EXCELLENT PUBLISHERS

International Journal of Current Research and Academic Review

ISSN: 2347-3215 Volume 2 Number 12 (December-2014) pp. 64-70

www.ijcrar.com

Carotid artery intima media thickness as a predictor of coronary artery disease in population of North Karnataka, India

Sanjeev L Sajjannar[1*] and Deepa S Sajjannar[2]

[1]Department of Cardiology, BLDU'S Shri B. M Patil Medical College, Hospital and Research Centre, Bijapur, India
[2]Department of Biochemistry, BLDU'S Shri B. M Patil Medical College, Hospital and Research Centre, Bijapur, India
Corresponding author

KEYWORDS

Coronary arteriosclerosis, carotid intima media thickness (IMT), B-mode ultrasound

A B S T R A C T

Coronary artery disease (CAD) is a major cause of morbidity and mortality in developed and developing world .The important predisposing factor to coronary artery disease is atherosclerosis of coronary arteries. Carotid artery intima media thickness (IMT) can be used as a measure of generalized atherosclerosis. Ultrasound B mode serves as a simple ,safe, cost effective and noninvasive method for measuring carotid artery intima media thickness, hence this study was undertaken to evaluate association of carotid IMT in prediction of CAD in local population. Carotid IMT was measured with a B-mode USG in 50 cases of coronary artery disease and 50 age and sex matched controls. IMT values more than 0.8 mm were labeled as significant for correlating the association between IMT and CAD. On univariate analysis mean IMT was 1.098±0.2938 as against 0.606±0.1530 which was statistically significant with a 'p' value of 0.001. In subgroup analysis, the mean IMT in hypertensive cases was higher than the controls and was statistically significant and also the mean IMT in diabetic cases was significantly higher than the non diabetic controls. A statistically significant increase in carotid IMT was also observed in smokers than in nonsmoking controls. Carotid artery intima media thickness can be measured by B- mode ultrasound which is a simple, non invasive and reproducible technique. Carotid artery intima media thickness is a marker of atherosclerosis which is strongly associated with traditional risk factors and could be used as asurrogate marker in prediction of atherosclerosis and CAD in Indians.

Introduction

The incidence of coronary artery disease has been steadily rising in developing countries like India and is also a major cause of morbidity and mortality. In the last three decade the prevalence of coronary artery disease has increased and is 4.5%in rural

India and 10%in urban India (Gupta et al., 2008)**.** Coronary artery disease represents a spectrum of condition with acute ST segment elevation myocardial infarction (MI) at one end and non ST segment elevation MI non Q-wave MI, unstable angina and chronic stable angina to silent myocardial ischemia at other end of spectrum. The important predisposing factor to coronary artery disease is atherosclerosis of coronary arteries.

Carotid artery intima media thickness value in general population varies between 0.4 to 1.0 mm. Age is an important determinant factor. It increases 0.01 to0.03 mm/year. This progression of thickness is 0.03to 0.06 mm/yr in person with coronary artery disease. Of all the risk factors, age has the strongest independent association with carotid atherosclerosis. Male sex is strongly and independently associated with carotid atherosclerosis (Suzan et al., 1997). Hypertension strongly influence carotid atherosclerosis.[3] Hypertension increases flow velocity and wall shear stress, which are considered to be important factors that induce intima media hypertrophy and thickness.

Carotid artery intima media thickness (IMT) is a measure of generalized atherosclerosis. Arterial vessel wall changes occur during a presumably long subclinical lag phase of endothelial damage and gradual diffuse thickening of intima. This early phase can be studied by two dimensional B-mode ultrasound. This technique yields information on atherosclerotic wall changes that cannot be obtained by conventional contrast angiography. Carotid arteries are most suitable for study because of their superficial localization, size and limited movement. Hence measurement of carotid artery IMT is helpful in detecting atherosclerosis and hence CAD. Carotid artery IMT can be measured by ultrasound B mode, which is noninvasive, cost effective, simple, safe and reproducible. American heart association has also recommended B-mode ultrasound for documenting atherosclerosis.

In this study carotid IMT measurement by ultrasound B-mode is undertaken to demonstrate presence of atherosclerosis which could predict CAD.

The aims and objectives of this work are (1) To study carotid artery intima media thickness in subjects with coronary artery disease and in controls without coronary artery disease and compare the results and (2) To evaluate the association of carotid artery intima media thickness in the prediction of coronary artery disease.

Materials and Methods

In this study, 50 subjects with diagnosis of coronary artery disease admitted in Karnataka medical college hospital and research center, Karnataka, Hubli were taken as cases and 50 age and sex matched controls were taken from the hospital wards without coronary artery disease. Informed consent was taken by all the subjects involved in the study.

The individuals with already proved coronary artery disease as evident with history of angina, ECG changes like ST segment elevation ≥1mm in limb leads and ≥ 2mm in chest leads, ST segment depression > 1mm, significant Q wave- 0.04 sec duration and 0.3 mV in amplitude or symmetrical pointed and inverted T waves were enrolled as cases, and to reduce the confounding errors those subjects who were on long term oral hypolipidemic drugs were excluded. 50 subjects without CAD were

taken as controls, who were age and sex matched with cases.

They were further subdivided into 3 subgroups in context to risk stratification for CAD: diabetes mellitus; hypertension; and diabetes with hypertension. The ages of the subjects ranged from 30 to 80 yrs. Mean age in males was 54 yrs and in female it was 56.5 yrs.

Each patient from case and control group, were subjected to a detailed history and thorough clinical examination; which included blood pressure measurement, general physical examination with anthropometric measurement and body mass index and in detail examination of cardiovascular system and other systems.

5 ml of fasting blood was drawn from both cases and controls with sterile disposable syringe which was transferred into centrifuge tubes. The samples were centrifuged at 3000 rpm for 10 minute and serum was separated. Biochemical assessment included fasting blood sugar, lipid profile and blood urea, serum creatinine on both cases and controls.

Ultrasonographic scanning of the carotid arterial wall was performed in the supine position with neck extended and head turned away from the site of examination, using a high frequency imaging probe (7.5 mHZ) with Larsen- Turbo scanner. The carotid vessels were followed from the clavicular head cephalad to their bifurcation and 3-4 cm of the proximal internal and external carotid arteries were studied. The IMT was measured at different points on both sides in the far wall of carotid arteries. Maximum carotid IMT was taken into consideration for calculating the results. Plaques were not included in calculating IMT, but their presence was noted.

IMT values more than 0.8 mm were labeled as the higher quartile (significant) for correlating the association between IMT and CAD.

Plaque was defined as localized thickening > 1.2 mm that does not involve whole common carotid artery or carotid bulb. Films were recorded in all subjects for documentation.

Statistical analysis: In the present study values are expressed as mean± 1 standard deviation. Variables are compared by ´ Z' test or ´t' test for 2-sample mean. Attributes are compared by odds ratio and standard error of difference between two proportions and chi-square test. In this study the strength of association is said to be significant if p value ≤ 0.05.

Result and Discussion

Coronary artery disease is a major cause of mortality and morbidity in developed world and in developing countries the incidence is rising. Atherosclerosis is the major cause of CAD.

Atherosclerosis can be detected and documented in early stage by examining carotid artery intima media thickness (IMT). Ultrasonography is reliable and accurate technique to determine IMT in superficial arteries. Reproducibility of IMT determination is best in common carotid artery of healthy subjects and patients with advanced atherosclerosis. B-Mode ultrasound scan of carotid IMT is of clinical value in the screening of patients with CAD.

In this study, we have compared 50 cases with proved CAD with 50 controls, who were age and sex matched. We studied all risk factors for atherosclerosis in cases and

controls and measured carotid IMT by B-mode ultrasound.

Age and sex

The mean age was 55.06± 11.80 yr in the study group, majority of the cases were in the age group 50-69 yrs (60%), males constituted 74% and females constituted 26%.

The mean age in the study conducted by (Jadhav and Kadam, 2001) was 52.8± 8.1 yr and males constituted 65% and females 35%.In the ARIC study (Burke et al., 1995; Crouse et al., 1996), the mean age was 55± 6 yr, whereas, in Rotterdam study (Bots et al., 1997) mean age was 70.6 year and in Cardiovascular Health study (O' leory et al., 1992) it was 72.5± 5.6 years. In Suita study (Mannami et al., 1997) the mean age was 63.4 ±7.7 year.

Smoking status

In our study 40% of the patients with CAD were smokers, where as no. of smokers in control group was 20%. There was significantly higher number of smokers in CAD group than controls ($p<0.05$). Jadhav and Kadam (2001) noted that, smoking incidence was 31.3% in CAD group and was significantly higher compared to controls. In Rotterdam study (Bots et al., 1997), the incidence of smoking was 26.5% and in cardiovascular health study[7] it was 12.2%. Smoking incidence was comparatively higher in our study group.

Hypertension

In our study 44% of the patients with CAD had hypertension while only 20% of the controls had hypertension. The mean systolic blood pressure (SBP) in cases was 139.64± 29.52 mm Hg and diastolic blood pressure (DBP) was 85.32 ±11.2964 mm Hg.

In Rotterdam study (Bots et al., 1997), the hypertension was noted in 32% of case. The mean SBP was 141 ±23 mm Hg and DBP was 71± 12 mm Hg. In cardiovascular health study (O' leory et al., 1992), hypertension was noted in 39.9 % of cases, which was comparable to our study.

In the study conducted by Jadhav and Kadam (2001) it was 18.2% and in ARIC study (1990) (Burke et al., 1995; Crouse et al., 1996) it was 27%. The mean SBP was comparable to that seen in Rotterdam study (Bots et al., 1997) (141 ±23 mm Hg) and cardiovascular health study (O' leory et al., 1992) (136.13 ±21.5 mm hg). The mean DBP was higher in our study 85.32± 11.29 mm Hg compared to Rotterdam study (Bots et al., 1997) (71± 1.2 mm hg) and Cardiovascular health study (O' leory et al., 1992) group (71 ±11.3).

Diabetes mellitus

In our study 30% of the cases were diabetic while only 12% of the controls in CADs were found to be diabetic. The incidence of diabetes mellitus in CAD group was statistically significant ($p<0.05$) compared to control group. Incidence of diabetes mellitus was 51.5 % in the study conducted by Jadhav and Kadam (2001) and in Rotterdam study (Bots et al., 1997) it was 10.5% while in ARIC study (1990) (Burke et al., 1995; Crouse et al., 1996) it was 9%.

Body Mass Index (BMI)

The mean BMI in patients with CAD was 25.46± 2.62 kg/m2 and in controls, it was 22.79 ±3.63 kg/m2.The BMI was significantly higher in cases than controls ($p<0.05$).

The mean BMI in study conducted by Jadhav and Kadam (2001) was 25.5± 3.37 kg/m2. It was comparable to our study. The BMI in Rotterdam study (Bots et al., 1997) was 26.4 kg/m2 and was comparable to our study.

Lipid profile

The mean total cholesterol in cases was 222.36± 67.93mg/dl and in control it was 161.88± 43.9 mg/dl. Total cholesterol was significantly higher in cases with CAD than controls ($p<0.05$).

In the study conducted by Jadhav and Kadam (2001) total cholesterol was 208.4 ±43.4 mg/dl which was comparable to our study. The mean LDL cholesterol in cases with CAD was 147.26± 65.19 mg/l where as in control it was 96.31 ± 33.65 mg/dl. LDL cholesterol was significantly higher in cases than controls ($p<0.05$).

The LDL cholesterol levels were comparable to that seen in ARIC study in which LDL cholesterol value was 140 ±37 mg/ dl (Burke et al., 1995; Crouse et al., 1996). The mean triglyceride level in our study, in cases with CAD was 195.62 ± 88.43 mg/dl, while in controls, it was 154.16 ± 65.54 mg/dl. It was significantly higher in cases compared to controls $p<0.05$. Jadhav and Kadam (2001) and Mohan *et al*., (2000) found similarly high triglyceride level in Indian subjects which was comparable to our study. The mean HDL cholesterol level in cases was 35.76 mg/dl.

HDL level in the study done by Jadhav and Kadam (2001) was 41.7 ±7.7 mg/dl and in ARIC study (Burke et al., 1995; Crouse et al., 1996) it was 45.14 mg/dl and in cardiovascular health study (O' leory et al., 1992) it was 55.65± 11.8 mg/dl.

So, in our study HDL cholesterol level was comparatively lower than all other studies.

Intima media thickness (IMT)

In our study, IMT in patients with CAD was 1.098± 0.29and in controls it was 0.606 ±0.15 mm. In cases, IMT was significantly higher than controls $p<0.001$.

In cardiovascular health study (O' leory et al., 1992) the mean IMT was 1.03 ± 0.2 mm which was comparable to our study. Jadhav and Kadam (2001) noted higher IMT levels in cases than controls.

The mean IMT in hypertensive cases was 1.176± 0.31 mm. this correlated with findings of Jadhav and Kadam (2001) and ARIC study (1990) (Burke et al., 1995; Crouse et al., 1996). Salonen and Salonen (1993) reported that each 0.1 mm increase in IMT, the risk of myocardial infarction increased by 11% and maximal IMT remains statistically significant predictor of acute MI. ARIC study reported that carotid IMT was 10% greater in patients with MI (Burke et al., 1995; Crouse et al., 1996). Johannes Hulthe *et al*., (1997) reported that presence of plaque and increased IMT in carotid artery is associated with CAD.

Rotterdam study (Bots et al., 1997) also showed that higher the base line IMT, the greater is the myocardial infarction risk. The mean IMT in diabetic patient was 1.4 mm. CUPS study (Mohan *et al*., 2000) showed that carotid atherosclerosis i.e., IMT more than 1.1 mm is seen in diabetics than non diabetics, which was comparable to our study. Diabetes mellitus predispose to atherosclerosis and is risk factor for carotid atherosclerosis and coronary atherosclerosis.

Rotterdam study (Bots et al., 1997), cardiovascular health study (O' leory et al., 1992), ARIC study (Burke et al., 1995; Crouse et al., 1996) and Craven *et al*., (1990) Kuopio ischemic heart disease risk factor study (Salonen and Salonen, 1993) and Jadhav and Kadam (2001) showed that IMT is significantly higher in hypertensive patient.

In smokers, the case group the IMT was 1.08± 0.25mm which was significantly higher than control group (0.7± 0.15 mm) with p value of <0.05.

Smoking is strong predictor of carotid IMT. Craven et al., (1990) Salonen and Salonen (1993) and Baldassarre *et al*., (2000) reported that smoking is a strong risk factor for carotid atherosclerosis.

In conclusion, the carotid IMT was found to be higher in patients with CAD and there was statistical difference between cases and controls. The odds ratio for IMT exceeding 0.8 mm is 55 in cases against those of controls making it an important marker of CAD.

The carotid IMT was found to be higher in the cases with traditional risk factors like smoking, diabetes mellitus, hypertension and hyperlipedemia. Thus our study shows that carotid IMT is a marker of atherosclerosis, which is strongly associated with traditional risk factors and can be used as a surrogate marker in prediction of atherosclerosis and CAD. Carotid B- mode ultrasound is a safe, non invasive and reproducible procedure, which helps in early identification of clinical and preclinical CAD

Table.1 Source of the knowledge of family planning

Parameters	**CAD(n=50)**	**Non CAD(n=50)**	**P value**
Smoking (%)	40	24	<0.001
Hypertension (%)	44.4	20	<0.001
Diabetes mellitus (%)	30	12	<0.001
Mean Body mass index(kg/m^2)	25.46± 2.6108	22.792±3.633	<0.05
Mean Total cholesterol levels (mg/dl)	222.36 ±67.7322	161.88± 43.90978	<0.01
Mean LDL- c levels (mg/dl)	147.26 ±65.954	96.36± 33.659	<0.001
Mean HDL-c levels (mg/dl)	35.46± 6.2972	32.04±4.5846	<0.05
Mean Triglycerides levels (mg/dl)	195.26± 88.4316	154.96± 65.5448	<0.001
Intima media thickness(mm)	1.098±0.2938	0.606± 0.1530	<0.001

Table.2 Intima media thickness (IMT) and coronary artery disease (CAD) cross tabulation

	Cases (CAD)	**Controls (without CAD)**
IMT>0.8 mm	45	7
IMT<0.8 mm	5	43

Table.3 Mean intima media thickness (IMT) in subgroup

	Hypertensive	**Diabetic**	**Smoker**
Cases	1.170±0.3128	1.40±0.3464	1.08± 0.2426
Controls	0.79±0.149	0.8±0.1549	0.7±0.1549
p-value	<0.01	<0.001	<0.001

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