IP Indian Journal of Neurosciences 2020;6(3):183–187

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IP Indian Journal of Neurosciences

Journal homepage: www.ipinnovative.com

Original Research Article

# Pattern of intracranial versus extracranial atherosclerotic cerebrovascular disease in indian patients with stroke: An angiography study

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ARTICLE INFO

*Article history:*
Received 25-06-2020
Accepted 17-07-2020
Available online 18-09-2020

*Keywords:*
Angiography
Multiple lesions
Single lesions
Atherosclerotic stenotic disease

ABSTRACT

**Background:** The atherosclerotic stenotic disease forms an important cause of secondary prevention of stroke. In the recent past with the availability of various imaging modalities and cerebral digital subtraction angiography (DSA) for the evaluation of stroke patients, the number of atherosclerotic stenotic diseases is at rising. This study analyses retrospectively and prospectively angiographic data in ischemic stroke patients referred to our center, which is a territory care hospital.

**Materials and Methods:** Between January 2016 to March 2019, 224 cerebral DSA was performed in the patients referred to us in university medical college, who had small or large vessel disease diagnosed by Doppler, CTA, or MRA.

The degrees of stenosis of bilateral cervical carotid arteries, vertebrobasilar system, and their major intracranial branches were recorded. Lesions were described as being single or multiple according to the number of lesions.

**Results:** Of the total 1024 patients, 224 patients were enrolled in the study, 54 were females. The mean age was 54years. A total of 404 lesions were present in 224 patients. Amongthese patients, single lesions were found in 64 (15.8%) and multiplelesions in 340 (84.15%). Of the single lesion, 40 were extracranial and 14 were intracranial stenosis. Out of 340 multiple lesions 88 (25.88%) were intracranial, 186(57.70%) extracranial, and combined in 66(19.41%). Lesions were located in the anterior circulation in 132 patients(58.9%) and the posterior circulation 62 patients (27.67%) and at the combined location in 30 patients (13.39%).

**Conclusion :**This study is the first report from the Indian subcontinent depicting a higher incidence of intracranial stenosis based on angiography. The reason for relatively higher incidence could be shared geographical region (Asia) in concordance with Chinese and Korean studies but relatively lower incidence from this population may be due to different prevalence of risk factors in this population.



## 1. Introduction

The atherosclerotic stenotic disease forms an important cause of secondary prevention of stroke. In the recent past with the availability of various imaging modalities and cerebral digital subtraction angiography (DSA) for the evaluation of stroke patients, the number of atherosclerotic stenotic diseases is at rising. The distribution of atherosclerotic disease in the cerebral vasculature can be broadly divided into two subsets, namely extracranial (EC) location involving large vessels in the neck region and intracranial (IC) location involving medium-sized vessels in intradural segments of the cerebrovascular tree.

Atherosclerotic lesions in the cerebral arteries are distributed heterogeneously among different races. Intracranial carotid lesions are reported to be more common than extracranial carotid lesions among Japanese, Korean, Chinese and African American as documented by

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https://doi.org/10.18231/j.ijn.2020.037

Angiographic and autopsy studies in stroke patients, which is in sharp contrast to the pattern of cerebral atherosclerosis in whites.[1–12]

Whites were more likely than blacks to have extracranial carotid artery lesions (33% versus 15% but the proportion of patients with intracranial lesions was similar (24% versus 22%).[13] Intracranial steno-occlusive lesions (> or =30% stenosis or occlusion) were found in 56.3% in Korean patients with stroke.[12] In a study by magnetic resonance angiography (MRA) in Taiwan Chinese, approximately 24% of patients had the only extracranial carotid disease, and about 26% had only intracranial carotid artery disease.[9] Indian data regarding intracranial and extracranial stenosis are lacking.[14]

This study analyses retrospectively and prospectively angiographic data in ischemic stroke patients referred to our center, which is a territory care hospital, These patients had evidence of large or small vessel disease on Doppler, CT angiography, MRA and cerebral angiography. This study was aimed to see, whether the higher incidence of intracranial incidence in Japanese, Korean and Chinese is due to racial differences with the rest of the population of the world, or is it a reflection of Asian trends. With the advent of endovascular technique, it is becoming possible to modify intracranial stenotic lesions by stent angioplasty with reasonable safety. This may open up a new dimension in secondary prevention of stroke.

## 2. Materials and Methods

Between January 2016 to March 2019, 224 cerebral DSA was performed in the patients referred to us in university medical college, who had small or large vessel disease diagnosed by Doppler, CTA, or MRA.

All patients with symptoms or signs of an ischemic stroke related to atherosclerosis who were referred to our department for cerebral angiography during the study interval were included in this study. Cardioembolic disease and cerebral hemorrhage cases were excluded. The degrees of stenosis of bilateral cervical carotid arteries, vertebrobasilar system, and their major intracranial branches were recorded. Potential vascular risk factors for each patient were obtained from medical records which include hypertension, diabetes mellitus, hyperlipidemia, coronary arterial disease, previous history of cerebral stroke, smoking, and age greater than 60 years.

The percentage diameter stenosis was calculated by dividing the narrowest linear diameter at the stenotic segment by the distal diameter at the normal-looking vessel (diameter of most severe stenotic segment/diameter of healthy-looking distal vessel multiplied by 100 to get % stenosis) while for intracranial vessels normal diameter of proximal vessel was taken as per WASID method as distally intracranial arteries become tapered and more tortuous. (WASID study group). If it was difficult to define the normal-looking vessel wall distal to the stenotic segment, the diameter of the imaginary wall of the vessel was used as the denominator. They were categorized as nonsignificant stenosis (0% to 49%), significant stenosis (50% to 99%), and total occlusion.[14] Locations of severe stenosis were categorized as being in the anterior or posterior circulation and the intracranial or extracranial vessels. The distinction of the intracranial and extracranial vessels was based on the observation that the internal carotid artery pierced the inner dura immediately proximal to the origin of the ophthalmic artery in the anterior circulation. Therefore, the intracranial vessels were involved when a lesion was distal to the ophthalmic artery. For the vertebral artery, the distinction was made at the point where the artery pierced the dura at the level of the 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 P1-P2 segments of the posterior cerebral artery. A cortical branch lesion beyond this level was not included. The characteristic angiographic findings of atherosclerosis included vessel wall irregularity, an atheromatous plaque with or without ulceration, tortuosity, stenosis, and occlusion or ectasia of the vascular lumen. Patients were excluded if they had moyamoya disease, vasculitis, stenosis, or occlusion caused by trauma or dissection. Lesions were described as being single or multiple according to the number of lesions.

## 3. Results

This study evaluated cerebral DSA data in ischemic stroke patients referred to us, who had evidence of large vessel disease on carotid Doppler, magnetic resonance imaging (MRA), or computed tomography angiography(CTA). Of the total 1024 patients, 224 patients were enrolled in the study, 54 were females. The mean age was 54years. A total of 404 lesions were present in 224 patients. Among these patients, single lesions were found in 64 (15.8%) and multiplelesions in 340 (84.15%). Of the single lesion, 40 were extracranial and 14 were intracranial stenosis. Out of 340 multiple lesions 88 (25.88%) were intracranial, 186(57.70%) extracranial, and combined in 66(19.41%). Lesions were located in the anterior circulation in 132 patients(58.9%) and in the posterior circulation 62 patients (27.67%) and at a combined location in 30 patients(13.39 %).Therefore, more lesions were located in the anterior than in the posterior circulation ($P < .05$). 142 lesions were intracranial and 262 were extracranial. The most commonly involved vessels werethe extracranial internal carotid artery, the extracranialvertebral artery, and the M1 segment of the middle cerebralartery.

### *3.1. Single Lesion*

Among the 64 patients with single severe stenosis, the lesion was located intracranially in 24 patients (37.5%)

and extracranially in 40 (62.5%). Lesions were located in the anterior circulation in 42 patients (65.62%) and in the posterior circulation in 22 (34.37%).

### 3.2. Multiple Lesions

Among the 340 stenoses in the 160 patients with multiple lesions, 38 (23.75%) patients had 88 lesions in the intracranial vessels, and 92 patients (57.5%) had 186 lesions in the extracranial vessels solely and both intra and extracranial combined in 30(18.75%) patients harboring 66 lesions. Of these combined location lesions 30 were intracranial and 36 were extracranial. A total of 240 lesions (70.58 %) were in the anterior circulation and 100 lesions (29.41%) in the posterior circulation. (Table 1)

**Table 1:** Distribution of severe (>50%) stenosis, intracranial versus extracranial

| Location | No. of Lesions |
|---|---|
| **Intracranial arteries** | **142** |
| Anterior circulation | 76 |
| Posterior circulation | 66 |
| **Extracranial arteries** | **262** |
| Anterior circulation | 206 |
| Posterior circulation | 56 |
| **Total** | **404** |

**Table 2:** Distribution of severe (>50%) stenosis, single versus multiple stenosis

| Group and Location | No. of Lesions |
|---|---|
| **Single lesion** | **64** |
| Intracranial | 24 |
| Extracranial | 40 |
| **Multiple lesions** | **340** |
| Intracranial | 88 |
| Extracranial | 186 |
| Both (IC+EC) | 66 |

## 4. Discussion

There have been reports of racial and ethnic differences in the distribution of central nervous disease vascular disease.[15] There are significant differences in the prevalence of risk factors and stroke types between Whites, Hispanics, and Native Americans in[a] hospital-based population, Although the three races, appear to respond to risk factors similarly.[16] Identification of specific features of stroke in specific populations should lead to more effectively focused treatment and prevention. The concept of the word 'ethnicity' may be confounded with race ("black"), a common language or culture ("Hispanic"), a shared geographic origin ("Asian"), or a presumed common descent with diffuse boundaries ("Caucasian"). Ethnic categories are usually not defined in scientific reports, which results in dubious findings that are difficult to compare.[17] The trend toward more intracranial stenotic disease in the Asian population remains unclear, although numerous studies from the past 2 decades have shown that coronary heart disease, stroke, hypertension, and diabetes mellitus are associated with more extensive cerebral atherosclerosis. An angiographic study of patients with stroke in a mixed white and African American population showed that ischemic heart disease is more common in patients with disease involving the extracranial internal carotid artery, whereas diabetes mellitus is more often noted in patients with the intracranial arterial disease.[18] In contrast to nonatherosclerotic disease, patients with intracranial disease were younger, more often with hypercholesterolemia and insulin-dependent diabetes.[19] The white race, male sex, and coronary heart disease and/or hypercholesterolemia are more commonly associated with occlusive disease of the extracranial arteries while certain races and other factors (eg, Hispanic Americans, blacks, Asians, female sex, diabetes, and younger age) are more commonly associated with occlusive disease of the intracranial arteries.[2,18,20,21] Our study shows that severe stenosis in Korean patients was intracranial in 52% and extracranial in 48%. Intracranial distribution of severe stenoses is thus more common in Koreans than in whites,[2,4] but it is less common than in the Chinese.[2,9] This difference is more definite and statistically significant when single severe stenosis is present. This increased incidence is also noted in Chinese and Japanese populations, although studies in these groups were not based on the same angiographic analysis.[4,6,9,22]

Indian population is extremely heterogeneous with varying skin colour, different races but enlarging the majority of the Indian population is Aryan descendent especially in north India where this study was carried out. It would worthwhile to compare various zonal Indian populations like north India, south India, and northeast population to have a clearer picture as India is the second-largest country in terms of population and one of the largest in the area also.

There are different methods to determine the location and degree of carotid stenosis in various studies. Kieffer et al compared angiographic findings in 42 white patients and 35 Japanese patients, but they did not mention the exact anatomic border between the intra- and extracranial internal carotid arteries[2] Feldman et al compared the clinical and angiographic findings in 48 patients, who included 24 white and 24 Chinese individuals. The investigators categorized the anterior circulation as being at the beginning point of the internal carotid siphon and defined the posterior circulation as being at the level between C1 and C2. They regarded the stenosis as severe when it was greater than 50%. Leung et al did not include the internal carotid arterial portion through the skull base because they analyzed

**Table 3:** Showing intracranial versus extracranial stenosis in the different population group

| Study | Investigation | Population | Pt. Number | ECS | ICS |
|---|---|---|---|---|---|
| Wityk et al | Duplex, TCD | White v/s Black | 274 | 33% v/s 15% | 24% v/s 22% |
| Suh et al | Angio | Korean | 268 | 34% | 40% |
| Lee et al | Angio | Korean | 142 | — | 56.3% |
| Liu et al | MRA | Taiwan Chinese | 108 | 24% | 26% |
| Padma et al | MRA | Indian | 100 | 26% | —— |

Angio: conventional angiography/ DSA, ECS (extracranial stenosis), ICS (intracranial stenosis)

the distribution of stenosisin the intracranial vessels and that in the extracranial carotidarteries separately in 114 consecutive human autopsies[20] Gorelicket al reported angiographic findings and risk factorsin 71 black patients and white patients. They classified theextracranial vessels up to the internal carotid siphon and regardedthe stenosis as severe when it was greater than 75%. In the Northern Manhattan stroke study, 73 patients with atherosclerotic stroke were assigned to extracranial andor intracranial categories based on extracranial duplexand transcranial Doppler findings or angiographic results, without definite anatomic division.

In this study, the intra- and extracranial vessels demarcated at the point where the internal carotid artery passes the inner dura just below the origin of the ophthalmic artery, as Gorelicket al and Suh et al did[23] In the posterior circulation where the vertebral artery passes the dura at the level of theforamen, magnum was labeled as intracranial. The rationale behind this classification is that firstly environment around the vessel is markedly different beyond the inner dura because of subarachnoid fluid surroundingthe vessels. Secondly, there is an inconsistent muscular layer and thinner intima beyond this level. Because of the anatomic difference and risk of vascular rupture, the therapeutic strategy forstenosis differs as far as angioplasty or stent placementis concerned. Apart from this, the branches of the internal carotidartery up to the level of the inner dura are only minor contributing factors when an occlusion is present in the extracranial portionof the internal carotid artery.

The higher incidence of intracranial atherosclerotic arterialstenosis in this study compared to western study but lesser than Chinese and Korean study is significant. Moreover, this study included fewer internal carotid arteries than that of Feldmann et al, who regarded the intracranialvessels beginning at the starting point of the carotid siphon.This study included stenoses of more than 70% because symptomaticstenosis greater than 70% is clinically significant and asit can be treated effectively with endarterectomy.[20]

Being hospital- and angiography-based, this study differs fromconsecutive human autopsy studies[6] and cohort studies.[1]

## 5. Conclusion

This study is the first report from the Indian subcontinent depicting a higher incidence of intracranial stenosis based on angiography compared to another MRA based Indian study depicting 26% stenosis of extracranial stenosis. It was studied from a tertiary care center from Capital city which might reflect the trend in population. The reason for relatively higher incidence could be shared geographical region (Asia) in concordance with Chinese and Korean studies but relatively lower incidence from this population may be due to different prevalence of risk factors in this population.

## 6. Source of Funding

None.

## 7. Conflict of Interest

None.

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**Cite this article:** Vajpeyee A, Tiwari S, Yadav LB, Gupta S, Vajpeyee M. **Pattern of intracranial versus extracranial atherosclerotic cerebrovascular disease in indian patients with stroke: An angiography study**. *IP Indian J Neurosci* 2020;6(3):183-187.