COMMON CAROTID ARTERY INTIMA-MEDIA THICKNESS IN MALE AND FEMALE PATIENTS WITH STROKE

Muhammad Amir[1], Attiya Sabeen Rahman[1], Tanvir Ahmed[1], Shaista Ahmed[1], Tahir Husain[1]

ABSTRACT

Objectives: *To determine significant intima-media thickness (IMT) of common carotid artery (CCA) in male and female patients with hemorrhagic and ischemic stroke and to see the risk factors of stroke.*

Methodology: *A total of 150 patients aged > 40 years of age and of both sexes with hemorrhagic and ischaemic stroke were included in this study. Patients with history of endartectomy, head injury, space occupying lesion and on anticoagulation were excluded. Thickness of common carotid artery intima-media of > 0.5 mm was considered significant. Analysis was performed through SPSS-10.0. Chi-square test was applied to see association of increased wall thickness of common carotid artery with stroke and gender.*

Results: *Male predominance was observed with M: F=1.23: 1. Mean age was 59.54±12.1 years. Among 150 patients of stroke, 13 (8.7%) patients had CCA-IMT of > 0.5 mm on the left side and 8 (5.3%) patients had CCA-IMT of > 0.5 mm on the right side. All patients with significant CCA-IMT thickness were of increasing age. The difference between proportions of an increased left and right wall thickness of common carotid artery between genders (p=0.225 & p=0.484) was not significant. Hypertension was the commonest risk factor in 93 (62%) patients followed by diabetes mellitus in 36 (24%) patients and smoking in 32 (21.3%) patients.*

Conclusion: *There was no significant association between intima-media thickness of common carotid artery with gender in patients with hemorrhagic and ischemic stroke. Hypertension and diabetes were the commonest risk factors of stroke.*

Key Words: *Stroke, Carotid Artery, Intima-Media Thickness, Ischaemic Stroke, Haemorrhagic Stroke.*

This article may be cited as: Amir M, Rahman AS, Ahmed T, Ahmed S, Husain T. Common carotid artery intima-media thickness in male and female patients with stroke. Khyber Med Univ J 2012;4(3):87-91.

INTRODUCTION

Common carotid artery intima-media thickness (CCA-IMT) represents marker for subclinical atherosclerosis and an opportunity for early detection of pre-symptomatic individuals.[1] Studies have shown association of CCA-IMT with all modifiable (e.g. hypertension, high blood cholesterol, smoking, diabetes) & no-modifiable risk factors (like age, gender), all ischaemic stroke subtypes,[1,2] occurrence of future carotid plaque,[1,3] with a high risk of incidental myocardial infarction, stroke and vascular death.[1,4] Therapeutic interventions with antihypertensives,[1,5] lipid lowering agents,[1,6] as well as multifactorial interventions in diabetics[1,7] can slow the progression of or even reduce CCA-IMT.[1] CCA-IMT has been recognized recently as a surrogate marker by which evaluation of therapeutic interventions in atherosclerotic disease.[1] Prospective population based studies in Europe and United States have documented that CCA-IMT are positively associated with the subsequent incidence of stroke[8].Stroke is the third leading cause of mortality worldwide. Both ischaemic and haemorrhagic strokes are common and devastating disorders. More than 80% deaths are due to stroke in middle income countries[9,10] (economies are divided according to 2011 GNI per capita, calculated using the World Bank Atlas method. The groups are: low income, $1,025 or less; lower middle income, $1,026 - $4,035; upper middle income, $4,036 - $12,475; and high income, $12,476 or more).

The annual incidence of stroke in developed countries is about 2/1000 population but the exact figure depends on the age structure of the population as the incidence rises steeply with increasing age[11]. According to world health organization (WHO) estimates for the year 2020, stroke will remain the second leading cause of death along with ischaemic heart disease (IHD) both in developing and the developed world[11,12]. The overall burden of stroke will be greater in developing countries than in the developed world mainly due to aging of population and transition to burden of chronic disease. The hospital based studies conducted in Pakistan revealed 31-40% cases of stroke due to cerebral haemorrhage and 60-69% due to ischaemia,[11,13,14]A few studies have

1 Department of Medicine, Karachi Medical & Dental College and Abbasi Shaheed Hospital, Karachi, Pakistan

Address for Correspondence:

Dr. Attiya Sabeen Rahman
Department of Medicine, Karachi Medical & Dental College and Abbasi Shaheed Hospital, Karachi, Pakistan
Email: asabeenrahman@hotmail.com
Date Submitted: May 18, 2012
Date Revised: September 25, 2012
Date Accepted: September 26, 2012

shown increased CCA-IMT in Pakistani patients with familial hypercholesterolemia and diabetes mellitus which are important risk factors of stroke.[15,16] However there is no local data available on CCA-IMT in stroke patients specially in male and female patients. So we planned this study to determine the intima-media thickness of common carotid artery in male and female patients with hemorrhagic and ischemic stroke and to see the risk factors of stroke in our population.

METHODOLOGY

This study was conducted in the department of medicine of Abbasi Shaheed hospital from October 2008 to March 2009. A total of one hundred and fifty patients were selected. All patients of more than 40 years of age of both sexes presenting with complete stroke (hemorrhage or infarction) were enrolled in the study. All patients were registered in a pre-tested questionnaire. Complete history including personal and demographic information including age, gender, past medical history and personal habits like smoking etc. were recorded on the questionnaire. After a complete clinical examination, random blood sugar, complete blood count and a fasting lipid profile were done to screen the risk factors. Patients were diagnosed as having a history of hypertension if they had a systolic blood pressure of $\geq$140 mmHg or a diastolic blood pressure of $\geq$ 90 mmHg (Joint National Committee seventh report) or if they have received anti hypertensive medication. A history of myocardial infarction, angioplasty, coronary artery bypass grafting (CABG) or angina pectoris was recorded as ischaemic heart disease. Diabetes mellitus was diagnosed if fasting blood sugar was more than 126 mg/dl or random blood sugar of more than 200 mg/dl (as per WHO criteria) or the patient was on oral hypoglycemic or insulin.

CAROTID ULTRASOUND STUDIES: All cases were examined in a supine position with head turned 45^0 from the site being scanned. Both carotid arteries were scanned longitudinally to visualize the IMT in the farwall artery. The reference point was the beginning of the carotid bulb. The best images of the far wall that could be obtained were used to determine the CCA. Measurements were made on frozen images, magnified to standard size online. Subjects were examined by an experienced sonographer who was unaware of any clinical or radiological information about the patients. Ultrasound Doppler was done on TOSHIBA ECOCEE with probe frequency of 10 mhz. No preparation or premedication was required for sonographic examination. Evaluation of intima media thickness was performed on the basis of the 2004 mannheim IMT consensus. IMT was assessed with B-mode ultrasound (Toshiba ECOCEE with probe frequency of 10mhz). The right and left common carotid arteries were scanned in longitudinal projections with the focus depth adjusted to the far wall. Plaques were defined on the basis of the 2004 mannheim IMT consensus as focal structures encroaching into the arterial lumen at least > 0.5 mm in the course of common carotid artery will be taken as significant[17]. Type of stroke was find out by TOSHIBA XPRESS GX computed tomographic (CT) scanner.

INCLUSION CRITERIA:

- Patients more than 40 year of age
- Patients of both sexes
- Patients with hemorrhagic and ischaemic stroke

EXCLUSION CRITERIA:

- Patients with history of endartectomy
- Patients with history of head injury resulting in stroke
- Patients with history of space occupying lesion resulting in stroke
- Patients on anticoagulation resulting in stroke
- Patients suffering of transient ischaemic attack (TIA)

STATISTICAL ANALYSIS:

Data analysis was performed through SPSS version-10.0. Patient's age was presented by Mean $\pm$ Standard deviation. Frequencies and percentages were computed to present all categorical variables including gender, presenting symptoms / co-morbid factors, stroke type and wall thickness of common carotid artery in terms of (< 0.5 mm or > 0.5 mm). Chi-square test was applied to see the association of increased wall thickness of common carotid artery with cerebrovascular accident. Chi-square test was also applied to compare the difference of wall thickness of common carotid artery between both sexes. Statistical significance was taken at $p < 0.05$. Relative risk (RR) was also computed through Epi-info version 6.0 to analyze the association of sex and stroke types with increased wall thickness of common carotid artery.

RESULTS

A total of 150 patients were included in the study. Male predominance was observed as there were 83 (55.3%) male and 67 (44.7%) female patients with M: F = 1.23: 1. The mean age of these patients was 59.54 $\pm$ 12.1 (Range= 41 to 65) years (figure-1). Among 150 patients of stroke, 89 (59.3%) had ischaemic stroke and 61 (40.6%) had hemorrhagic stroke. Hypertension was the commonest risk factor observed in 93 (62%) patients followed by diabetes mellitus in 36 (24%) patients and smoking in 32 (21.3%) patients. Hyperlipidemia was found to be 25 (16.7%). Ischemic heart diseases were found in 16 (10.7%), atrial fibrillation in 9 (6%) patients due to turbulent blood flow and valvular heart disease in 6 (4%) patients (Table I). Thirteen (8.7%) patients had an increased *left* intima-media thickness of common carotid artery (> 0.5 mm) while 137 (91.3%) had the normal measurement (< 0.5 mm) (Table II). An increased *right* intima-media thickness of common carotid artery > 0.5 mm) was found

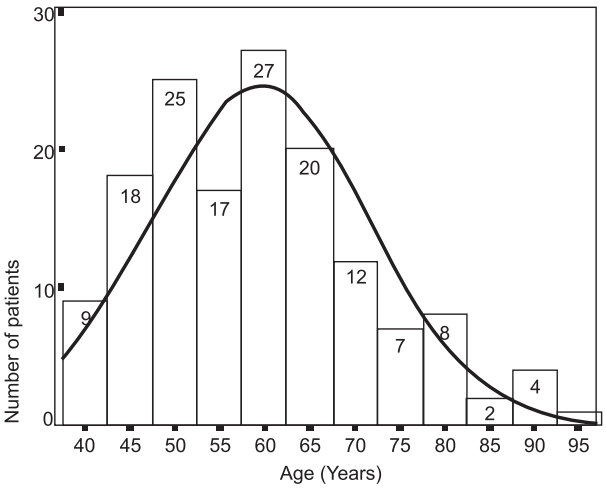

Fig. 1: Age distribution of the patients

DISTRIBUTION OF CO-MORBID VARIABLES IN THE PATIENTS

Co-morbid variables	No. of patients	Percentage
Hypertension	93	62.0
Diabetes mellitus	36	24.0
Smoking	32	21.3
Hyperlipidemia	25	16.7
Ischemic heart diseases	16	10.7
Atrial fibrillation	9	6.0
Valvular Heart disease	6	4.0
History of Oral contraceptive	2	1.3

Table I

ASSOCIATION OF WALL THICKNESS OF LEFT AND RIGHT COMMON CAROTID ARTERY WITH CEREBROVASCULAR ACCIDENT PATIENTS

Site	Common Carotid artery intima-media thickness (CCA-IMT)	
	Increased CCA-IMT	Normal CCA-IMT
Left	13 (8.7%)	137 (91.3%)*
Right	8 (5.3%)	142 (94.7%)*

*Significantly high proportion in normal wall thickness of common carotid artery; shows no association with cerebrovascular accident $p < 0.05$.

Table II

in 8 (5.3%) patients while 142 (94.7%) had normal measurement (table-2). The proportion of an increased left

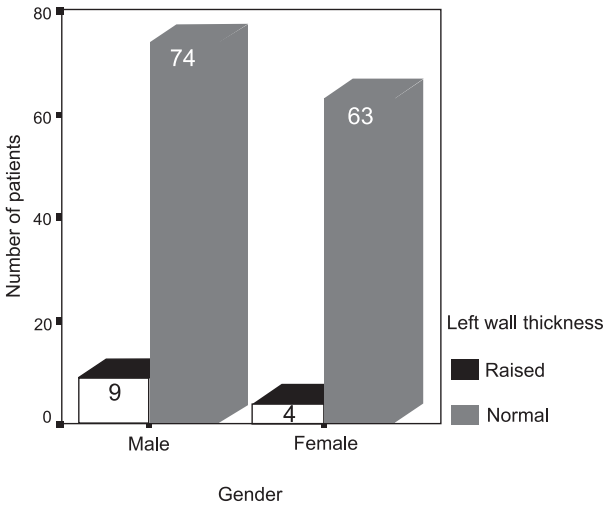

Fig. 2: Association of wall thickness of the left common carotid artery with gender

(*Insignificant difference of left wall thickness of common carotid artery between both genders (Fisher's Exact test: $p = 0.225$).

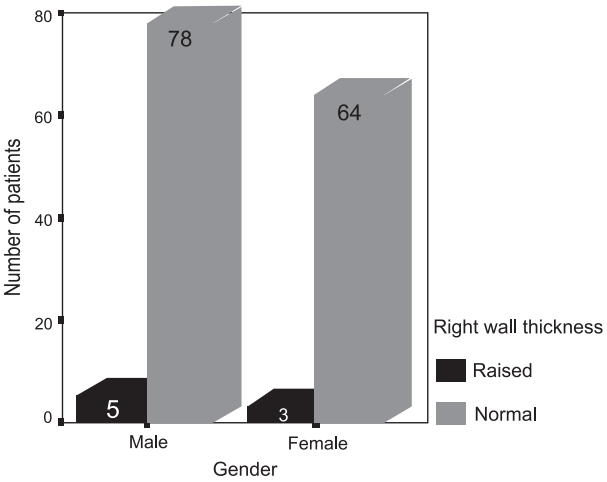

Fig. 3: Association of wall thickness of the right common carotid artery with gender:

(*Insignificant Difference Of Right Wall Thickness Of Common Carotid Artery Between Both Genders Fisher's Exact Test: $P = 0.484$).

intima-media thickness of common carotid artery (> 0.5 mm) in male patients was higher than female patients (10.8% vs. 6.0%, $p = 0.225$, RR = 1.82 respectively) (figure-2). However this difference was not statistically significant. The proportion of an increased right wall thickness of common carotid artery (> 0.4 mm) in male patients was higher than female patients (6.0% vs. 4.5%, $p = 0.484$, RR = 1.35), (figure-3) however this difference was not statistically significant. The CCA-IMT thickness in patients with stroke compared among both genders was not statistically significant, but were seen with increasing age.

DISCUSSION

This was an observational study, in which stroke was more common in males than females. Similarly it was seen in a study[11] of 100 patients in which 64 were male and 36 patients were female. Mean age for men was 64 years and for women were 49 years which was similar to our study which showed a mean age of 59.54+12.1 years. A study conducted in India in rural and urban population who showed stroke to be more common in females than males, while the median age of stroke patients was 67 years, which did not differ between urban and rural populations. The incidence rates increased steadily with age for both genders[18].In our study ischaemic stroke (59.3%) was found to be more common than hemorrhagic (40.6%) stroke. This finding is consistent with other local studies from Pakistan.[11,13,14] A study carried out in India also showed a significant increase in the prevalence of hemorrhagic stroke of 32% [18]. Two other studies from south Asian countries also showed similar distribution of stroke subtypes[17]. A study conducted in china showed stroke to be more common in males with a mean age of 64.9 years for men and 66.6 years for women. The stroke subtypes were found to be 1.8% subarachnoid hemorrhage, 27.5% intracranial hemorrhage, 62.4% were cerebral infarction and 8.3% were undetermined stroke[19].Hypertension was the commonest risk factor of stroke which was seen in 62% of patients followed by diabetes mellitus (24%), smoking (21.3%), hyperlipidemia (16.7%) and ischaemic heart disease (10.7%). Atrial fibrillation and valvular heart disease was found in 6% and 4% respectively. History of oral contraceptive pills (OCPs) were found in only 1.3% of women. Local studies have shown that hypertension is the most common risk factor for both ischemic and haemorrhagic stroke.[11,13,20] It was seen similarly that hypertension was the most common risk factor found in 60%, diabetes and hyperlipidemia was found in 28% of patients respectively. Smoking was found in 22%, IHD in 18%, atrial fibrillation in 12%, history of OCPs in 10% and toxemia of pregnancy in 2% of patients[11]. The distribution of conventional stroke risk factors in India were found to be, 85% had hypertension, half had diabetes, a quarter had dyslipidemia and one-fifth males smoked tobacco[16]. It has been estimated that hypertension causes 54% stroke mortality in low-income and middle-income countries, followed by high cholesterol (15% and tobacco smoking (12%).[21]Carotid intima-media thickness measurements are being applied widely as a measure of atherosclerosis in studies on determinants of presence and progression of atherosclerosis and in studies on atherosclerosis as determinants of cardiovascular disease.[22,23] Carotid IMT has been shown to be related to cardiovascular risk factors, prevalent cardiovascular diseases and atherosclerosis in peripheral, coronary, and femoral arteries. Recently evidence became available indicating that an increased carotid IMT is a strong predictor of coronary heart disease and stroke[22,23]. In Taiwanese population common carotid IMT independently predicted future ischaemic stroke[24]. In the present study 8.7% had increased left carotid IMT while 91.3% had normal measurement. An increased right carotid IMT was found in 5.3% while 94.7% had normal measurements. The CCA-IMT in patents with stroke compared among both genders was not significant but seen with increasing age. While Su et al.[25] showed that CCA-IMT increases with increasing age and in men is greater than women. A community based Gutenberg study in Germany showed greater CCA-IMT in men than women, but gender differences in IMT became non-significant in older subjects.[25]

CONCLUSION

There was no significant association between intima-media thickness of common carotid artery with gender in patients with hemorrhagic and ischemic stroke. Hypertension, diabetes mellitus and smoking were the commonest risk factors of stroke.

REFERENCES

1. Touboul PJ, Labreuche J, Vicant E, Amarenco P. Carotid intima-media thickness, plaques and Framingham risk score as independent determinants of stroke risk. Stroke 2005; 36: 1741-45.
2. Touboul PJ, Elbaz A, Koller C, Lucas C, Adrai V, Chedru F, et al. Common carotid artery intima-media thickness and brain infarction. Circulation 2000; 102: 313-18.
3. Zureik M, Touboul PJ, Bonithon-Kop C, Courbon D, Berr C, Leroux C, et al. Cross-sectional and 4-year longitudinal associations between brachial pulse pressure and common carotid intima-media thickness in a general population: The EVA study. Stroke 1999; 30: 550-5.
4. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK. Carotid artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. N Engl J Med 1999; 340: 14-22.
5. Zanchetti A, Bond MG, Hennig M, Neiss A, Mancia G, Dal Palu C, et al. Calcium antagonist lacidipine slows down progression of asymptomatic carotid atherosclerosis. Circulation 2002; 106: 2422-7.
6. Smilde TJ, Van Wissen S, Wollersheim H, Kastelein JJP, Stalenhoef AFH. Effect of aggressive versus conventional lipid lowering on atherosclerosis progression in familial hypercholesterolemia (ASAP). Lancet 2001; 357: 577-81.
7. The diabetes and complications trial/epidemiology of diabetes intervention and complication research group. Intensive diabetes therapy of carotid intima-media thickness in type-I diabetes mellitus. N Engl J Med 2003; 348: 2294-303.
8. Kitamura A, Iso H, Imano H, Ohira T, Okada T, Sato S, et al. Carotid intima media thickness and plaque characteristics as a risk factor for stroke in Japanese elderly men. Stroke 2004; 35: 2788-94.

9. Sahoo R, Krishna MV, Subrahmaniyan DKS, Dutte TK, Elangoven S. Common carotid intima-media thickness in acute ischaemic stroke: A case control study. Neurol India 2009; 57(5): 627-30.

10. Goyal A, Yousuf S. The burden of cardiovascular disease in Indian sub-continent. Indian J Med Res 2007; 124: 235-44.

11. Alam I, Haider I, Wahab F, Khan W, Taqweem MA, Nowsherwan. Risk factors stratification in 100 patients of acute stroke. J Postgrad Med Inst 2004; 18(4): 583-71.

12. Vohra EA. Stroke: The challenge and response. Pak J Med Sci 2001; 17(2): 65-6.

13. Vohra EA, Ahmed WU, Ali M. Aetiology and prognostic factors for outcome of patients admitted in stroke. J Pak Med Assoc 2000; 50: 234-6.

14. Sherin A, Khan A, Rehman S, Shah NH, Shabbier G, Zarif M. Comparability and validity of Siriraj stroke score and Allen stroke score in differentiation of acute ischemic and haemorrhagic stroke J Postgrad Med Inst 2011; 25: 206-16.

15. Khan SP, Ahmed KZ, Yaqub Z, Ghani R. Carotid intima-media thickness correlation with lipid profile in patients with familial hypercholesterolemia versus controls. J Coll Physicians Surg Pak 2011; 21(1): 30-3.

16. Sarwar HJ, Tahira QUA, Kubra KT. Assessment of common carotid artery intima media thickness in diabetics compared with non diabetics by b-mode ultrasonography. Pak Armed Forces Med J 2012; 62(3):

17. Rosenkranz M, Thomalla G, Havemeister S, Wittkugel O, Cheng B, Krutzelmann A, et al. Older age and greater carotid intima-media thickness predict ischaemic events associated with carotid artery stenting. Cerebrovasc Dis 2010; 30: 567-72.

18. Sridharan SE, Unnikrishan JP, Sukumaran S, Sylaja PN, Nayak SD, Sarma PS. et al. Incidence, types, risk factors and outcome of stroke in developing country: The trivandrum stroke registry. Stroke 2009; 40: 1212-18.

19. Zhang LF, Yang J, Hong Z, Yuan GG, Zhou BF, Zhao LC, Huang YH, et al. Proportion of different subtypes of stroke in China. Stroke 2003; 34: 2091-96.

20. Sherin A, Shabbier G, Rehman S, Shah NH, Zarif M. Hypertension in acute ischemic and haemorrhagic stroke. J Postgrad Med Inst 2005; 19(2): 220-5.

21. Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. Lancet Neurol 2007; 6: 182-7.

22. Sol AID, Moons KGM, Hollander M, Hoffman A, Koudstaal PJ, Grobbee DE, et al. Is carotid intima-media thickness useful in cardiovascular disease risk assessment?: The Rotterdam study. Stroke 2001; 32: 1532-38.

23. Bots ML, Hoes AW, Koudstaal PJ, Hofman A, Grobbee DE. Common carotid intima-media thickness and risk of stroke and myocardial infarction: The Rotterdam study. Circulation 1997; 96: 1432-37.

24. Chuang SY, Bai CH, Chen JR, Yeh WT, Chen HJ, Chiu HC, Shiu RS, et al. Common carotid end diastolic velocity and intima-media thickness jointly predict ischaemic stroke in Taiwan. Stroke 2011; 42: 1338-44.

25. Su TC, Chien KL, Jeng JS, Chen MF, Hsu HC, Torng PL, et al. Age and gender associated determinants of carotid intima media thickness: A community based study. J Atheroscler Thromb 2012; 19: 872-80.

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

MA: Conception and design

ASR: Analysis and interpretation of data, Drafting the manuscript

TA: acquisition of data,

SA: Critical revision

TH: Final Approval of the manuscript

CONFLICT OF INTEREST

Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE

NONE DECLARED

KMUJ web address: www.kmuj.kmu.edu.pk

Email address: kmuj@kmu.edu.pk