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CT Angiographic Evaluation of Pattern and Distribution of Stenosis and its Association with Risk Factors Among Indian Ischemic Stroke Patients

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Summary

Background: Stroke is the major cause of disability and third major cause of death. Ischemia causes about 80% of stroke cases; stenosis and occlusion are the predominant cause of stroke. Our purpose for this study was to evaluate the pattern and distribution of stenosis and its association with risk factors in Indian ischemic stroke patients and in other countries, for comparison.

Material/Methods: We evaluated 60 patients after ischemic stroke with CT angiography. The degree of stenosis was measured by the North American Symptomatic Carotid Endarterectomy Trial (NASCET). The results were analyzed by descriptive statistics and chi-square test.

Results: Out of 60 cases, 32 cases were positive for significant stenosis and a total number of stenotic segments was 45. Out of 45 stenotic segments, 29 were single stenotic segments (16 intracranial and 13 extracranial) and 16 were multiple stenotic segments (8 intracranial and 8 extracranial). In the total number of stenotic segments (single and multiple), there were 24 (53.33%) intracranial and 21 (46.67%) extracranial. The most commonly involved intracranial stenosis segment was MCA, present in 10 (41.6%) out of 24 intracranial segments. Most commonly involved extracranial stenosis segment was ICA, present in 14 (66.6%) out of 21 extracranial segments. Diabetes is found to be the most common risk factor of intracranial stenosis while hypertension and hypercholesterolemia are the major risk factors of extracranial stenosis.

Conclusions: In the Indian population, intracranial stenosis is more common than extracranial one, anterior circulation stenosis is more common than posterior circulation stenosis; single stenosis is more common than multiple stenosis.

MeSH Keywords: **Carotid Stenosis • Cerebral Angiography • India • Stroke**

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Background

Stroke is a sudden loss of brain function resulting from an interference with blood supply to the brain as defined by the National Institute of Neurologic Disorders and Stroke (NINDS), USA. Stroke is an acute vascular phenomenon that includes ischemic and hemorrhagic types of strokes. [1]

Stroke is the major cause of disability and third major cause of death following cardiovascular disease and cancer. It ranked as the sixth leading cause of disability-adjusted life years (DALY; one DALY is one lost year of healthy life) in 1990 and is projected to become the fourth leading cause by the year 2020. Developing countries bear more than two-thirds of the global burden of stroke, where the average age of patients with stroke is 15 years lower than in the developed countries [1].

The first population-based study in India to determine the incidence of stroke was conducted in the Southern Indian town of Vellore in 1969-71, where a population of 258,576 in and around Vellore was kept under surveillance for two years. An incidence of 13 per 100,000 per year was obtained [2].

Epidemiological surveys from different regions of India analyzed a crude stroke prevalence rate of about 203 per 100,000 people above 20 years of age, amounting to a total of about 1 million cases [3]. As per WHO report from 1990, there were 619,000 deaths due to stroke out of 9.4 million deaths in India. This gives a stroke mortality rate of 73 per 100,000. For comparison, this figure is 22 times the number of deaths from malaria, 1.4 times that due to tuberculosis, 4 times that due to rheumatic heart disease, and almost equal to that due to ischemic heart disease [4]. It is believed that 1.2% of total deaths in India are due to stroke. As compared with the developed nations, stroke mortality rates among Indians were been found to be two to three times higher, suggesting thereby that Indians are at a higher risk of stroke-related death than Caucasians [5–7].

Ischemia causes about 80% of stroke cases and 20% are caused by hemorrhage. Stenosis and occlusion are the predominant cause of stroke. Commonly, patients with acute stroke are examined with unenhanced CT of the brain to exclude intracranial hemorrhage or other causes of stroke.

With aggressive but promising new therapies for treating stroke, early recognition of an ischemic-related disease placed diagnostic neuro-imaging at the forefront of stroke management.

The principal cause of cerebral infarction is atherosclerosis and its sequelae. Atherosclerotic plaques are eccentric focal fibro-fatty intimal thickening and affect large, medium and small arteries [8–12].

The clinical pattern of stroke and the angiographic distribution of the stenotic segment is different in different countries and races [13–16]. For example, intracranial stenosis is more common in Japan, China and Korea. Extracranial stenosis is more common in white people and in Iran. No data is available for the Indian population. For patients with major stroke, the mortality rate in a subsequent stroke is 40%, hence stroke prevention is an important concept. Ability to accurately assess the site of stenosis has become important to identify the patient who would benefit from surgical/radiological intervention [17].

Catheter angiography is the gold standard for diagnostic neuro-angiography. Catheter angiography is an expensive and invasive procedure with a morbidity and mortality rate of 1.5–2% [18–20]. Accurate imaging of the vascular anatomy of the head and neck requires excellent spatial resolution for visualization of small and tortuous vessels. In addition, speed is needed to avoid venous enhancement. The entire lengths of the carotids or cerebral arteries are scanned in a few seconds. The finest anatomic detail can be achieved by this isotropic data set providing high-quality 2D and 3D renderings of the vascular anatomy through different reconstruction techniques. CTA (Computed Tomography Angiography) is the current non-invasive modality of choice because it is faster, cheaper, sensitive to the presence of calcium, available in smaller centers, displays bony landmarks and can be used in patients with aneurysmal clips. CTA depends on volume expansion and opacification of blood in the vessels and hence it is more accurate [21–25].

Objectives of the study were to evaluate the pattern and distribution of stenosis and its association with risk factors among ischemic stroke patients in the Indian population and in other countries for comparison.

Material and Method

A cross-sectional study was conducted from May 2008 to April 2010. An ethical approval was obtained from the Institutional Ethics Committee. Purposive sampling was performed for 60 known cases of all age groups having the clinical diagnosis of stroke and ischemic stroke on imaging. Written consent was obtained from all the participants. Patients with moyamoya disease, vasculitis, stenosis or occlusion caused by trauma or dissection, stenosis or occlusion of the cortical branches beyond A2 (A2: vertical segment of the anterior cerebral artery), M2 (insular segment of the middle cerebral artery), and P4 (calcarine segment of the posterior cerebral artery), subarachnoid hemorrhage, heart disease, which could have led to embolism were excluded from the study.

We evaluated CT angiography in patients with ischemic stroke. CT angiography was performed on a 16-slice whole-body GE Light Speed scanner. CT angiography evaluates the area from the arch of the aorta to the vertex for a cervico-cerebral study.

The used parameters were as follows:

KVp – 120–140, **mAs** – 200–350, **slice thickness** –1.25-mm cuts with 1-mm overlap, **pitch** – 3 for the head (1.25 mm/3.75 mm/rev) and 6 for the neck (1.25 mm/7.5 mm/rev), **rotation time** – 0.5 second, **contrast** – 120 mL of contrast at a rate of 4 mL/sec, **bolus tracking** – when threshold attenuation of 100 HU was reached as detected by region of interest (ROI) placed in one of the common carotids, the scan started automatically, **reformation** – images were reformatted with section thickness of 1.25 mm, overlap of 1 mm at a narrow field of view of 120 mm.

Locations of significant stenosis were categorized as intracranial or extracranial and further in the anterior or posterior circulation. The stenosis was labeled as intracranial when the lesion was distal to the ophthalmic artery. Intracranial location was beyond the point where the vertebral artery passes through the dura at the level of the foramen magnum. Lesions were described as single or multiple based on the number. The degree of stenosis was measured according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) [26,27].

The axial data were transferred to a workstation for 3D reconstructions. Shaded Surface Display (SSD) image was generated by selecting a CT value above a defined density threshold. The maximum intensity projection (MIP) image

Table 1. Distribution of type of stenosis according to segments.

Type of stenosis	Segment		Total
	Intracranial	Extracranial	
Single	16 (66.67%)	13 (61.9%)	29 (64.44%)
Multiple	8 (33.33%)	8 (38.10%)	16 (35.56%)
Total	24 (100.0%)	21 (100.0%)	45 (100.0%)

χ^2=0.109, P>0.05.

Table 2. Association between site of stenosis and risk factors.

Risk factor	Segments		Total (N=45)	χ^2	p-value
	Intracranial (n=24)	Extracranial (n=21)			
Diabetes mellitus	21 (65.62%)	11 (34.38%)	32 (100.00%)	5.123	<.05
Hypertension	11 (36.67%)	19 (63.33%)	30 (100.00%)	8.136	<.01
Previous episode	7 (46.67%)	8 (53.33%)	15 (100.00%)	0.402	>.05
Obesity	3 (50.00%)	3 (50.00%)	6 (100.00%)	0.069	>.05
Smoking	10 (52.63%)	9 (47.37%)	19 (100.00%)	0.006	>.05
Hypercholesterolemia	10 (83.33%)	2 (16.67%)	12 (100.00%)	6.944	<.01

was obtained by projection of imaginary rays through the image data and mapping the maximum attenuation values. The vessel lumen, calcium and thrombus were well delineated, but depth information was totally lost. The degree of stenosis was calculated accurately, but there could be overlapping of vessels with bones. SSD (surface shaded display) computed all surfaces connecting neighboring pixels above a particular threshold. It preserved the depth information but lost the attenuation information. It did not show interiors of the vessels, thrombus or wall calcification, and underestimated stenosis. Volume rendering (VR) allowed integration of all available information through the most advanced 3D rendering algorithm. It overcame many problems seen with MIP and SSD.

The detailed history regarding potential risk factors associated with atherosclerotic ischemic stroke was obtained from each patient and from the medical records. Patients were labeled as hypertensive if their blood pressure surpassed 160 (systolic) and/or 95 (diastolic) mmHg on repeated measurements during hospitalization or when taking anti-hypertensive medications. A diagnosis of diabetes mellitus was based on the fasting serum glucose level. If the patient had smoked 10 or more cigarettes daily for more than 10 years, he/she was considered as positive for cigarette smoking. The total fasting serum cholesterol level of 220 mL/dL was considered as hypercholesterolemia [28–33].

Data were entered into a database (Microsoft Office Excel 2007). Statistical analyses were performed using statistical software SPSS 16.0, SPSS Inc.,Chicago,USA. The results were analyzed by descriptive statistics and chi-square test.

Results

Out of 60 cases, there were 40 males and 20 females. Stenosis was present in 24 males and 8 females. There was no association between stenosis and sex (χ^2=2.148 and p>0.05).

The mean age for males was 57.97+10.75 years and for females 56.65+9.04 years. The numbers of patients below 50 years, between 50–60 years and above 60 years was 15, 22 and 23, respectively. There was no association between stenosis and age (χ^2=0.385 and p>0.05).

Paresis was present in 66.67% of patients. Plegia was present in 10% of patients. The most common presentation was hemi-(paresis/plegia), in 51.67% of patients. Ataxia and others were present in 28.33% of patients.

In cases of a single type of stenosis, the total number of stenotic sites was 29, including 16 intracranial stenoses and 13 extracranial stenoses. In cases of multiple types of stenosis, the total number of stenotic sites was 16, including 8 intracranial stenoses and 8 extracranial stenoses. There was no association between stenosis and type of stenosis (χ^2=0.109 and p>0.05) (Table 1).

In the total number of 24 intracranial stenosis segments, 18 (75%) were present in male patients and 6 (25%) in female patients. In a total number of 21 extracranial stenosis segments, 18 (85.71%) were present in male patients and 3 (14.29%) in female patients.

There was no association between extracranial and intracranial stenosis and sex (χ^2=0.273 and p>0.05).

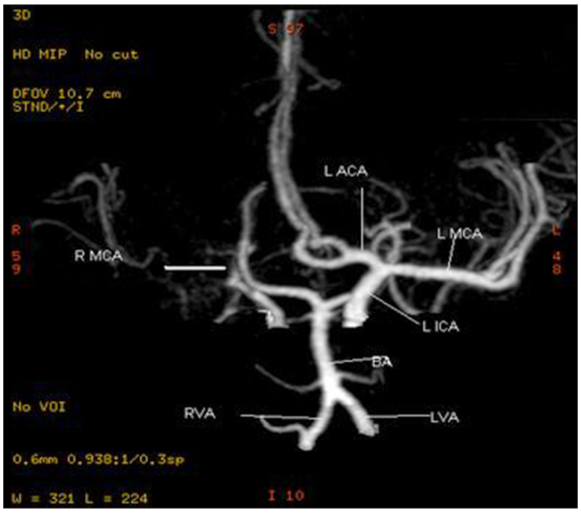

Figure 1. CT MIP image of right MCA stenosis.

Table 3. Frequency of stenosis in intracranial segments.

Intracranial segment	Number of stenosis	%
MCA	10	41.67
ACA	7	29.17
PCA	3	12.50
V4	2	8.33
VBJ	1	4.17
BA	1	4.17
Total stenosis	24	100.00

Intracranial and extracranial stenosis had an association with risk factors like diabetes mellitus, hypertension, previous episode, obesity, smoking, hypercholesterolemia. Diabetes mellitus was significantly associated with intracranial stenosis (χ^2=5.123 and $p<0.05$). Hypertension was significantly associated with extracranial stenosis (χ^2=8.136 and $p<0.05$). Hypercholesterolemia was significantly associated with extracranial stenosis (χ^2=6.944 and $p<0.01$) (Table 2).

In total, 24 intracranial stenotic segments were present. The most commonly involved segment was the middle cerebral artery (MCA) – 10 (41.67%) (Figure 1). It was followed by the anterior cerebral artery (ACA), posterior cerebral artery (PCA), intracranial segments of the vertebral artery (VA), basilar artery (BA), and vertebrobasilar junction (VBJ), with the following number of stenotic segments: 7 (29.17%), 3 (12.5%), 2 (8.33%), 1 (4.17%), 1(4.17), respectively (Table 3).

A total of 21 extracranial stenotic segments were present, among which the most commonly involved segment was the internal carotid artery (ICA) – 14 (66.67%) (Figure 2). Stenosis was present in the intracranial segments of the vertebral artery, common carotid artery (CCA), external carotid artery (ECA) and subclavian artery: 3 (14.29%), 2 (9.52%), 1 (4.76%), and 1 (4.76%), respectively (Table 4).

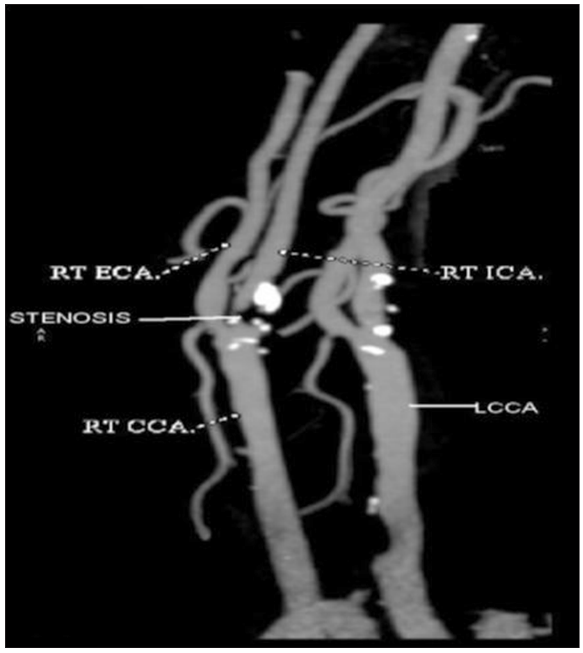

Figure 2. CT MIP image of right ICA stenosis.

Table 4. Frequency of stenosis in extracranial segments.

Intracranial segment	Number of stenosis	%
ICA	14	66.67
Vertebral	3	14.29
CCA	2	9.52
ECA	1	4.76
Subclavian	1	4.76
Total stenosis	21	100.00

Out of all 45 stenotic segments, 34 (75.56) were present in the anterior circulation, with 17 stenotic segments in the intracranial region and 17 stenotic segments in the extracranial region. The posterior circulation consisted of 11 (24.44) stenotic segments, with 7 segments in the intracranial region and 4 in the extracranial region.

Discussion

A CT angiography-based study was conducted, being non-invasive in nature, fast and sensitive to calcification, available in small centers and displaying bony landmarks. We focused only on stenotic segments present in the extracranial and intracranial region and then evaluated the exact site of stenosis and compared the results with similar studies in other countries.

We considered a stenosis of more than 50% as significant. Stenosis was calculated by dividing the narrowest diameter at a stenotic segment by the distal diameter at a normal-looking vessel distal to the stenotic segment [17].

We used CT angiography as the modality for investigation. Catheter angiography is the gold standard but it is an expensive and invasive procedure. Magnetic resonance angiography (MRA) and colour Doppler ultrasound are some non-invasive alternatives but limitations of MRA include motion artifacts, long examination time, loss of signal due to turbulence and in-plane saturation leading to exaggeration of stenosis, poor demonstration of calcium and bony landmarks, and limitations in evaluating post-operative patients with metallic clips and stents. Colour Doppler is operator-dependent and limited in evaluating the intracranial vasculature [34]. CTA is the current noninvasive modality of choice for neuro-angiography because it is faster, sensitive to the presence of calcium, available in smaller centers, displays bony landmarks and can be used in patients with aneurysmal clips. CTA depends on volume expansion and opacification of blood in the vessels and hence is more accurate.

The incidence of ischemic stroke segments was the highest in patients above 61 yrs. and the male: female ratio was 2:1. The incidence of stroke increased with age. The most common presentation was hemiparesis, present in 40 (66.6%) patients.

Out of 60 cases of stroke, 32 patients had significant stenotic segments (>50%). A total number of stenotic segments in 32 positive cases was 45, including 29 single stenotic segments (16 intracranial and 13 extracranial) and 16 multiple stenotic segments (8 intracranial and 8 extracranial).

In a total number of stenotic segments (single and multiple), there were 24 (53.33%) intracranial and 21extracranial ones (46.67%). Extracranial stenotic segments were present in 18 male patients and 3 female patients. Intracranial stenotic segments were present in 18 male patients and 6 female patients.

In 24 intracranial stenotic segments, the distribution of stenosis was as follows: MCA 10 (41.67%), ACA 7 (29.17%), vertebral 2 (8.33%), basilar 1 (4.17%), VBJ 1 (4.17%), and PCA 3 (12.5%). The most common site of intracranial stenosis was MCA, supported by Dae et al. [35]. The horizontal segment of the middle cerebral artery (M1segment) was the most commonly involved one.

In 21 extracranial stenotic segments the distribution of stenosis was as follows: ICA-14 (66.67%), ECA 1 (4.76%), CCA 2 (9.52%), subclavian 1 (4.76%), vertebral 3 (14.29%). The most common site of extracranial stenosis was ICA, supported by Dae et al. [35]. The cervical segment of the internal carotid artery (C1 segment) was the most commonly involved one.

Hypertension, diabetes mellitus, history of previous episode, obesity, and smoking were risk factors. Diabetes was most significantly associated with intracranial stenosis, present in 32 stenotic segments, among which 21 (65.62%) were intracranial and 11 (34.38%) extracranial. (χ^2=5.123 and $p<0.05$). That was supported by Framingham [12], Mendes et al. [31], Ralph et al. [36] and Hossein Zarei et al. [37] Hypertension was most significantly associated with extracranial stenosis. Among all 30 stenotic segments associated with hypertension, 19 (63.33%) were extracranial and 11 (36.67%) were intracranial (χ^2=8.136 and $p<0.05$). That was supported by Bogousslavsky et al. [28], JR Crouse et al., [29] Framingham [12], and Hossein Zarei et al. [37] Hypercholesterolemia was significantly associated with extracranial stenosis (χ^2=6.944 and $p<.01$). This was in agreement with the study conducted by Ralph et al. [36].

Single stenotic segments were more common than multiple stenotic segments. In 32 positive cases, there were 45 stenotic segments, including 24 (53.33%) intracranial and 21 (46.67%) extracranial. In our study, intracranial stenosis (24 cases, 53.33%) was more common than extracranial stenosis (21 cases, 46.67%). This was in line with the studies conducted in the South Korean Population (52% intracranial and 48% extracranial stenosis) (Dae et al.) [35] and China population (52% intracranial stenosis and 48% extracranial stenosis) (Wong KS et al). [38] However, that was in contrast with the studies conducted in the white population (Wityk RJ et al.) [39] and Iranian population (Hossein Zarei et al.) [37] where extracranial stenosis (58% and 57% respectively) was more common than intracranial stenosis (42% and 43% respectively).

The most commonly involved intracranial stenosis segment was MCA, present in 10 (41.6%) out of 24 intracranial segments. The most commonly involved extracranial stenosis segment was ICA, present in 14 (66.6%) out of 21 extracranial segments. Anterior circulation had more stenosis segments (i.e. 34, 75.56%) as compared to the posterior circulation stenosis (11, 24.44%).

The exact cause of intracranial stenosis is not known, but it may possibly be due to genetic differences. Another possibility is that in our study the most common risk factor was diabetes mellitus and it was associated with intracranial stenosis.

A different interventional procedure can be planned on the basis of the results of our study. The effects of antiplatelet, anticoagulant, and lipid-lowering drugs can be evaluated in the treatment of extracranial and intracranial stenosis with the help of the present study. Limitation of the present study was that the CT angiography findings were not compared with the gold-standard technique, like DSA. Further studies can be conducted by performing a large multicentric study in a different demographic population of India and can be correlated with DSA findings.

Conclusions

Intracranial stenosis is more common than the extracranial one, anterior circulation stenosis is more common than posterior circulation stenosis, single stenosis is more common than multiple stenosis, MCA stenosis is the most common in intracranial location and ICA stenosis is the most common in extracranial location in the Indian population.

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