Original Article

Correlation of intracranial atherosclerosis with carotid stenosis in ischemic stroke patients

Manas Ghosh, Kaushik Ghosh[1], Atri Chatterjee[2], Ambarish Bhattacharya[3], Amitava Acharya[4], Sisir Chakraborty[5], Bhaskor Ghosh[6]

Department of Medicine, Murshidabad Medical College, Murshidabad, [1]Department of Medicine, Burdwan Medical College, Burdwan, [2]Department of Neurology, Nil Ratan Sircar Medical College, Kolkata, [3]Department of Medicine, Charnock Hospital, Kolkata, [4]Research Associate, J. B. Roy State Ayurvedic Medical College and Hospital, Kolkata, [5]Department of Medicine, College of Medicine and Sagar Dutta Hospital, Kolkata, [6]Department of Neurology, Baba Ramrick Singh Hospital, Kolkata, West Bengal, India

Abstract

Introduction: Carotid stenosis is a major risk factor for ischemic stroke. However, the effect of carotid stenosis on the site of stroke is still under investigation. **Aims:** This study aimed to elucidate how the presence of carotid stenosis influenced the pattern of stroke and also how it interacted with other risk factors for stroke. **Materials and Methods:** Thirty-eight patients with ischemic stroke were included in this study and were investigated with carotid artery Doppler and magnetic resonance angiography for carotid stenosis and intracranial stenosis in the circle of Willis, respectively. Other known risk factors of stroke were also studied in and compared between the subgroups with and without carotid stenosis. **Results:** In patients without carotid stenosis, anterior cerebral artery was the commonest site of stenosis. In patients with carotid stenosis, middle cerebral artery was the commonest site of stenosis. Overall, middle cerebral artery was the commonest territory of stroke. Patients with hypertension, diabetes and history of smoking had preferential stenosis of the anterior cerebral artery.

Key Words

Carotid stenosis, intracranial atherosclerosis, ischemic stroke

For correspondence:
Dr. Kaushik Ghosh, Assistant Professor, Department of Medicine, Burdwan Medical College and Hospital, Burdwan - 713101, West Bengal, India.
E-mail: drkaushikghosh@gmail.com

Ann Indian Acad Neurol 2015;18:412-414

Introduction

Stroke is the foremost cause of disability across the world. In United States, 800,000 patients have stroke every year; 87% of them have ischemic stroke.[1] Again, 87% of all stroke-related deaths occur in low-to middle-income nations.[2] In India, age-standardized prevalence rate of stroke is 545 per 100,000 and mortality rate in stroke is 7.5 per 1000.[3]

Carotid stenosis is an established risk factor of ischemic stroke. In patients with carotid stenosis < 75%, annual incidence of stroke is 1.3%.[4] Intensive medical management of carotid stenosis can reduce the risk of stroke to 0.34%.[5] On the other hand, ischemic stroke patients have a higher likelihood of having carotid stenosis. However, the site of stroke is not clearly related to the degree and site of the carotid stenosis.

The incidence of intracranial atherosclerosis is high in Asians. Outcome of stroke is poor in this group, with a mortality of 101-125 per 100,000 patients.[1] Recent studies have shown that the outcome of stroke deteriorates and risk of recurrent stroke increases with intracranial atherosclerosis.[6] Stenosis of the major intracranial vessels progresses at the rate of 9-12% over six months and a patient with more than 50% stenosis has approximately 40% risk of suffering a vascular event over the next two years.[7] Intracranial atherosclerosis has been shown to correlate well with atherosclerosis at other sites like carotid arteries and the aorta.[8]

Access this article online	
Quick Response Code:	Website: www.annalsofian.org
	DOI: 10.4103/0972-2327.165473

Materials and Methods

A cross-sectional descriptive study was conducted at multiple tertiary care centers during a period of two years between 2009 and 2011. The institutional ethics committee approved

the study protocol prior to the commencement of the study. Patients admitted with first occurrence of ischemic stroke were included in the study. All participants provided an informed consent for inclusion as study subjects. Critically ill patients and those who were unwilling to participate in study were excluded.

The participants underwent clinical examination at the time of admission. Information regarding demographic background and risk factors were collected. Initial blood investigations included complete blood count, blood glucose, renal and liver function tests, lipid profile and electrolytes. Dyslipidemia was defined as the presence of any one of the following — high-density lipoprotein < 40 mg/dl, low-density lipoprotein > 130 mg/dl. Atrial fibrillation was defined as documentation of the same in at least one electrocardiograph recording at any point of time.

Each patient underwent magnetic resonance imaging (MRI) of brain in a 1.5 Tesla Toshiba scanner with 8-channel head coil. The MRI protocol included T1, T2, T2-FLAIR and DWI sequences. At the same time, time-of-flight magnetic resonance angiogram (TOF MRA) was obtained. The sites of stenosis in the intracerebral circulation were compared in subgroups based on age, risk factors and extent of carotid artery stenosis. All statistical computations were performed with R programming language.

Results

The summary of the demographic variables of the patients and prevalence of the risk factors are shown in Table 1. The study population was predominantly male and hypertension was identified as the commonest risk factor among the patients. Total 11.11% patients had anterior cerebral artery (ACA) territory stroke, 55.56% had middle cerebral artery (MCA) territory stroke and 36.11% had posterior cerebral artery (PCA) territory stroke.

Intracranial stenosis was found in 52.78% patients and extracranial stenosis was found in 13.89% patients. Among the patients who had extracranial stenosis, 80% patients had concurrent intracranial stenosis. The relationship between the site of stroke and the sites of arterial stenosis is shown in Table 2. In patients with internal carotid artery (ICA) stenosis greater than or equal to 70%, stem of the MCA was the most prevalent site of stenosis, followed by ACA. In those who had ICA stenosis less than 70%, A1 segment of the ACA was the commonest site of stenosis. Overall, ACA was the commonest site of stenosis, even though MCA was the commonest territory of stroke.

Table 3 shows the relationship of the risk factors to the site of stenosis. Notably, hypertension, diabetes and smoking had stronger association with ACA stenosis. On the other hand, all patients with atrial fibrillation had MCA stenosis.

Discussion

The burden of intracranial atherosclerosis has been reported in different populations worldwide. The incidence of intracranial atherosclerosis is very high in northern India and it is responsible for 30-50% of ischemic strokes in Asian population.[9] Major risk factors for intracranial atherosclerosis are hypertension, diabetes, smoking and dyslipidemia.[10] Stenosis of the large branches of the Circle of Willis can lead to stroke by hypoperfusion or by artery-to-artery embolism.[11] Our study shows three aspects of intracranial atherosclerosis. First, it shows the spatial pattern of stenosis. Second, it correlates the pattern with the presence of carotid artery stenosis. Third, it re-evaluates the relationship of intracranial pathology with the risk factors.

Carotid artery stenosis contributes significantly to the total burden. Patients with more than 70% stenosis of carotid artery had a stroke rate of 28% at 18 months.[12] Carotid artery stenosis can lead to stroke by multiple mechanisms - embolism, thrombotic occlusion, dissection or hypoperfusion. On the other hand, carotid stenosis is considered as a marker of systemic atherosclerosis and has a significant correlation with

Table 1: Demographic and risk factors in the study population

Variable (%)	Male	Female
Mean age (years)	58.1	54.4
Hypertension	89.6	100
Diabetes	61.9	57.1
Dyslipidemia	6.9	28.6
Ischemic heart disease	6.9	0
Atrial fibrillation	3.5	0
Smoking	41.3	0
Family history	6.9	28.7

Table 2: Relationship between site of stroke and site of arterial stenosis. All the figures are in percentage points

ICA stenosis (%)	Vascular territory of stroke	Site of intracranial stenosis					
		ACA		MCA			PCA
		A1	A2	Stem	M1	M2	
≥70	ACA	–	–	–	–	–	–
	MCA	30	14	36	16	4	–
	PCA	–		22.2	11.1	–	33.3
<70	ACA	32	18	12	8	5	–
	MCA	40	10	15	12.8	–	22.2
	PCA	18.1	6.9	12.6	10.2	2.2	33.3

Table 3: Relationship of risk factors and site of intracranial stenosis

Risk factor	ACA (%)	MCA (%)	PCA (%)	Combined (%)	Concurrent (%)
Hypertension	48.5	30.3	27.3	27.3	100
Diabetes	52.9	29.4	17.6	29.4	20
Dyslipidemia	22.2	11.1	22.2	22.2	20
Ischemic heart disease	0	50	0	0	0
Atrial fibrillation	0	100	0	0	0
Smoking	41.7	16.7	16.7	25	0

Stenosis in 2 or more arterial territories was considered as combined, Stenosis in ICA or CCA along with stenosis in at least one intracranial artery was considered concurrent

myocardial infarction.[13] Therefore, the correlation of carotid stenosis with intracranial atherosclerosis becomes a pertinent topic of investigation. Also, in patients with coexistent stenosis of intracranial and extracranial vessels is expected to alter the pathophysiology of stroke. We have investigated the spatial aspect of this process. Our results show that patients with extracranial stenosis almost always have associated intracranial stenosis but the reverse is not true in the majority. Another important aspect of our results is that ACA stenosis, rather than MCA stenosis, was present in greater proportion of patients. The reason why ACA stenosis is less likely to manifest as stroke is not clear and requires further evaluation.

Risk factors for carotid artery stenosis and intracranial stenosis are largely similar, and include age, hypertension, diabetes mellitus, smoking and dyslipidemia. We have included ischemic heart disease as well as a marker of systemic atherosclerosis. In our study, all the risk factors except ischemic heart disease and atrial fibrillation were associated with ACA stenosis. No risk factor preferentially caused atherosclerosis in multiple territories. Concurrent atherosclerosis in extracranial and intracranial arteries was also studied. Hypertension emerged as the strongest risk factor for concurrent stenosis, followed by diabetes and dyslipidemia. Hypertension was similarly indicted in literature as well.[14]

Main limitations of our study are the small number of patients and lack of invasive studies. According to the Stroke Outcomes and Neuroimaging of Intracranial Atherosclerosis (SONIA) trial, cerebral catheter angiography (CTA) is the gold standard for the diagnosis of intracranial atherosclerosis and not MRA, though both methods fail to accurately detail the degree of intracranial stenosis.[15] Fractional flow reserve identifies hemodynamically significant pressure gradient across stenotic lesions. TOF circle of Willis images often overestimate the degree of stenosis in the presence of significant neck vessel stenosis. However as non-invasive methods, TOF MRA and high resolution MRI are getting wide recognition.

In conclusion, we would like to state that ACA was the most prevalent site of stenosis in patients without ICA stenosis and had the strongest association with risk factors like hypertension, diabetes and smoking, even though MCA territory is the commonest affected by stroke. Additionally, presence of ICA stenosis was associated with MCA stenosis in preference to other sites. The biological reason for this pattern needs to be studied in larger populations.

Acknowledgment

We acknowledge the help of Mr. Shamba Chatterjee in preparation of this manuscript.

References

1. Ovbiagele B, Nguyen-Huynh MN. Stroke epidemiology: Advancing our understanding of disease mechanism and therapy. Neurotherapeutics 2011;8:319-29.
2. Mehndiratta MM, Singhal AB, Chaturvedi S, Seemant MR, Moonis M. Meeting the challenges of stroke in India. Neurology 2013;80:2246-7.
3. Das SK, Banerjee TK. Stroke: Indian scenario. Circulation 2008;118:2719-24.
4. Norris JW, Zhu CZ, Bornstein NM, Chambers BR. Vascular risks of asymptomatic carotid stenosis. Stroke 1991;22:1485-90.
5. Spence JD, Pelz D, Veith FJ. Asymptomatic carotid stenosis: Identifying patients at high enough risk to warrant endarterectomy or stenting. Stroke 2014;45:655-7.
6. Wang Y, Zhao X, Liu L, Soo YO, Pu Y, Pan Y, *et al.*, CICAS Study Group. Prevalence and outcomes of symptomatic intracranial large artery stenoses and occlusions in China: The Chinese Intracranial Atherosclerosis (CICAS) Study. Stroke 2014;45:663-9.
7. Pu Y, Dou X, Liu L. Natural history of intracranial atherosclerotic disease. Front Neurol 2014;5:125.
8. Chatzikonstantinou A, Ebert AD, Schoenberg SO, Hennerici MG, Henzler T. Atherosclerosis in intracranial, extracranial, and coronary arteries with aortic plaques in patients with ischemic stroke of undetermined etiology. Int J Neurosci 2014.
9. Holmstedt CA, Turan TN, Chimowitz MI. Atherosclerotic intracranial arterial stenosis: Risk factors, diagnosis and treatment. Lancet Neurol 2013;12:1106-14.
10. Rincon F, Sacco RL, Kranwinkel G, Xu Q, Paik MC, Boden-Albala B, *et al*. Incidence and risk factors of intracranial atherosclerotic stroke: The Northern Manhattan Stroke Study. Cerebrovasc Dis 2009;28:65-71.
11. Liebeskind DS, Cotsonis GA, Saver JL, Lynn MJ, Turan TN, Cloft HJ, *et al.*, Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) Investigators Collaterals dramatically alter stroke risk in intracranial atherosclerosis. Ann Neurol 2011;69:963-74.
12. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med 1991;325:445-53.
13. Wiebers DO, Whisnant JP, Sandok BA, O'Fallon WM. Prospective comparison of a cohort with asymptomatic carotid bruit and a population-based cohort without carotid bruit. Stroke 1990;21:984-8.
14. Man BL, Fu YP, Chan YY, Lam W, Hui AC, Leung WH, *et al.* Lesion patterns and stroke mechanisms of concurrent atherosclerosis of intracranial and extracranial vessels. Stroke 2009;40:3211-5.
15. Feldmann E, Wilterdink JL, Kosinski A, Lynn M, Chimowitz MI, Sarafin J, *et al.*, Stroke Outcomes and Neuroimaging of Intracranial Atherosclerosis (SONIA) Trial Investigators. The stroke outcomes and neuroimaging of intracranial atherosclerosis (SONIA) trial. Neurology 2007;68:2099-106.

How to cite this article: Ghosh M, Ghosh K, Chatterjee A, Bhattacharya A, Acharya A, Chakraborty S, *et al*. Correlation of intracranial atherosclerosis with carotid stenosis in ischemic stroke patients. Ann Indian Acad Neurol 2015;18:412-4.
Received: 21-03-15, **Revised:** 13-04-15, **Accepted:** 29-05-15

Source of Support: Nil, **Conflicts of Interest:** None declared.