independently correlated with CAD and conventional risk factors

Key Words: Coronary Artery Disease,. Carotid Intima Media Thickness(IMT) Carotid Stenosis(CAD).

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Introduction:

It is said that by the year 2020 atherosclerotic cardiovascular disease will be the major cause of death worldwide[1,2] The Asian Indians have much higher incidence of CAD as compared to all ethnic groups. CAD among Asian Indians has been found to be more severe, diffuse & associated with serious complications & increasing mortality in young age[3]. An underlying genetic susceptibility associated with the conventional risk factors (for CAD) like male gender, hypertension, diabetes, smoking, dyslipidemia, increased BMI, alcohol & sedentary lifestyle makes CAD assume a malignant course in Asian Indians[3,4] Carotid artery intima-media wall thickness and carotid artery luminal stenosis have been reported to be a useful marker for the presence of CAD[5]. Number of studies have shown this association and found that B-mode ultrasound score is strongly and independently associated with CAD and is at least as useful as well known risk factor for atherosclerotic CAD[6]. Assessment of carotid intima media thickness is a simple non invasive and reproducible tool to evaluate atherosclerosis and predict coronary artery disease in Indian subjects. Carotid intima media thickness is also reported to have significant correlation with extent and severity of coronary artery disease.[7]

Material and Methods:

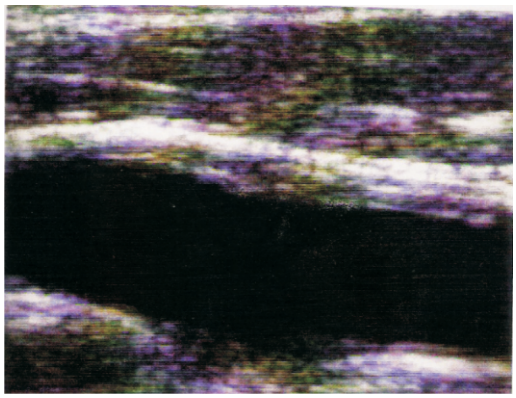
This hospital based, observational case control study was carried out in the Dept. of Medicine at Indira Gandhi Govt. Medical College and Hospital, Nagpur during the period of August 2005 to November 2007 Permission from institutional ethical committee was obtained before starting the study. Total 52 consecutive cases above 35 years of age having coronary artery disease (angiographically proved) and 26 age and gender matched controls without significant coronary artery disease (having normal angiogram) were included. Subjects with acute myocardial infarction, acute cerebrovascular episode, hepatic, renal failure, cases with neck pathologies likely to produce changes in carotid arteries were excluded.

All the subjects were evaluated clinically.Anthropometric measurements were obtained. Both the cases and controls were assessed for conventional cardiovascular risk factors like hypertension, smoking, diabetes, dyslipidemia, BMI, waist hip ratio. Biochemical investigations were done viz fasting and post prandial blood sugar, serum lipids ,liver and kidney function tests . Hypertension was defined according to JNC VII criteria. Diabetes mellitus was defined as fasting blood sugar more than 126mg% or history of DM on oral antidiabetic medication[9] BMI >25KG/M^2 was considered a risk factor for coronary artery disease [8,,9]

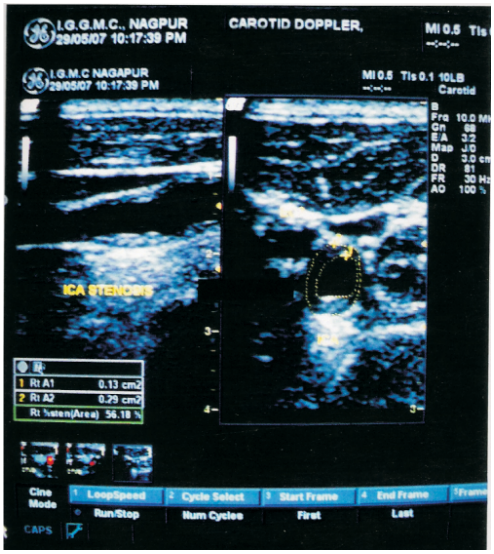
Dyslipidemia was defined as per NCEP ATP III guidelines[10] Coronary artery disease was labelled when coronary angiography revealed 50% or more block in one or more coronary arteries [11,12]

All cases and controls underwent B mode Ultrasonography & colour doppler study for the evaluation of extra cranial carotid arteries for atherosclerotic changes in the form of increased intima media thickness, presence of plaque and degree of carotid artery luminal stenosis. (See Fig).

Fig : Photograph of Carotid artery Doppler study



Increased common carotid intima thickness



Internal carotid artery plaque and luminal stenosis

The intima media thickness is defined as distance in mm between lumen intima and media interfaces. Plaques

were defined as a focal widening relative to adjacent segments, with protrusion into the lumen composed either of only calcified deposits or a combination of calcification and non calcified material.[12] IMT >0.8mm was considered as significant [7], [13]

An attempt was made to correlate external carotid artery abnormalities (intima media thickness, presence of plaque and degree of luminal stenosis) and presence of conventional cardiovascular risk factors with coronary artery disease. Statistical analysis was performed by using "SPSSversion 12" software. Chi square test, paired and unpaired students 't'test were applied

Results:

The study included 52 coronary angiographically proven coronary artery disease cases having 50% or more stenosis in one or more of coronary arteries and 26 controls without coronary artery disease (angiographically proven). The mean age of cases was 55±9. 5yrs & those of controls was 56.6±9. 6yrs. Male to female ratio was 1.4:1.in cases and 1.6:1 in controls. There were 16 (30.7%)cases with Single vessel disease,16 (30.7%) cases with Double vessel disease. and 20 (38.4%) cases with Triple vessel disease Subjects having more than 2 risk factors were significantly more in cases than controls (76.9% &65.3%, X^2-4.33,S)which is statistically significant. Physical inactivity was the commonest risk factor in the present study, next being dyslipidemia ***(Table. no. 1)***

The mean CIMT was 1.06 ± 0.2mm & 0.744 ± 0.1 in cases & controls respectively. Which is statistically significant (p= <0.05). Mean carotid luminal stenosis was significantly more in cases (43.2±15.9) as compared to controls (9. 4) (p= <0.05) ***(Table no 2)***

Increased in intima media thickness (>0.8mm) was present in 42 cases (80.7%) as compared to10 controls (19.3%) difference was also statistically significant (X^2 - 12.3,p = 0.05 s)

IMT was maximum (1.1±0.2) in cases with tripple vessel disease. Mean CIMT values showed increment as per number of coronaries involvement. However this difference was statistically insignificant (p-0.39, 0.55, 0.12) .

Triple vessel disease had higher degree of carotid stenosis (54.3±13.6%) as compared to Single vessel disease (36.7±16. 6) and Double vessel disease (39. 1±12. 8). As the number of coronary arteries involved increased, the degree of mean percentage of carotid arteries luminal stenosis was also increased and the difference was statistically significant. (p = < 0.02) ***(Table no. 3)***

It was also found that as the number of risk factors increased, the CIMT also increased in cases and controls. The mean CIMT in cases with two and more than two risk factors was significantly more in cases compared to controls (1.06±0. 2 & 1.1±0.2mm Vs 0.75±0.1 & 0.77± 0. 2mm p=0.009). Similarly cases with more than two risk factors had increased carotid luminal stenosis compared to controls (45.6 ± 16.7 Vs14, pvalue <0. 05s).

In univariate analysis using carotid stenosis and CIMT as dependent variable and various conventional risk factors for CAD as independent variables, age, hypertension, dyslipidemia, Diabetes Mellitus, smoking, and male gender were associated positively with CIMT and Hypertension, Diabetes Mellitus, Dyslipidemia, and male gender were associated with carotid stenosis. HDL was associated negatively with carotid intima media thickness and carotid stenosis .

In multivariate analysis independent association of carotid stenosis was evident with LDL-C, BMI, PPBS and negatively with HDL-C.However, multivariate analysis did not reveal independent association of CIMT with confounding factors. CIMT and carotid stenosis were found to be independent risk factors for coronary artery disease. ***(Table no.4)***

Discussion:

It is thought that conventional risk factor assessment may not be sufficient to assess total risk of cardiovascular disease. CIMT can be considered as a non invasive method that is intended to be a surrogate marker for coronary artery atherosclerosis. It represents an independent marker, separate from traditional risk factors for cardiovascular disease and stroke. However, It is yet not clear if the assessment of carotid arteries by Doppler ultrasonography provides benefit above traditional risk factors or has an effect on clinical outcome [14 15,16]

There is increasing evidence day by day that coronary artery disease and carotid atherosclerosis are related and reflects atherosclerotic changes in these arterial beds. Extracranial Carotids are easily accessible and the Doppler study of these vessels being a noninvasive, easily reproducible and relatively inexpensive, could be of great

assistance in predicting and monitoring the coronary artery disease.

In the present study, the mean CIMT & mean percentage of carotid artery luminal stenosis was significantly higher in cases than controls.

The mean CIMT was also higher in cases who had more than two risk factors than those having two or less number of risk factors.CIMTin the present study increased significantly in relation to number of coronary arteries involved but difference was statistically not significant. The results of the present are comparable to similar studies performed by others.[7,12,15.]

The results of Atherosclerosis Risk in communities Study (ARIC) revealed that mean CMIT is a non invasive predictor of future coronary events.[17] Several other authors have also performed same kind of studies & concluded that carefully performed CIMT can add incremental information to traditional risk factors assessment.[15,17,18]

The present study showed significant increase of mean percentage of carotid artery luminal stenosis in cases as compared to controls & also observed that as the coronary artery disease severity goes on increasing the degree of external carotid artery luminal stenosis also goes on increasing in a statistically significant manner in cases The percentage of carotid artery luminal stenosis was significantly more in cases having more than 2 risk factors than having less number of risk factors.These observations are consistent with other authors.[14,15,19]

As previously reported coronary heart disease risk is largely associated with the presence of non obstructive or obstructive plaque rather than IMT.[15,20] However detailed assessment of type of plaque was not done in present study.

In univariate analysis strong association was found between CIMT and carotid stenosis & conventional risk factors. Multivariate analysis revealed independent association of carotid luminal stenosis with LDL-cholesterol, BMI, post prandial Blood Sugar, HDL –cholesterol correlated negatively with carotid Doppler abnormality

Conclusion:

It can be concluded that carotid intima media thickness >0.8mm is an independent risk factor for coronary artery disease and degree of carotid stenosis is related to severity and extent of coronary artery disease. Physical inactivity was the commonest risk factor. Extra Cranial Carotid Doppler assessment is a sensitive,cheaper & reproducible test to evaluate atherosclerotic changes in patients of coronary artery disease.

However, whether to implicate CIMT,plaque assessment by Doppler ultrasonograhy in population,for evaluation as a risk factor in asymptomatic individuals- needs further studies. Even if CIMT is increased, at what level subjects would be symptomatic,at which stage treatment interventions should be initiated-needs to be further assessed by prospective studies.

Limitations of the study-present study had a small sample size, and it is a cross sectional study, only angiographically significant and clinically manifested coronary artery disease cases have been included in the present study .

Table 1: Risk Factors in Cases and Controls.

SR. NO.	PARAMETERS	CASES (n=52)	CONTROLS (n=26)	P VALUE
1	MALE GENDER	31(59.6%)	16(61.5%)	0.39, NS
2	DYSLIPIDEMIA	24(48%)	7(6.9%)	0.22, NS
3	HYPERTENSION	20(38.4%)	7(6.9%)	2.17, NS
4	**DIABETES**	**17(32.6%)**	**8(30.7%)**	**4.5, S**
5	**BMI>25KG/M^2**	**10(19.2%)**	**2(7.6%)**	**42.9, S**
6	**SMOKING**	**10(19.2%)**	**3(11.5%)**	**36.9, S**
7	PHYSICAL INACTIVITY	47(90.3%)	22(84.6%)	2.62, NS
8	ALCOHOL	4(7.6%)	0	-

Table 2: Table Showing Carotid IMT and Luminal Stenosis As demonstrated by Carotid Doppler Ultrasound In Cases and Controls.

SR. NO.	CAROTID DOPPLER ABNORMALITY	CASES (n=52)	CONTROLS (n=26)	P Value
1	MEAN IMT(mm)	1.06±0.2	0.744±0.1	p=0.000….p<0.05
2	% LUMINAL STENOSIS	43.2±15.9	9.4	p=0.000….p<0.05

Table 3: Relation of Carotid Artery Luminal Stenosis and Pattern of Coronary Artery Involvement.

SR. NO.	CORONRY ARTERY INVOLVEMENT	MEAN % STENOSIS	P-VALUE
1.	Single Vessel Disease (n=16)	36.7± 16.6	0.74
2.	**Double Vessel Disease (n=16)**	**39.1±12.8**	**0.007**
3.	**Triple Vessel Disease (n=20)**	**54.3±13.6**	**0.02**

Table No 4.: Multivariate analysis for carotid artery stenosis: Coefficients

		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
Model		B	Std. Error	Beta		
1	(Constant)	.453	.903		.501	.630
	AGE	8.021E-03	.018	.180	.435	.675
	SEX	8.330E-02	.269	.096	.309	.765
	H.T.	6.790E-02	.168	.071	.405	.696
	D.M.	.226	.238	.248	.951	.370
	L.D.L.C	.763	.228	.714	3.351	.010
	H.D.L.C	.614	.229	.526	2.684	.028
	V.L..D.L.	3.038E-03	.022	.037	.141	.891
	T.G.	-.720	.341	-.546	-2.108	.068
	SMOKING	.227	.204	.195	1.112	.298
	F.B.S.	.929	.351	.588	2.649	.029
	S.B.P.	-.354	.332	-.268	-1.064	.318
	D.B.P.	5.888E-02	.303	.050	.195	.851
	B.M.I.	.601	.268	.380	2.242	.055
	P.M.STATE	-.569	.357	-.532	-1.594	.150
	REG.EXERCISE	9.742E-02	.498	.083	.196	.850
	BLD.UREA	-2.311E-02	.012	-.285	-1.972	.084
	SR.CREATININE	-.539	.527	-.221	-1.022	.336

a Dependent Variable: STENOSIS(%)

b Selecting only cases for which CAT = 0

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