CAROTID INTIMA-MEDIA THICKNESS IN PATIENTS PRESENTING WITH ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Aim: To assess the role of carotid intima-media thickness in patients with acute myocardial infarction as compared to without it. **Methods:** It's a prospective case control study in 50 patients with acute myocardial infarction defined as clinical presentation of acute coronary syndrome and elevated Troponin I and data was compared with 54 age and sex matched control subjects. All patients had their carotid intima-media thickness measured within 1 cm from carotid bulb in the common carotid artery on both sides, and average and maximum values were calculated from at least 3 measurements on each side. The measured values were compared with ARIC (Atherosclerosis Risk in Communities; a large epidemiological study) values for the appropriate age categories. **Result:** Eight percent of MI had occurred below age 45 years. Twenty six (52%) cases and 18 (33%) of control subjects were hypertensive. Eighteen percent of cases and 4% of control had diabetes. More than 50% of total patients were past or current smokers. Fifty one percent of cases had non-ST elevation MI and 27% had inferior wall STEMI. Mean CIMT in MI group was 0.69±0.19 mm and 0.74±0.19mm in right and left side and in control group was 0.61±0.18 mm and 0.59±0.19 mm in right and left side respectively (P = 0.037 for right CCA CIMT, P= 0.0001 for left CCA CIMT). The number of patients with CIMT value above the 75th percentile value of ARIC were 24 in cases and 15 in

control in right side (P=0.03) and 24 in cases and 10 in control in left side (P=0.001). **Conclusion:** Increased value of CIMT is significantly associated with incident MI. The easy, cheap and non-invasive test can be used as surrogate marker of atherosclerosis.

KEYWORDS: Atherosclerosis; carotid intima-media thickness; myocardial infarction; Nepal; common carotid artery; coronary artery disease.

INTRODUCTION

Atherosclerosis is the major cause of death and premature disability in the developed world. The burden is increasing in particular in developing countries. Over 80% of CVD deaths take place in low- and middle-income countries.[1] Atherosclerosis is an inflammatory disease that often begins early in life with impairment of endothelial function, which leads to the formation of lesions in large and medium elastic and muscular arteries.[2] Symptomatic cardiac events occur when the atherosclerosis progresses to flow limiting disease that cause ischemia or when a thrombus forms on an existing plaque as a result of plaque rupture or erosion. So it is imperative to shift focus on disease prevention on individuals at risk of developing CVD but still clinically asymptomatic.

Atherosclerosis is a generalized process that affects all arterial beds, including carotid and coronaries arteries. In 1986, Pignoli et al from Italy reported the results of an in-vitro study of human aorta and common carotid artery, which compared direct measurement with B mode ultrasound images.[3] There was no significant difference between the two measurements. The carotid artery lends itself to study by high-resolution ultrasound devices because it is superficial in location, is relatively stationary and runs in parallel to the surface of the neck, at least to the level of carotid bifurcation. At the current time, it is not possible to distinguish between intima and media by ultrasound. Studies done in Western countries have suggested increased CIMT predict future cardiovascular event risk and can also detect presence of CAD.[4-8] However, data on Nepalese patients are sparse who differ substantially from the Western population in cardiovascular risk profile, morbidity and mortality. The study aims to assess the role of CIMT in patient presented with acute myocardial infarction by measuring it and comparing with 75th percentile value or above provided by large epidemiological study of ARIC (atherosclerosis risk in community) study[9] done in 4 US communities from 1987 to 1993 as recommended by American Society of Echocardiography consensus statement.[10]

METHODS

This is a prospective case control study done in patients presented to ManMohan Cardiothoracic Vascular and Transplant Centre with 50 acute myocardial infarction and 54 control patients from August 2011 to December 2012. Age 25 to 74 years, chest discomfort consistent with myocardial ischemia or angina equivalent and positive Troponin I test (qualitative assay from cardiac specific troponin I from Acon Laboratories, Inc., San Diego, CA, USA with lower detection limit of 0.5 ng/ml) the index hospital admission were taken as inclusion criteria. The standard of care was given by the treating physician to all cases. Echocardiography (Vivid™ 7 dimensions from GE medical system) and measurement of CIMT was done by the investigator in all cases. The CIMT was measured by 10MHz linear array transducer at posterior wall of distal common carotid artery within 1 cm from the carotid bifurcation. At least 3 measurements were measured on each side and average value was recorded. The measurement was done manually at the time of image acquisition. As the values were compared with ARIC study values which gave 25th, 50th and 75th percentile value for males and females for right and left side for age range 45 to 65 years, for patients below and above 45 and 65 years of age, values taken were same as for 45 years and 65 years respectively. If the measured value was above 75th percentile for the age range, it was regarded as increased CIMT. Data were analyzed in IBM SPSS ver. 20 with standard statistical tests: independent T-test for quantitative data and χ^2 test for qualitative data. Logistic regression analysis was done for studying the correlation of various risk factors with increased CIMT. One sided P value of < 0.05 was considered statistically significant. The study was approved by the Institutional Review Board of Institute of Medicine.

RESULTS

Table 1: Baseline characteristics of MI group and control group

	MI group	Control group
No of patients	50	54
Age (years)	57.14 ± 10	52.89 ±14.8
Males	34 (68%)	25 (46%)
Hypertension	26 (52%)	18 (33%)
Diabetes mellitus	9 (18%)	2 (3.4%)
Smoking	28 (56%)	29 (53%)
Family history of premature CAD	3 (6%)	3 (6%)

CAD: Coronary artery disease, MI: Myocardial infarction

The baseline characteristics of the study groups are shown in Table 1. There was no statistically significant difference between the two groups, except that diabetes mellitus was

more prevalent in myocardial infarction group. The mean and maximum carotid intima-media thickness values are given in Table 2. Except maximum right CCA IMT (P= 0.167), all other parameters were statistically significant between cases and control (P= 0.037 for right mean IMT, P= 0.0001 for left mean IMT, P= 0.002 for left maximum IMT).

Table 2: Mean and Maximum CIMT values in cases and control

	Cases of acute MI (N=50)	**Control (N=54)**
Right CCA – mean IMT (mm)	0.69 ± 0.19	0.61 ± 0.18
Left CCA- mean IMT (mm)	0.74 ± 0.19	0.59 ± 0.19
RightCCA–maximum IMT (mm)	0.80 ± 0.18	0.74 ± 0.19
Left CCA- maximum IMT (mm)	0.85 ± 0.20	0.71 ± 0.21

The distribution of right and left mean CCA CIMT value above 75th percentile value of ARIC CIMT value is provided in figures 1 and 2 respectively.
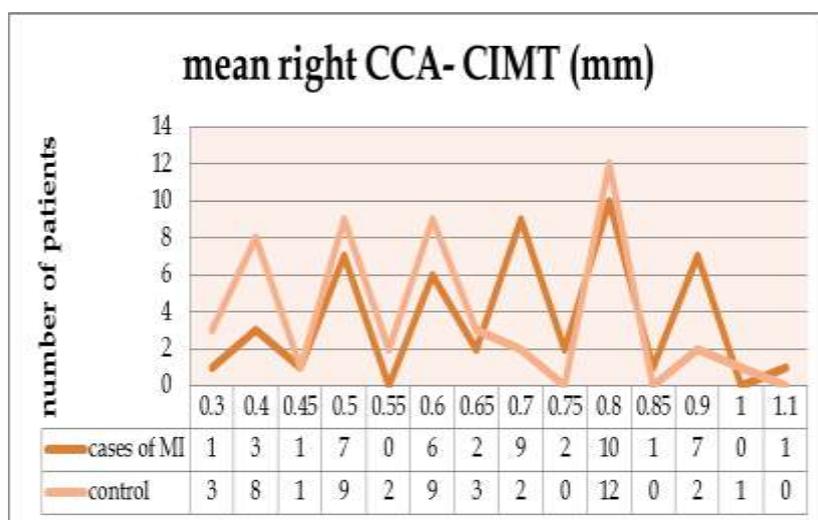
Fig 1: Mean right-CCA CIMT value distribution in cases and control
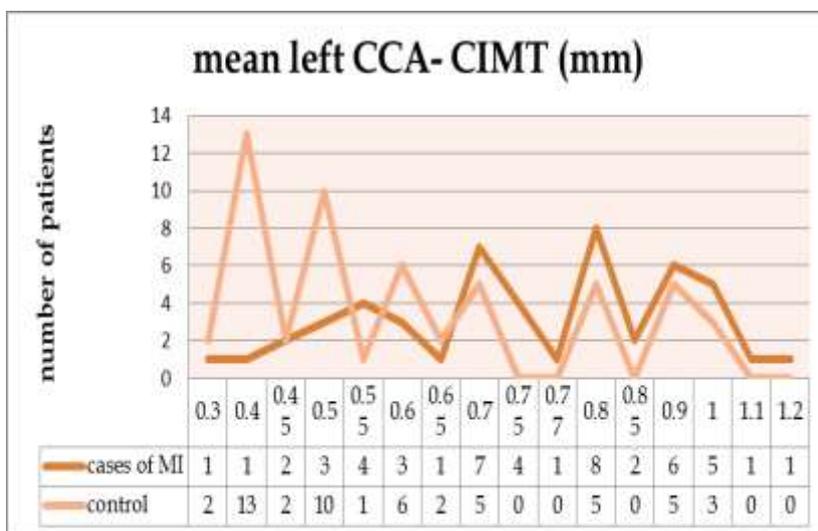
Fig 2: Mean left-CCA CIMT value distribution in cases and control

On multiple logistic regression analysis, CIMT values higher than 75th percentile value were found as the only independent predictors of acute myocardial infarction among the variables studied (Table 3).

Table 3: Multivariate analysis using acute Myocardial Infarction as a dependent variable

Variable	B	SE	P value
Age	0.006	0.004	0.144
Hypertension	0.099	0.098	0.317
Diabetes mellitus	0.283	0.154	0.070
Smoking	0.055	0.098	0.575
Family history of premature CAD	-0.088	0.203	0.667
Right CIMT value more than 75th percentile	0.019	0.130	0.025
Left CIMT value more than 75th percentile	0.305	0.133	0.024

B= estimated coefficient, CAD= coronary artery disease, CIMT= carotid intima-media thickness, SE= standard error

DISCUSSION

The development of new non-invasive tools for the detection of atherosclerosis including CIMT has added a new dimension to cardiovascular research and clinical cardiology practice. Mean CIMT in particular has added a lot of interest because it is easy to directly visualize the ongoing atherosclerotic process. Various prior studies have shown cross-sectional association between CCA CIMT and cardiovascular risk factors in Europe and United States.[11, 12]

The prospective cross sectional study done in cases of acute myocardial infarction group and control group without incident MI, our study showed mean right CCA-IMT 0.69 mm and 0.61 mm in right side and 0.74 mm and 0.59 mm in the left side respectively. Compared to 50th percentile value of ARIC (atherosclerosis risk in communities study)[12] values done in 4 communities in America on general population to find out distribution of CIMT, the mean right CIMT value was not significant statistically (P=0.09) but comparing 50th percentile value of left CIMT and 75th percentile value of both right and left CIMT mean values were significant between the MI group and control group (P= 0.29, 0.033 and 0.001 respectively). These findings are all consistent with previous studies.

As a part of the Cardiovascular Health Study (CHS), a population-based cohort of adults aged ≥ 65 years, Mukamal et al examined the 10 year risk of myocardial infarction, stroke and cardiovascular death in 782 older adults with diabetes.[13] In this study, novel biomarkers did

not improve discrimination or classification. The addition of ankle-brachial index, electrocardiographic left ventricular hypertrophy and internal carotid intima-media thickness modestly improved discrimination (C statistic 0.68; p = 0.002) and classification (net reclassification improvement [NRI] 0.12; p = 0.01), mainly in those remaining free of CVD. In a study in Indian population by Hansa et al carotid intima-media thickness was measured using high-resolution B-mode ultrasonography in 101 patients with coronary artery disease and 140 control subjects. The maximum and average carotid intima-media thickness was significantly higher in the coronary disease group compared to the controls (1.02 vs. 0.80 mm and (0.82 vs. 0.67 mm respectively).[14] Our study had mean CCA-IMT of 0.69 and 0.74 mm in right and left side in acute MI group and 0.61 and 0.59 mm in the control group and the findings are similar. On multivariate logistic regression analysis, carotid intima-media thickness was the only factor found to be an independent predictor of coronary artery disease. There was a significant association between risk factor count and the average and maximum intima-media thickness values in the combined study population. These results indicate that raised values of average and maximum carotid intima-media thickness are significantly associated with the presence of coronary artery disease and this association is independent of the presence of other conventional cardiovascular risk factors.

Our study also showed that only diabetes mellitus was statistically significant for the presence of increased carotid intima thickness. But if CIMT values >75th percentile were considered, only age was found to be significant; history of hypertension, measured SBP & DBP at the examination, history of diabetes, family history of premature atherosclerosis and lipid profile were not. This is because of small sample size and different primary endpoints. Moreover, we studied consecutive cases of myocardial infarction and control group and there is obvious limitation of non-randomized study.

In a case control study done in Nepal by Sharma et al designed to evaluate carotid intima-medial thickness (IMT) in hypertensive and normotensive individuals, high-resolution carotid ultrasound was done in 203 hypertensive patients (cases) and 101 normotensive individuals (control) with mean age from 35 to 65 years. Scanning of bilateral common carotid artery (CCA) was performed in anteroposterior projections. Mean IMT was significantly high in hypertensive patients compared to the control group, p<0.001 (in cases, IMT in right side was 0.968 mm and that of left side was 0.969 mm and in control group IMT of right side was 0.551 mm and that of left side was 0.555 mm). A significant difference in IMT of bilateral

common carotid arteries was found between the smoker and non-smoker hypertensive patients (p<0.02).[15]

Our study gives some of important findings of public health importance. Almost 50% of patients in both cases and control were smokers, which will cause its ill-effects in years to come not only coronary artery disease, cerebrovascular disease and peripheral artery disease but also chronic obstructive lung disease, carcinomas and various other illnesses. The prevalence of diabetes was about 20% in cases and 5% in control group. With change in eating habits and physical inactivity, diabetes incidence and its huge burden on overall health will definitely increase if not actively sought and preventive measures taken in time. Many patients in the control group had valvular heart disease and commonest lesions were mitral regurgitation with or without mitral stenosis implying the fact that rheumatic heart disease is still the major disease. Though LDL-Cholesterol was increased only in 12% of cases, 47.7% showed low HDL-Cholesterol.

So the carotid intima-media thickness, when consistently and uniformly measured, has been found in a quite number of studies as independent marker of subclinical atherosclerosis showing statistical significance with cardiovascular risk factors, incident and prevalent vascular events and predicting future cardiovascular events in prospective studies. Our study also found a strong association of mean far-wall common carotid artery intima-media thickness in patients presented with acute myocardial infarction in Nepalese population.

CONCLUSION

As compared to population without incident myocardial infarction, the mean far wall common carotid artery CIMT higher than 75th percentile value of ARIC in both sides were significantly higher. Easy applicability and noninvasive nature of B-mode ultrasonography make it suitable for use as surrogate marker to measure atherosclerosis burden. This study suggests a significant association between CIMT and presence of myocardial infarction in Nepalese patients also. However, more data are needed to establish CIMT as a noninvasive tool for detection of CAD in symptomatic or asymptomatic individuals.

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