Original Research Article

Study of carotid intima media thickness and lipid profile in cases of ischaemic stroke

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Abstract

Background: Stroke is one of the leading reasons for mortality throughout the world. Measurement of carotid intima media thickness (CIMT) is a reliable marker for the development of atherosclerosis and ischemic stroke (IS). **Aims**: To study the carotid Intimal-medial thickness in patients with Ischemic stroke proven by computed tomography or MRI. To study the correlation between the increase in carotid artery intimal medial thickness & dyslipidemia in patients with ischemic stroke proven by computed tomography or MRI. **Materials and methods:** Our study is a cross-sectional study of hundred patients, Hundred patients admitted with acute ischemic stroke confirmed by computer tomography (CT)/MRI admitted in our Hospital. The blood collected within 24 hrs of admission for lipid-profiles. eg., sr. cholesterol, TG, HDL, LDL, VLDL. Carotid Doppler study in patients of ischemic stroke. Patients, who met the inclusion-criteria, are included in the study. **Results:** A total of 144 patients were screened in 81% patients with CT proven ischemic stroke, there is an increase in intimal- medial thickness of common carotid-internal carotid artery. A statistically significant correlation was found between increased intimal-medial thickness in patients of ischemic stroke and abnormal triglycerides & HDL. **Conclusion**: CIMT measurement and lipid profile can be used as primary preventive measure for prediction of stroke in elderly population.

Keywords: Carotid Intima Media Thickness(CIMT), Dyslipidemia, Triglycerides

Introduction

Stroke is one of the leading causes of morbidity and mortality in the world today. There has been a constant effort on the part of medical researchers to analyze this problem and search for factors that may aid in its prevention. Atherosclerosis afflicts multiple vascular beds, accounting for nearly all of coronary heart disease and some proportion of ischemic strokes[1]. An increased cross-sectional carotid intimal-medial thickness, a measure of carotid artery atherosclerosis, has been associated with unfavourable levels of cardiovascular risk factors, prevalent cardiovascular disease, and atherosclerosis elsewhere in the arterial system. There is a growing belief that carotid intimal medial thickness can be regarded as an indicator of generalized atherosclerosis. There are few studies showing an association between increased intimal-medial thickness and stroke. The risk of stroke increases gradually with increasing intimal-medial thickness[2]. Drugs which retard the progression of intimal-medial thickening of the artery may prevent stroke and are the subjects of current trials all over the world. Elevated low density lipoproteins, cholesterol and triglyceride levels are significant independent risk factors in patients with proven atherothrombotic cerebrovascular disease manifesting as stroke or transient ischemic attack [3]. Dyslipidemia also identified as risk factors for coronary artery disease and stroke[4].

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Early detection of dyslipidemia reduces the risk of stroke & decreases the morbidity & mortality. It is proposed to study the association of an increase in carotid artery intimal medial thickness as well as dyslipidemia in patients with ischemic stroke proven by computed tomography or MRI. Recognition of atherosclerosis in subclinical stage is of paramount importance in planning for prevention of diseases like coronary artery disease (CAD), stroke and peripheral vascular disease(PVD). The importance of preventive screening, risk stratification and management of atherosclerosis cannot be over emphasized. Technologies have been developed to identify atherosclerosis in subclinical phase. Conventional Contrast Angiography is the gold standard test for evaluation of coronary and cerebral arteries. However this method is invasive, costly, equipment and expertise oriented, carries risk of anesthesia and cannot be repeated frequently. Alternative to this are computed tomography angiography(CTA),Magnetic resonance Angiography(MRA),Electron beam computed Tomography(EBCT),Brachial artery reactivity testing(BART) and Ankle Brachial index(ABI).These techniques have Disadvantages of high cost, limited availability, advanced setup, exposure to radiation and contrast and decreased sensitivity and specificity. Thus there is a need for a technique which is cheap, simple, noninvasive, reproducible, and available at peripheral center, carries low risk, sensitive and specific. It is often said that when one cerebral or coronary vessel is involved with atherosclerosis, four peripheral vessels also share the misery. Autopsy studies have also confirmed close histological relationship between coronary, cerebral and carotid atherosclerotic disease.

Ultrasound assessment of easily accessible arteries have been advocated as a surrogate marker for coronary and cerebral arterial systems which are less accessible. Intima media thickness(IMT)refers

to endothelial cells, connective tissue and smooth muscles in the vessel wall. It is the site of lipid deposition and plaque formations. Measurement of IMT by B-mode ultrasound is a well validated procedure to detect early stages of atherosclerosis. Ultrasound imaging also provides details on plaque presence and type calcification and wall diameter. It has the advantage of being cheaper, reproducible 4 and non invasive. It is sensitive in detecting early atherosclerosis and plaques at risk of rupture.

Use of ultrasound imaging for assessment of atherosclerotic changes in carotid arteries was first reported in 1991[5]. Absolute definition of a cutoff for IMT is problematic because of strong influence for age, gender and race and hypertension related increase in IMT. Average and maximum CIMT in healthy adults were 0.67 and 0.7 mm respectively. CIMT can also be used to assess the influence of risk factors, therapies and diet on progression and regression of atherosclerosis. It has been found that risk of myocardial infarction and stroke increases by 10-18 % with each 0.1 mm increase in CIMT .CIMT can be used as a surrogate marker to assess atherosclerotic burden independent of other risk factors.

Materials and methods

Our study is a cross-sectional study of hundred patients, Hundred patients admitted with acute ischemic stroke confirmed by computer tomography (CT)/MRI admitted to department of medicine from Osmania medical college. The blood collected within 24 hrs of admission for lipid-profiles as Serum cholesterol, TG, HDL, LDL, VLDL. Carotid Doppler study in patients of ischemic stroke. Patients, who met the inclusion-criteria, are included in the study. The study period is between January, 2012, to October, 2013 for twenty-two months. This study has the approval of the ethical committee

Inclusion Criteria

Presenting with symptoms at the time of admission to the hospital, CT Brain / MRI Brain proven infarct, Patients amenable for transportation to the radiology department for carotid Doppler.

Exclusion Criteria

CT/MRI brain was normal, Scan showing hemorrhage/lacunar infarcts, Patients with recurrent stroke, valvular heart disease, thrombophilic state, stroke more than two weeks and the Patients on statin therapy for more than a year for any indication.

All patients enrolled were questioned with a detailed proforma. Complete postal address with name and telephone number of near relative, occupation, educational status and financial status were noted. Detailed questioning regarding time of onset of symptoms, time to presentation to hospital, activity at the time of onset of symptoms was recorded. Patients were questioned with respect to symptoms suggestive of raised intracranial tension, side of weakness of limb, associated sensory or cranial nerve palsies, aphasia, brainstem or cerebellar signs were noted. Vitals of all patients including pulse, blood pressure were recorded. All patients were carefully auscultated for carotid bruit. Cardiovascular, cerebrovascular event, atrial fibrillation, diabetes mellitus, hypertension, hypercholesterolemia along with personal habits of smoking and alcohol use were elicited. All patients who fulfilled inclusion criteria underwent CT scan. Blood was withdrawn from all patients for creatinine, hemoglobin, mean corpuscular volume, fasting lipid profile, fasting blood sugar, sr. electrolytes, and Hs Crp, . All patients underwent ECG and 2D echo for evidence of ischemic heart disease. All patients fit to be transported were shifted to the Radiology and underwent carotid Doppler imaging using B-mode ultrasound (Siemens Acuson x300).

Infarcts were detected by neuro-imaging, Hypertension was defined according to the 7th JNC guidelines Or patient on anti-hypertensive medication. Diabetes mellitus is defined as fasting blood glucose >126mg/dl on two consecutive assessments or patient on any OHA or Insulin therapy. The fasting blood sample was analyzed on ERBA Smart Lab auto analyzer using the ERBA REKT201 kit.

Stroke is defined as an abrupt onset of focal neurological deficit of vascular region lasting more than 24 hours. Intima media thickness (IMT) refers to endothelial cells, connective tissue and smooth muscles in the vessel wall. 10 ml of blood after was collected within 24hrs of admission for the analysis of lipid profile. The analysis was done on auto analyzer ERBA Smart Lab ERBA test kit REKT104 for total cholesterol, REKT40 for triglycerides and REKT106 for HDL, LDL cholesterol was calculated using the Freidwald formula,

LDL cholesterol=Total cholesterol-HDL cholesterol- triglycerides/5

The levels of the individual fractions of the lipid profile were interpreted as follows, in accordance with the ATP III guidelines.

History of smoking, was included, whether the patient have ever smoked, is smoking or have stopped smoking and how many cigarettes per day.

Intimal Medial Thickness

All patients were examined in supine position with neck extended with a pillow under the shoulder. Ultrasonography of the common carotid artery, carotid bifurcation, and internal carotid artery of the left and right carotid arteries was performed with a 7.5-MHz linear-array transducer (Siemens Acuson x300).

On a longitudinal, two-dimensional ultrasound image of the carotid artery, the anterior (near) and posterior (far) walls of the carotid artery are displayed as two bright white lines separated by a hypoechogenic space. The distance between the leading edge of the first bright line of the far wall (lumen-intima interface) and the leading edge of the second bright line (media-adventitia interface) indicates the intima-media thickness. For the near wall, the distance between the trailing edge of the first bright line and the trailing edge of the second bright line at the near wall provides the best estimate of the near-wall intima media thickness. Longitudinal scan of carotid ultrasonogram. Measurement of CCA-IMT (*large arrows*) at the far wall of the common carotid artery is shown. The carotid plaque (*small arrows*) in the distal common carotid artery is seen. The *arrowhead* represents carotid bifurcation

Left carotid was examined first and then the right. Three sites were selected in each carotid artery. The carotid artery bulb was traced and the first reading is taken 1 cm proximal to the carotid bulb. The second reading is taken within the bulb and the site with maximum diameter recorded. The third reading is taken 1 cm distal to the carotid bulb along the internal carotid artery. For all three sites both near wall and far wall measurements are taken. The recordings are taken upto 2 decimal points. An average of each artery is computed taking into account all six readings. Head Position and Probe Orientation for C.Ul-Sound Scan. IMT measured on the frozen frame of a suitable longitudinal image with the image magnified to achieve a higher resolution of detail. The IMT measurement obtained from the 3 sites are averaged and the average of 6 measurements used The CIMT readings were recorded as

A= far wall of common carotid
B=near wall of common carotid
C=far wall of carotid bulb
D=near wall of carotid bulb
E=far wall of internal carotid
F=near wall of internal carotid
Thus, the mean CIMT = A+B+C+D+E+F/6

Results

A total of 144 patients were screened between January 2012 and October, 2013 and of these, 100 patients who fulfilled the inclusion criteria were included in the study. CT scan showed hemorrhage in 20 patients and were excluded. CT scan was not feasible in 5 patients and was excluded and 19 patients were too ill to be transported to the radiology department for Doppler study and they were also excluded. A total 44 patients were excluded. A total of 100 patients were studied.

Of the total 100 patients, the largest group was in the age range of 61-70 years (35%).The mean age was 60.13 years with minimum of 40

years and maximum of 80 years. There were 59(59%) males and 41(41%) females in the study (Table:1).

Table 1: Age and sex wise distribution of cases in study group

Age (Yrs)	Sex		Total (%)
	Male (%)	Female (%)	
41 – 50	23	4	27
51 – 60	18	12	30
61 – 70	14	21	35
> 70	4	4	8
Total	59	41	

Chi-square = 5.13, P>0.05 Mean age =60.13 SD = 12.22 Range= 80-40

Table:2: Hypertension-wise distribution of cases in the study group

Hypertension	No of cases	Percentage
Normal	10	10
Pre hypertension	10	10
Stage I	42	42
Stage II	38	38
Total	100	100
IMT (mm)		
< O.67 (Normal)	19	19
≥ 0.67 (Abnormal)	81	81
Total	100	100

Of the 100 patients, 10% had Prehypertension, Stage 1 hypertension in 42% and Stage 2 hypertension in 38% of patients. Only 10% of patients had a normal blood pressure According to JNC 7 criteria.

Of the total 100 patients, 81 (81%) patients had an IMT > or = to 0.67mm and 19(19%) patients had an IMT < 0.67 mm.

Table 3: Association between Carotid Intima thickness (IMT) and sex in study group

IMT (mm)	Male (%)	Female (%)	Total (%)
<0.67 (Normal)	12	7	19
≥ 0.67(Abnormal)	47	34	81
Total	59	41	100

Chi-square = 0.05, P>0.05

Of the total 100 patients, 81 (81%) patients had an IMT > or = to 0.67mm and 19(19%) patients had an IMT < 0.67 mm. Out of those 81 patients, 47 males & 34 females had an IMT >or = to 0.67mm and Out of those 19 patients, 12males & 7 females had an IMT < 0.67mm

Table 4: Correlation between lipid profile and Carotid Intima thickness (IMT) in study group

Sr. Cholesterol	IMT (mm) (%)		Total (%)	
	<0.67	≥ 0.67 (Abnormal)		
≥200	0	3	3	0.916
<200	19	78	97	
Total	19	81	100	
Sr. LDLmg/dl				
>100	6	31	37	0.779
<100	13	50	63	
Sr. Triglyceride				
≥150	5	59	64	0.0000406
<150	14	22	36	
Sr. HDL				
≥40	5	9	14	0.002
<40	14	72	86	

Out of 100 patients,3(3%) patients had abnormal total cholesterol. Out of those 3(3%) patients,3(3%)patients had abnormal IMT & 0(0%)patients had normal IMT. 97(97%) patients had normal total cholesterol & out of those 78(78%) patients had abnormal IMT & 19(19%) patients had normal IMT. This relation is statistically not significant with p > 0.05.

Out of those 81(81%) patients, 31(31%) patients had abnormal LDL & 50(50%) patients had normal LDL. 50 19(19%) patients had normal IMT & out of those 19(19%) patients,6(6%) patient had abnormal LDL & 13(13%) patients had normal.

Out of 100 patients,81(81%) patients had abnormal IMT & out of those 81(81%) patients,59(59%) patients had abnormal TG &22(22%) patients had normal TG. 19(19%) patients had normal IMT,out of those 19(19%) patients, 5(5%) patients had abnormal TG & 14(14%) patients had normal TG. The relation is highly significant

Out of 100 patients, 81(81%) patients had abnormal IMT. out of 81(818%) patients, 72(72%) had abnormal HDL &9(9%) patients had

normal HDL. 19(19%) patients had normal IMT & out of those 14(14%) patients had abnormal HDL & 5(5%) patients had normal HDL. The relation is statistically significant with p< 0.01.

Discussion

Early detection of atherosclerosis is desirable to prevent the occurrence of atherosclerotic events like stroke and myocardial infarction. The carotid intima media thickness is a non invasive technique used in the diagnosis of atherosclerotic disease which is 70.7% sensitive and 59.0% specific in predicting CAD[7]. Similarly, the risk of stroke increases with increasing intimal-medial thickness [IMT][8].Our study was carried out in 100 patients fulfilling inclusion criteria from January, 2012 to October, 2013. The mean age of our study population was 60.13 years with minimum of 40 years and maximum of 80 years. Males comprised 59% and females 41% of the study population. Uncontrolled hypertension was found to be the single most important risk factor for the development of strokes in the Monica report published in 1997[9]. In our study, also the single most common risk factor was hypertension with 80% of patients having a blood pressure recording of >=140/90.Most scientists studying the relation of intimal medial thickness with atherosclerosis have concentrated their efforts on coronary artery disease & the relation between intimal medial thickness and stroke. Four major randomized controlled trials have studied the relation of intimal medial thickness and stroke or coronary artery disease. At three years of follow up, the stroke risk increased gradually with increasing IMT. The odds ratio for stroke per standard deviation increase in IMT (0.163 mm) was 1.41. When subjects with a previous myocardial infarction or stroke were excluded, the odds ratio was 1.57 for stroke. Thus, increased common carotid IMT is associated with future cerebrovascular and cardiovascular events[10]. Increased intima-media thickness, an indicator of subclinical disease, may reflect the consequences of past exposures to risk factors. The addition of measurements of intima-media thickness to risk equations may help to identify asymptomatic persons who would benefit from aggressive preventive measures.

In our study, the mean IMT of the common carotid-internal carotid artery measured by carotid artery Doppler in patients of ischemic stroke was 1.6 mm with a minimum of 0.5mm and maximum of 2.7mm. Thus, we summarize that in patients of ischemic stroke, there is an increase in the intimal-medial thickness of the common carotid-internal carotid artery. The uniform standard cut off value of carotid IMT has not been defined with values in different studies. Sun, Y et al[11] have taken the cut off value as 0.68 mm. Taking this cut off value, asymptomatic individuals with carotid IMT >0.68mm had increased risk of carotid atherosclerosis. Geroulakos, G et al[12] took IMT > or = 0.85 mm as a criterion for the prediction of coronary artery disease. Lemne, C et al[13] have found 0.72mm of carotid IMT to be significant in their studies of carotid intima-media thickness and plaque in borderline hypertension. Lacroix, P et al[14] have demonstrated that carotid IMT >0.7 mm was a predictor of secondary events after coronary angioplasty (p=0.03) in univariate analysis. The CIMT expected for age of the patient was calculated using the formula CIMT = (0.009×Age) + 0.116. The mean expected CIMT was 0.67 mm calculated according to the age of the study patients. Therefore CIMT > 0.67 mm is considered as the abnormal value It is a reasonable assumption, however, that an IMT of > or = 0.67mm is abnormal & is likely to be associated with sonographically visible plaque. Thus considering the data from the above mentioned studies, a cut-off of 0.67 mm for Carotid IMT was selected as being significant by us.

In our study, Of 100 patients,80% were hypertensive. 10% had Pre hypertension, Stage 1 hypertension in 42% and Stage 2 hypertension in 38% of patients. Only 10% of patients had a normal blood pressure. Thus, we observed that majority of our patients in study group were hypertensive. (Using the JNC VII classification)[15].In our study, the cut off value for normal total cholesterol is taken as < 200 mg/dl and for normal IMT as < 0.67mm.Out of 100 patients 3(3%) patients had abnormal total Cholesterol. Out of those 3(3%) patients,3(3%)patients had abnormal IMT & 0(0%)patients had normal IMT 97(97%) patients had normal total cholesterol & out of those 97(97%) patients 78(78%) patients had abnormal IMT & 19(19%) patients had normal IMT. This relation is statistically not significant with p > 0.05.

In our study, The cut off value for normal LDL was taken as < 100 mg/dl and for normal IMT as <0.67 mm. Out of 100 patients, 81(81%) patients had abnormal IMT. Out of those 81(81%) patients, 31(31%) patients had abnormal LDL & 50(50%) patients had normal LDL. 19(19%) patients had normal IMT .Out of those 19(19%) patients,6(6%) patient had abnormal LDL & 13(13%) patients had normal LDL In our study, The cut off value for normal Triglycerides was taken as < 150 mg/dl and for normal IMT < 0.67mm.Out of 100 patients,81(81%) patients had abnormal IMT & out of those 81(81%) patients,59(59%) patients had abnormal TG & 22(22%) patients had normal TG.19(19%) patients had normal IMT, out of those 19(19%)patients, 5(5%) patients had abnormal TG & 14(14%) patients had normal TG. The relation is highly significant with p < 0.0001. 56 In our study, The cut off value for HDL as abnormal was taken as < 40 mg/dl and for normal IMT < 0.67mm.Out of 100 patients, 81(81%) patients had abnormal IMT & out of those 72(72%) patients had abnormal HDL & 9(9%) patients had normal HDL.19(19%) patients had normal IMT & out of those 14(14%) patients had abnormal HDL & 5(5%) patients had normal HDL. The relation is statistically significant with p< 0.01. Thus, in our study, we found increase in the intimal-medial thickness of common carotid-internal carotid artery in patients with CT proven ischemic infarct. A statistically significant correlation was found between increased intimal-medial thickness in patients of ischemic stroke and abnormal serum triglycerides. The correlation of increased total cholesterol & increased serum LDL with intimal- medial thickness was not statistically significant. We also found statistically significant correlation of low serum HDL with increased intimal-medial thickness. These patients can be managed by dietary control, regular exercise, niacin, fibrates

Conclusion

In patients with CT proven ischemic stroke, there is an increase in intimal-medial thickness of common carotid-internal carotid artery. A statistically significant correlation was found between increased intimal-medial thickness in patients of ischemic stroke and abnormal serum triglycerides. The correlation of increased total cholesterol & increased LDL with increased intimal-medial thickness was not seen in our study. We also found statistically significant correlation of low serum HDL with increased intimal-medial thickness.CIMT measurement and lipid profile can be used as primary preventive measure for prediction of stroke in elderly population. These patients should be targeted for low HDL and high triglycerides. This may also be useful in preventing CAD

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