Extracranial and intracranial arterial stenoocclusive disease in acute ischemic stroke patients: A study from north India - Evaluation with MR angiography

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Abstract

Background: Asian, African, and Hispanic ancestry are at higher risk of intracranial atherosclerosis. In North America, extracranial carotid stenosis remains the most common vascular lesion in Caucasian. However the studies in Indian population are lacking.
Aims: The study was done to evaluate extracranial and intracranial arterial stenoocclusive diseases in acute ischemic stroke with MR angiography.
Material and Methods: This prospective study was conducted on 50 subjects of ischemic stroke. A thorough clinical examination, history of risk factors, routine baseline investigations for stroke, Brain CT/ MRI, and MRA study of extracranial and intracranial vessels (three-dimensional time-of-flight technique) were done in all patients.
Results: Twenty two (44%) have abnormal MRA with significant steno-occlusive lesions. The intracranial stenosis was more common than extracranial stenosis in our population and was statistically significant (p value < 0.05). The intracranial stenosis was more common in younger age (age < 60 years), diabetics and female sex while extracranial stenosis was more common in old age (age > 60 years), ischemic heart disease and male patients.
Conclusion: The intracranial stenosis was more common than extracranial stenosis in our studied population. The present study confirms racial difference between Indians and whites in location of lesion in cerebrovascular steno-occlusive. Further large scale population based studies are needed.

Keywords: Extracranial Stenosis; Intracranial Stenosis; MR Angiography.

Introduction

Atherosclerotic plaque may develop at any point along the carotid artery and the vertebrobasilar system, but the most common sites at extracranial arteries are bifurcation of the common carotid artery, the origin of internal carotid artery, origins of the vertebral arteries from the subclavian arteries.(1) Intracranial atherosclerosis affects intracranial portion of the internal carotid artery, middle cerebral artery, vertebrobasilar artery, and posterior and anterior cerebral arteries.(2-4)

For large artery atherosclerosis, carotid stenosis is the most common vascular lesion found in Caucasians in America and Europe and is extensively studied in terms of epidemiology, pathophysiology and treatment.(5,6) Based on widespread observation worldwide, that intracranial atherosclerosis is the most common vascular lesions in Asians, Hispanics and Africans, and Caucasians remain the only ethic group with a low frequency of intracranial atherosclerosis patients.(7-11) However, there are only few studies in Indians.

Cerebral angiography is the gold standard for imaging the carotid arteries as well as intracranial arteries but its disadvantages include invasive nature, high cost and risk of morbidity and mortality. MR Angiography (MRA), especially the three-dimensional time-of-flight technique, is useful non-invasive diagnostic tool for the evaluation of suspected extracranial and intracranial steno-occlusive disease. The correlation of MRA and conventional angiography was about 80% to 98% in the diagnosis of extracranial carotid artery diseases. The Overall sensitivities of 85% and 88% and specificities of 96% and 97% for the intracranial carotid artery and middle cerebral artery, respectively, have been reported.(12,13) Both transcranial doppler ultrasound and MRA non-invasively identify 50 to 99% intracranial large vessel stenoses with substantial negative predictive value.(14) Although MRA is not a good tool to evaluate VA ostium stenosis.

Carotid endarterectomy is the most common surgical procedure used to treat stenosis of the extracranial precerebral carotid artery.(15,16) Carotid angioplasty with stenting is also being performed, and there are many clinical trials comparing this procedure with carotid endarterectomy. For Intracranial atherosclerotic stenosis various revascularization strategies have been suggested during the past decades, but the method of choice is still controversial. Stent assisted angioplasty is now feasible for treatment of intracranial stenoses.(17)

The aim of this study was to evaluate extracranial and intracranial arterial stenoocclusive diseases in acute ischemic stroke with MRA in Indian population, as its literature is lacking.(18)

Material and Methods

This prospective study was conducted at MBG hospital associated with R.N.T. Medical College, Udaipur, Rajasthan, India. A total of 50 cases of acute

ischemic stroke were included in the study. Patients were designated as ischemic stroke as indicated by the clinical examination, and Brain CT/MRI (DWI, ADC, T2WI & FLAIR images) documented the acute infarction in clinically correlated territory.

All the patients underwent the baseline investigations e.g. complete blood count, Plasma glucose, Lipid profile, ECG and chest X-Ray. The patients with cardiogenic conditions such as atrial fibrillation or flutter, recent MI, valvular heart diseases, endocarditis, and is chemic cardiomyopathy were excluded from the study.

The history of potential vascular risk factors associated with atherosclerosis was obtained from each patient and from the medical records. A diagnosis of hypertension was made if the patient's blood pressure was above 140 (systolic) and/or 90 (diastolic)mm Hg on repeated measurements during hospitalization or if the patient was on antihypertensive drugs. A diagnosis of diabetes mellitus was based on fasting, postprandial serum glucose level, or sometimes the oral glucose tolerance test. History of cigarette smoking was positive if the patient had smoked 10 or more cigarettes daily for more than 10 years. Hypercholesterolemia was defined as a total fasting serum cholesterol level of ≥ 240 mg/dL. Ischemic heart disease (IHD) referred to the presence of history of angina pectoris, acute myocardial infarction, or electrocardiographic evidence of old myocardial infarction or ischemic changes.

Magnetic Resonance Angiography: All patients underwent MRA study on a 1.5 Tesla machine with a standard head coil. The MRA studies were performed within 1 month of the clinical onset suggestive of cerebrovascular disease. Two sets of MRA were performed separately at the cervical carotid and vertebral arteries, and the circle of Willis. We used the time-of-flight (TOF) angiography principle for imaging. Images were acquired in the axial planes by means of three-dimensional acquisition, gradient-echo technique with spoiling, and flow compensation. The repetition time, echo time, and flip angle were 22 milliseconds, 6.9 milliseconds, and 20° for the cervical carotid study and 23 milliseconds, 6.9 milliseconds, and 20° for the study in the circle of Willis, respectively. The slice thicknesses were 1 mm in the cervical portion and 0.7 or 0.8 mm in the region of the circle of Willis. One acquisition was obtained in each study. The scanning times were 7 minutes 53 seconds and 5 minutes 33 seconds, respectively.

All the intracranial and extracranial angiography findings were categorized as symptomatic side or contralateral side, according to the clinical history. The measurements of stenosis were computed directly on the maximum intensity projection views of MRA. Collapsed views were also taken into measurement in the evaluation of steno-occlusion of the intracranial tributary. The percent stenosis was computed by measuring the residual lumen diameter and the original diameter at the site of maximum stenos is in each segment of the artery and dividing the difference by the original diameter. Vessels in which a signal void on MRA was accompanied by evidence of regained flow distal to the proximal part were considered patent. The stenoses were recorded as (1) normal or clinically non-significant stenosis(i.e., <50% stenosis), (2) clinically significant stenosis(i.e., ≥50% stenosis), or (3) total occlusion. The locations of severe stenosis were categorized as being in the anterior or posterior circulation and in the intracranial or extracranial vessels. The intracranial segment for the internal carotid artery was considered to involve when a lesion is distal to the ophthalmic artery and for the vertebral artery at the point where the artery pierces the dura at the level of foramen magnum. The intracranial extent of the stenosis was included in this study up to the M2 and A2 segments in the anterior circulation and the P2 segment of the posterior cerebral artery. A cortical branch lesion beyond the level was not included.

Results

The study was conducted on 50 subjects of ischemic stroke out of which 32 were males and 18 females, age ranged from 32-78 years with mean of 61 years. The study subjects additionally suffering from hypertension (23), diabetes mellitus (15), ischemic heart disease (10) or had history of TIA (8). The baseline characteristics were shown in table 1. MRA (Table 2) did not reveal any significant stenosis in 28 patients (56%), 22 patients (44%) had abnormal angiogram with significant steno-occlusive lesions. Among these 22 patients, stenosis was exclusively extracranial in 8 cases (16%), exclusively intracranial in 10 cases (20%) and combined intra and extracranial in 4 cases (8%). Intracranial stenosis was more common than extracranial stenosis which was statistically significant (p value <0.05). Intracranial stenosis was more common in younger age (age <60 years), female sex and diabetics. Extracranial stenosis was more common in male sex, old age (age >60 years) and IHD patients. Stenoses of both intracranial as well as extracranial vessels were more common in patients with diabetes mellitus and IHD patients. There was no significant association found between smoking, alcoholism, obesity (BMI >25) with site of stenosis. Single stenosis was predominantly in the intracranial distribution whereas multiple stenosis in the extracranial distribution (Table 3 & 4).

Discussion

In the treatment of a patient with cerebral ischemia, location and severity of the occlusive disease within the extracranial or intracranial arteries are the major considerations for applying guidelines for care. Racial differences in the distribution of extracranial and intracranial cerebral vascular occlusive disease are well documented. However, most of the data were related to

white, black, and Japanese patients. Few reports discuss Indian populations, particularly regarding incidences of intracranial and extracranial lesions.[18,26]

The distinction of the intracranial and extracranial vessels was based on the observation that the internal carotid artery pierces the inner dura immediately proximal to the origin of the ophthalmic artery in the anterior circulation. Therefore, the intracranial vessel was involved when a lesion is distal to the ophthalmic artery. For the vertebral artery, the distinction was made at the point where the artery pierces the dura at the level of foramen magnum. The reason for applying these criteria is that the environment around the vessel is markedly different beyond the inner dura because of subarachnoid fluid surrounding the vessels. Because of the anatomic difference and the risk of vascular rupture, the therapeutic strategy for extracranial/ intracranial stenosis is applied differently when angioplasty or stent placement is considered.

The present study shows that intracranial stenosis is more common than extracranial stenosis in our population. This further supports that Asians are at higher risk of intracranial stenosis as in study of Caplan et al.[5] This increased incidence of intracranial stenosis is also noted in Chinese and Japanese populations.[19,20] The pathogenesis of the trend toward more intracranial occlusive lesions in the Asian population remains unclear.

In this study, among the patients with single stenosis, the intracranial distribution was more common than the extracranial distribution ($P< 0.05$) whereas in patients with multiple lesions, the extracranial distribution was more common than the intracranial distribution ($P<0.05$). Similar observation was also noted by Suh et al.[20] We observed that intracranial stenosis is more commonly associated with younger age (age < 60 years) while extra cranial stenos is with older age group (age > 60 years). While a study by Uehara et al found that older age is risk factor for both extracranial and intracranial stenosis.[22] Correlation of sex with site of stenosis shows that males have predominantly extracranial stenosis whereas females have higher incidence of intracranial stenosis. This correlates with Oslo Study,[23] however these findings does not correlate with the study of Caplan et al[5] which concluded male sex as a risk factor for intracranial stenosis. Correlation of DM with site of stenosis shows that intracranial stenosis as well as combined stenoses is significantly more common in diabetics while extracranial stenosis was found equal in diabetics and non-diabetics. These results correspond with previous studies.[22,24,25] Correlation of IHD with site of stenosis shows that extracranial arterial stenosis as well as combined stenoses was significantly more common in IHD patients. This corresponds with study of Uehara et al[22] however Suwanwela et al[24] found that IHD is a risk factor for intracranial stenosis. The above mentioned discordance in results of our study and previous studies regarding the distribution of stenosis and their relation with risk factors may be due to difference in patient population, small number of subjects and lack of cerebral DSA.

Conclusion

The intracranial stenosis was more common than extracranial stenosis in our studied population. Further large scale population based studies are needed in the Indian population to find out further details of clinical pattern of stroke and distribution of cerebral atherosclerosis. As, intracranial atherosclerotic disease causing strokes is probably more common in India as in other Asian countries, there is a need to find an optimal medical treatment and to develop resources for intracranial angioplasty and stenting.

Table 1: Baseline characteristics of the patients

Total no. of patients	**50**
Sex	32:18
Age (years)	61 (32-78)
Hypertension	23 (46%)
Smoking	14 (28%)
Diabetes mellitus	15 (30%)
Diabetes mellitus and Hypertension	10 (20%)
Ischemic heart disease	10 (20%)
Hypertension and Ischemic heart disease	6 (12%)
Transient ischemic attack	8 (6%)

Table 2: MR Angiogram findings of the patients

No significant abnormality	28 (56%)
Significant steno-occlusive lesions	22 (44%)
Exclusively intracranial stenosis	10 (20%)
Exclusively extracranial stenosis	8 (16%)
Combined intracranial & extracranial stenoses	4(8%)
Anterior circulation stenosis	16 (32%)
Posterior circulation stenosis	6 (12%)

Table 3: Correlation of number of stenotic lesion with age, sex, smoking, DM, HT, IHD, anterior/ posterior circulation and ECAS/ICAS

No. of Stenotic Lesion	**Age**		**p value**
	< 60 years	**> 60 years**	
Single 13	6	7	0.15
Multiple 9	7	2	
	Sex		
	Male	Female	
Single 13	8	5	0.46
Multiple 9	7	2	
	Smoker/Non-smoker		
	Non-smoker	Smoker	
Single 13	3	10	0.13
Multiple 9	5	4	
	DM		
	Yes	No	
Single 13	6	7	**0.04***

Multiple 9	8	1		
	HT			
	Yes	No		
Single 13	10	3		0.61
Multiple 9	6	3		
	IHD			
	Yes	No		
Single 13	3	10		**0.04***
Multiple 9	6	3		
	AC/PC			
	AC	PC		
Single 13	9	4		0.67
Multiple 9	7	2		
	ECAS/ICAS			
	ECAS	ICAS	Both	
Single 13	3	10	0	**0.03***
Multiple 9	5	1	3	

Abbreviations: DM: Diabetes mellitus, ECAS/ICAS: Extracranial arterial stenosis HT: Hypertension, ICAS: Intracranial arterial stenosis, IHD: Ischemic heart disease
* Statistically significant

Table 4: Correlation of site of stenotic lesion with age, sex, smoking, DM, HT and IHD

Site of Stenotic Lesion	Age		p value
	<60 years	>60 years	
ECAS 8	3	5	0.71
ICAS 10	7	3	
Both 4	3	1	
	Sex		
	Male	Female	
ECAS 8	7	1	**0.03***
ICAS 10	6	4	
Both 4	2	2	
Total 22	15	7	
	Smoker/Non-smoker		
	Non-smoker	Smoker	
ECAS 8	3	5	0.79
ICAS 10	3	7	
Both 4	2	2	
	DM		
	Yes	No	
ECAS 8	4	4	**0.04***
ICAS 10	8	2	
Both 4	4	0	
	HT		
	Yes	No	
ECAS 8	5	3	0.22
ICAS 10	7	3	
Both 4	4	0	
	IHD		
	Yes	No	
ECAS 8	6	2	0.83
ICAS 10	3	7	
Both 4	3	1	

Abbreviations: DM: Diabetes mellitus, ECAS/ICAS: Extracranial arterial stenosis HT: Hypertension, ICAS: Intracranial arterial stenosis, IHD: ischemic heart disease
* Statistically significant

References

1. Lernfelt B, Forsberg M, Blomstrand C, Mellstrom D, Volkmann R. Cerebral atherosclerosisas predictor of stroke and mortality in representative elderly population. Stroke 2002;33:224-229.
2. Aronow WS, Schoenfeld MR. Prevalence of atherothrombotic brain infarction and extracranial carotid arterial disease and their association in elderly blacks, Hispanics, and whites. Am J Cardiology 1993;71:999-1000.
3. Craig DR, Meguro K, Watridge C, Robertson JT, Barnett HJM, Fox AJ. Intracranial internal carotid artery stenosis. Stroke 1982;13:825-828.
4. Marzewski DJ, Furlan AJ, St Louis P, Little JR, Modic MT, Williams G. Intracranial internal carotid artery stenosis: longterm prognosis. Stroke 1982;13:821-824.
5. Caplan LR, Gorelick PB, Hier DB. Race, sex and occlusive cerebrovascular disease: a review. Stroke 1986;17:648-655.
6. Norris JW, Zhu CZ, Bornstein NM, Chambers BR. Vascular risks of asymptomatic carotid stenosis. Stroke 1991;22:1485-1490.
7. Frey J, Jahnke H, Bulfinch E. Difference in stroke between white, Hispanic, and Native American patients. Stroke1998;29:29-33.
8. Gorelick PB, Caplan LR, Hier DB, et al. Racial differences in the distribution of posterior circulation occlusive disease. Stroke 1985;16:785-790.
9. Gorelick PB, Caplan LR, Hier DB, Parker SL, Patel D. Racial differences in the distribution of anterior circulation occlusive disease. Neurology 1984;34:54-59.
10. Kittner SJ, McCarter RJ, Sherwin RW, Sloan MA, Stern BJ, Johnson CJ, et al. Black-white differences in stroke risk among young adults. Stroke 1993;24(suppl-I):13-15.
11. Wong LH. Racial distribution of intracranial and extracranial atherosclerosis. J Clin Neurosci 2003;10:30-34.
12. Masaryk AM, Ross JS, DiCello MC, Modic MT, Paranandi L, Masaryk TJ. 3DFT MR angiography of the carotid bifurcation: potential and limitation as a screening examination. Radiology 1991;179:797-804.
13. Heiserman JE, Drayer BP, Fram EK, Keller PJ, Bird R, Hodak JA et al. Carotid artery stenosis: clinical efficacy of two-dimensional time-of-flight MR angiography. Radiology 1992;182:761-768.
14. Feldmann E, Wilterdink JL, Kosinski A, Lynn M, Chimowitz MI, Sarafin J, et al. The Stroke Outcomes and Neuroimaging of Intracranial Atherosclerosis (SONIA) Trial. Neurology 2007;68:2099-2106.
15. European Carotid Surgery Trialists' Collaborative Group. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). Lancet 1998;351:1379-1387.

16. Estol CJ. Diagnosis and treatment of symptomatic and asymptomatic carotid disease. Rev Neurol 1999;29:1309-1321.
17. Meyers PM, Schumacher HC, Tanji K, Higashida RT, Caplan LR. Use of stents to treat intracranial cerebrovascular disease. Annu Rev Med 2007;58:107-122.
18. Padma MV, Gaikwad S, Jain S, Maheshwari MC, Misra NK. Distribution of vascular lesions in ischaemic stroke: a magnetic resonance angiographic study. Natl Med J India 1997;10:217-220.
19. Liu HM, Tu YK, Yip PK, Su CT. Evaluation of intracranial and extracranial carotid steno-occlusive diseases in Taiwan Chinese patients with MR angiography: preliminary experience. Stroke 1996;27:650-653.
20. Kieffer SA, Takeya Y, Resch JA, Amplatz K. Racial differences in cerebrovascular disease: angiographic evaluation of Japanese and American populations. AJR Am J Roentgenol1967;101:94-99.
21. Suh DC, Lee SH, Kim KR, Park ST, Lim SM, Kim SJ, et al. Pattern of atherosclerotic carotid stenosis in Korean patients with stroke: different involvement of intracranial versus extracranial vessels. AJNR Am J Neuroradiol. 2003;24:239-244.
22. Uehara T, Tabuchi M, Mori E. Occlusive lesions of carotid and intracranial arteries in patients with symptomatic lacunar infarction-evaluation by MR angiography. Rinsho Shinkeigaku 1997;37:796-801.
23. Holme I, Enger SC, Helgeland A, et al. Risk factors and raised atherosclerotic lesions in coronary and cerebral arteries: statistical analysis from the Oslo study**.** Atherosclerosis1981;1:250-256.
24. Suwanwela NC, Chutinetr A. Risk factors for atherosclerosis of cervicocerebral arteries: intracranial versus extracranial. Neuroepidemiology 2003;22:37-40.
25. Palomeras Soler E, Fossas Felip P, Cano Orgaz A, Sanz Cartagena P. Intracranial stenosis. Study and follow-up of 38 patients. Neurologia. 2004;19:254-259.
26. Kumar G, Kalita J, Kumar B et al. Magnetic Resonance Angiography Findings in Patients with Ischemic Stroke from North India. Journal of Stroke & Cerebrovascular diseases 2010.19:146-152.