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Association between Carotid Artery Intima-Media Thickness and Cerebrovascular Accident: Prospective Observational Study

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Abstract

Introduction: Ischemic cerebrovascular accident (CVA) is often a sequel of atherosclerotic disease. Common carotid artery intima-media thickness (CIMT) is a surrogate marker of early atherosclerotic changes. Aim of our study was to see if increased CIMT co-related with increased risk of stroke using carotid artery Doppler duplex ultrasonography. *Methods:* Ours was prospective observational study including 300 patients who were divided into 2 groups: CVA group (n = 150) and non-CVA group (n = 150). Noninvasive measurements of the intima and media of the common carotid artery (CCA) were performed with high-resolution ultrasonography in all the patients in both the groups. *Results:* Age range of the patients was 33 to 72. CIMT was significantly increased in CVA patients (0.77 ± 0.35 mm) compared to non-CVA patients (0.57 ± 0.15 mm) on both right and left CCA. The significance of difference persisted in patients with associated comorbidities, e.g. hypertension, diabetes mellitus and smokers. *Conclusion:* Increased CIMT of the CCA, measured noninvasively by Doppler ultrasonography are associated with increased risk of CVA.

Keywords: CIMT; Stroke; Duplex.

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Introduction

Stroke is a cerebrovascular accident (CVA) thatis the result of pathological changes in the cerebral vessels. Ischemic stroke accounts for 85% of the all the cases of stroke and it can be acute due to occlusion of cerebral vessels by emboli or chronic due to atherosclerotic occlusion of carotid arteries.[1] Presently, CVA risk stratification tools are focused on modifiable risk factors such as diabetes mellitus (DM), systemic hypertension (HTN), and dyslipidemia and smoking which in long-term may contribute to atherosclerotic changes in arterial thickness. Similar to other large systemic arteries, in carotid arteries also, early stage of atherosclerotic occlusion is the endothelial injury induced by multiple factors including DM, HTN, dyslipidemia and smoking that directly or indirectly injure the vessel wall. Among various factors, HTN is the most common cause for endothelial injury. Long-standing HTN induces a shear stress on the vessel wall that leads to an increased production of vaso-active substances such as nitric oxide (NO), prostaglandin E and prostacyclins from the endothelial cells. These substances induce the production of superoxide ions that further incites the increased endothelial permeability and injury.

Injured endothelial cells further release the pro-inflammatory cytokines that activates the leukocyte. This eventually induce a vicious cycle culminating into complete endothelial injury. Endothelial injury alters the vessel wall thickness through vascular remodeling that leads to reduction in the diameter of the blood vessel through hypertrophy or through an eutrophic inner remodeling process.[1,2] The net resultis the stiffening of vessel wall and the blood vessel becomes smaller in diameter, rigid and non-compliant.

Change in the combined thickness of the intima and media layers of the common carotid artery (CCA), i.e. common carotid artery intima-media thickness (CIMT) is believed to be a surrogate marker of generalized atherosclerosis and used as an indicator for the early detection of atheromatous changes. Studies have found that increased CIMT is significantly related to various cardiovascular risk factors including HTN, DM, hypercholesterolemia and smoking. Further, increased CIMT has also been related to future risk of myocardial infarction, CVA, and cardiovascular death.[3-7]

Since first proposed in the 1980s, the Doppler duplex ultrasound is increasingly being used as a non-invasive investigation to measure CIMT. However, there are still few studies showing an association between increased CIMT and stroke. In our institute, we investigated the hypothesis that increased CIMT is directly correlated with the incidence of stroke.[5]

Materials and Methods

Our study was prospective observational study included the patients admitted to emergency department of civil hospital, Ahmedabad. The study was approved by ethics committee of our hospital and informed and written consent was obtained from all the patients. Patients' age ranged from 33 to 72. The patients were categorized into 2 groups, stroke and non-stroke groups. There were 150 patients in the stroke group and 150 patients in the non-stroke group.

The carotid arteries of all patients were evaluated using high-resolution B-mode ultrasonography using a cross-sectional methodology. Doppler with a 0.75 MHz linear superficial probe in B-mode. The point of measurement was taken 1 cm proximal to the carotid bulb at the site of maximum thickness, avoiding the plaque area. The ultrasound machine used had a sensitivity range of 0.1 mm, i.e. each division was equivalent to 0.1 mm. The maximum intima-media thickness was used as the key variable in determining the correlation between CIMT and stroke. The maximal intima-media thickness of the CCA was defined as the mean of the maximal intima-media thickness of the near and far wall on both the left and right sides. The intima-media thickness was called abnormal if the thickness was more than 1 mm. Measurements were made by readers blinded to all clinical information.

Statistical analysis

Statistical analysis was performed using the software package SPSS for Windows 18.0. Association of the variables was tested using chi-square statistics. χ^2 statistics and independent *t*-test were used when appropriate to determine significance of difference among background variables compared.

Results

A total of 300 patients (229 males and 71 females) were included in our study. Patients with stroke (n = 150) (group 1) were compared with age and sex matched patients without stroke (n = 150) (group 2). Incidence of hypertension, type 2 diabetes mellitus (DM), dyslipidemia and smoking were comparable in both the groups.

Table 1: Baseline Characteristics of the Patients.

Characteristics	CVA group (n = 150)	Non-CVA group (n = 150)	*p*-value
Age (years) (SD)	59.34 ± 8.68	56.12 ± 10.16	0.0034
Male sex (%)	113 (75.3%)	116 (77.3%)	0.7859
HTN (%)	96 (64%)	92 (61.3%)	0.7203
Type-2 DM (%)	51 (34%)	47 (31.3%)	0.7119
DM with HTN (%)	35 (23.3%)	6 (4%)	<0.001
Dyslipidemia (%)	40 (26.7%)	41 (27.3%)	1.000
Smoking (%)	76 (51%)	70 (46.7%)	0.5636
Alcohol (%)	39 (26%)	43 (28.7%)	0.6975

DM—Diabetes mellitus, **HTN**—Hypertension

As shown in table 2, CVA group had higher mean right CIMT compared to non-CVA group and the difference was highly significant (p < 0.0001). Statistically significant difference was also observed when groups were compared for CIMT in patients with risk factors such as DM, HTN and smoking. When groups were compared for the left CIMT value, the CVA group was found to have higher values compared to non-CVA group (p < 0.001). This difference was statistically highly significant when groups were analyzed with risk factors such as HTN, diabetes, and smoking.

Table 2: Association between CIMT and other Risk Factors with Stroke

CIMT (mm)	CVA group (n = 150)	Non-CVA group (n = 150)	*p*-value
Right IMT (mm)	0.77 ± 0.35	0.57 ± 0.15	<0.0001
Left IMT (mm)	0.74 ± 0.31	0.58 ± 0.14	<0.0001
Right IMT with DM (mm)	0.87 ± 0.13	0.54 ± 0.17	0.06
Left IMT with DM (mm)	0.92 ± 0.12	0.62 ± 0.11	0.003
Right IMT with HTN (mm)	0.76 ± 0.17	0.62 ± 0.12	<0.0001
Left IMT with HTN (mm)	0.74 ± 0.18	0.61 ± 0.12	0.006
Right IMT with DM and HTN (mm)	0.76 ± 0.22	0.59 ± 0.13	0.06
Left IMT with DM and HTN (mm)	0.69 ± 0.19	0.72 ± 0.13	0.15
Right IMT in smokers (mm)	0.76 ± 0.12	0.56 ± 0.11	<0.0001
Left IMT in smokers (mm)	0.73 ± 0.16	0.54 ± 0.14	<0.0001

CIMT—Carotid artery intima-media thickness, **DM**—Diabetes mellitus, **HTN**—Hypertension.

Discussion

In our study, CIMT was measured in both the CVA and were found to be significantly higher in CVA group (0.77 ± 0.35 mm and 0.74 ± 0.31 mm) than in non-CVA group (0.57 ± 0.15 and 0.58 ± 0.14 mm; p < 0.001). Difference in the CIMT between CVA group and non-CVA group was also observed by Sahoo *et al*.[8] In their study on south Indian population, they reported a significantly higher mean CIMT in the CVA group (0.78 ± 0.19 mm) than in the non-CVA group (0.59 ± 0.98 mm; p < 0.0001). Similarly, Mukherjee *et al*.[9] also reported a significantly higher CIMT values among stroke patients as compared to the controls. The major limitation of their study was, however, the sample size and the controls were not matched with the cases.

Study by Cupini *et al*.[10] also found that CIMT >1 mm was significantly associated with the development of stroke and CIMT was significantly higher in patients with stroke compared to the controls (0.91 mm). However, the population in their study was more than 70 years of age and patients were of different ethnicity. In our study, patients were relatively young with mean age 59.34 years. In our study, mean CIMT in CVA patients was 0.74 mm in the left CCA and 0.77 mm in right CCA. Our results are in agreement with GENIC, a case control study[11] and study by Saxena *et al*.[12] In GENIC, a case control study and a study by Saxena, *et al*. similar mean CIMT values (0.79 mm and 0.77 mm, respectively) in CVA patients was found in patients with stroke. The basal characteristics of population in both the studies were similar to ours, except that both these studies included patients with older age and only in hypertensive patients.

In a study by Bamford *et al*. in Caucasian patients with CVA, higher values of CIMT was found in patients who had associated DM, HTN, and dyslipidemia and in smokers compared to patients who didn't have these risk factors[13]. In our study, we also found significantly higher value of CIMT among CVA patients who had associated comorbidities. Similar results were observed by Sahoo *et al*.[8] In their study, on subgroup analysis by risk factors such as HTN, DM, and smoking between the patients with CVA and the controls, they found significantly higher CIMT in patients who had associated risk factors. In a study by Das *et al*.[14] on patients with CVA in Indian population, they demonstrated significantly increased CIMT in CVA patients with varying grades of plaque in patients with Type II DM, HTN, and smokers. Study by Saha *et al*.[15] in 50–60 years of age group patients also found a higher value of CIMT among ischemic stroke patients with DM in both left and right carotid arteries as compared to the controls, but the difference was not statistically significant. Cross-sectional study by Harris in South-East Asia also showed a strong association of CIMT (>1.0 mm) and stroke (p = 0.008) in the Indonesian

population.[1] The author proposed that a direct correlation exists CIMT and stroke because CIMT is a marker of generalized atherosclerosis which plays an important role in the pathogenesis of cerebrovascular events such as stroke.

Limitations

A number of patients in our study were limited and the study was limited to single hospital and a small region of the country. We recommend studies involving larger number of patients from across the country to further validate our findings.

Conclusion

Our results extend the findings of previous studies and show that CIMT has a strong correlation, with the incidence of stroke even in younger age group. The association becomes further stronger in patients who have associated co-morbidities. Our results show that CIMT may be used as a predictor of cerebrovascular events across all age groups in Indian population.

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