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## Pattern of Atherosclerotic Carotid Stenosis in Korean Patients with Stroke: Different Involvement of Intracranial versus Extracranial Vessels

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**BACKGROUND AND PURPOSE:** The clinical pattern of stroke and the angiographic distribution of cerebral atherosclerosis in the Japanese and Chinese are different from those in whites. Our purpose was to evaluate the location and distribution of severe atherosclerotic stenoses in Korean patients by using cerebral angiography.

**METHODS:** We retrospectively reviewed the cerebral angiographic findings in 268 patients (219 male, 49 female; mean age, 56 years) with one or more severe atherosclerotic stenoses ( $\geq 70\%$ ), as shown on angiograms. These patients were selected from 1436 patients who were examined between 1996 and 1997. The analysis focused on the intracranial or extracranial location of the stenosis, the anterior and posterior circulations, and the multiplicity of the lesions. Statistical analysis was performed by using the  $\chi^2$  test. The data were then compared with data reported in other races and ethnic groups.

**RESULTS:** A total of 389 severe stenotic sites were detected in 268 patients. A single stenosis was found in 56 (21%), and multiple stenoses were found in 212 (79%). Lesions were located in the intracranial area in 52% and in the extracranial area in 48%. They were detected in anterior circulation in 59% and in posterior circulation in 41%. Thirty-seven (66%) of 56 single stenosis were located in the intracranial area, and 19 (34%) were in the extracranial area. Of 333 lesions, 167 (50%) were multiple stenoses in the extracranial area, and 166 lesions (50%) were located in the intracranial vessels. The prevalence of intracranial stenosis was significantly higher in the single-stenosis group than in the multiple stenosis group ( $P < .05$ ).

**CONCLUSION:** Korean patients with severe atherosclerotic stenoses tend to have more intracranial stenoses. In particular, those with an isolated stenosis have more intracranial stenoses, compared with those with multiple stenoses.

Stroke is the second leading cause of death in Korea (1), after cancer, and it is the third leading cause of death in the United States, after cardiac diseases and cancer (2). In Asians, the incidence and mortality rate due to stroke is higher than that in whites, although the rate of coronary heart disease is lower in Asians. Racial differences have been suggested in the distribution of cerebral atherosclerosis (2–6): Angiographic and autopsy studies in stroke patients have

shown that African American, Chinese, and Japanese individuals tend to have more intracranial vascular occlusions, whereas whites tend to have more extracranial lesions (7–12). However, reports of the differences in the distribution of cerebral atherosclerosis in Koreans and in whites have been few in number.

In this study, we analyzed the distribution of atherosclerotic stenosis, as depicted on angiograms obtained in 1996 and 1997, in patients admitted to our hospital.

### Methods

During the 2 years between January 1996 and December 1997, 1436 patients were admitted to our hospital and underwent transfemoral intra-arterial four-vessel cerebral angiography. Among these, 536 patients had stenosis in their cerebral vessels, and 268 of these 536 patients had severe ( $\geq 70\%$ )

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atherosclerotic stenosis. This group was included in this study; they were selected on the basis of their medical records and information obtained from the data bank at our hospital. 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. The male-female ratio was 219:49, and the mean patient age was 56 years. The patients had characteristic atherosclerotic stenosis, as detected using cerebral angiography, and one or more risk factors of atherosclerosis, eg, hypertension, diabetes mellitus, hyperlipidemia, coronary arterial disease, previous history of cerebral stroke, smoking (with a history of more than 20 pack-years), and age greater than 55 years.

The angiographic examinations were performed by three neuroradiologists (D.C.S., C.G.C., H.K.L.) and/or neuroradiology fellows or residents under the supervision of the neuroradiologists. Each neuroradiologist read the angiograms at the time of the examination unless a question or doubt existed. If the neuroradiologist raised a question, two or more neuroradiologists made the decision after discussion. When a stenosis was present, they measured its degree and categorized it as severe (30%), moderate (30–69%), or severe ( $\geq 70\%$ ). Angiographic assessments for this study were based on review of the findings from each examination (S.-H.L., D.C.S.) and on the interpretation report. If the degree of stenosis was not specified in the report, one of the authors (S.-H.L.) measured the degree of stenosis.

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. 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. Any disagreement among the independent examiners regarding the degree of stenosis was arbitrated and settled by means of angiographic review by two of the authors (D.C.S., S.-H.L.). Locations of severe stenosis were categorized as being in the anterior or posterior circulation and in 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 vessel was 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 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 P4 segment of the posterior cerebral artery. A cortical branch lesion beyond the level was not included. Each of the main branches of the cerebral vessels belonging to these vascular territories, such as the anterior choroidal artery, anteroinferior cerebellar artery, superior cerebellar artery, posteroinferior cerebellar artery, were included for measurement.

The characteristic angiographic findings of atherosclerosis included vessel wall irregularity, 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; stenosis or occlusion of cortical branches beyond A2, M2, and P4; subarachnoid hemorrhage, as depicted on CT scans; heart disease, which could have led to embolism; incomplete angiograms; multiple sclerosis; or mitochondrial encephalomyelopathy, lactic acidosis, and stroke-like episodes syndrome (MELAS). For the cardiac evaluation, we reviewed the results of all the medical records and medical examinations, which routinely included electrocardiography, echocardiography, and medical assessment.

We divided the sites of the lesions into intracranial or extracranial vessels and anterior or posterior circulation. Lesions were described as being single or multiple according to the number of lesions. Patients in the single-lesion group had

normal vessels except for one severe stenosis. Patients in the multiple-lesion group had at least one stenosis of  $\geq 70\%$  and multiple stenoses of variable degrees in other areas.

The distribution of the intracranial and extracranial locations in the two patients groups was statistically analyzed and compared by using the  $\chi^2$  test. Significance was defined as  $P < .05$ . Patients with multiple severe stenoses were categorized in groups with intracranial involvement, extracranial involvement, or both. We compared the distribution of intracranial and extracranial vascular involvement with published data.

## Results

A total 389 lesions were present in our 268 patients. Among these patients, single lesions were found in 56 (21%) and multiple lesions in 212 (79%). The 212 patients with multiple stenoses had a total of 333 lesions. One hundred twenty-three patients had at least one severe stenosis and a variable number (1–8) of mild to moderate stenoses in other vessels, and 89 patients had more than two severe stenoses.

Lesions were located in the anterior circulation in 231 patients (59%) and in the posterior circulation in 158 patients (41%). Therefore, more lesions were located in the anterior than in the posterior circulation ( $P < .05$ ). Lesions were located intracranially in 203 patients (52%) (Fig 1) and extracranially in 186 (48%) (Fig 2). The most commonly involved vessels were the extracranial internal carotid artery (30%), the extracranial vertebral artery (16%), and the M1 segment of the middle cerebral artery (15%) (Table 1).

### Single Lesion

Among the 56 patients with a single severe stenosis, the lesion was located intracranially in 37 patients (66%) and extracranially in 19 (34%). Therefore, the intracranial distribution was more common than the extracranial distribution ( $P < .05$ ). Lesions were located in the anterior circulation in 34 patients (61%) and in the posterior circulation in 22 (39%). The most commonly involved vessels were in the M1 segment of the middle cerebral artery ( $n = 16$ ) (Table 2).

### Multiple Lesions

Among the 333 stenoses in the 212 patients with multiple lesions, 166 (50%) were located in the intracranial vessels, and 167 lesions (50%) were in the extracranial vessels. A total of 197 lesions (59%) were in the anterior circulation and 136 lesions (41%) in the posterior circulation (Table 2).

Among the 89 patients with more than two severe stenoses, 28 patients (32%) had severe stenosis in only the intracranial vessels, whereas 27 patients (30%) had stenosis in only the extracranial vessels. The remaining 34 patients (38%) had lesions in both vessels. In 28 patients with 71 severe intracranial stenoses, M1 was the most common site ( $n = 19$ ). In 27 patients with 59 severe stenotic extracranial vessels, the extracranial internal carotid artery ( $n = 41$ ) was the most common location. In 34 patients with 80 severe stenoses in both intra- and extracranial vessels, 39 lesions (49%) were intracranial and 41 lesions

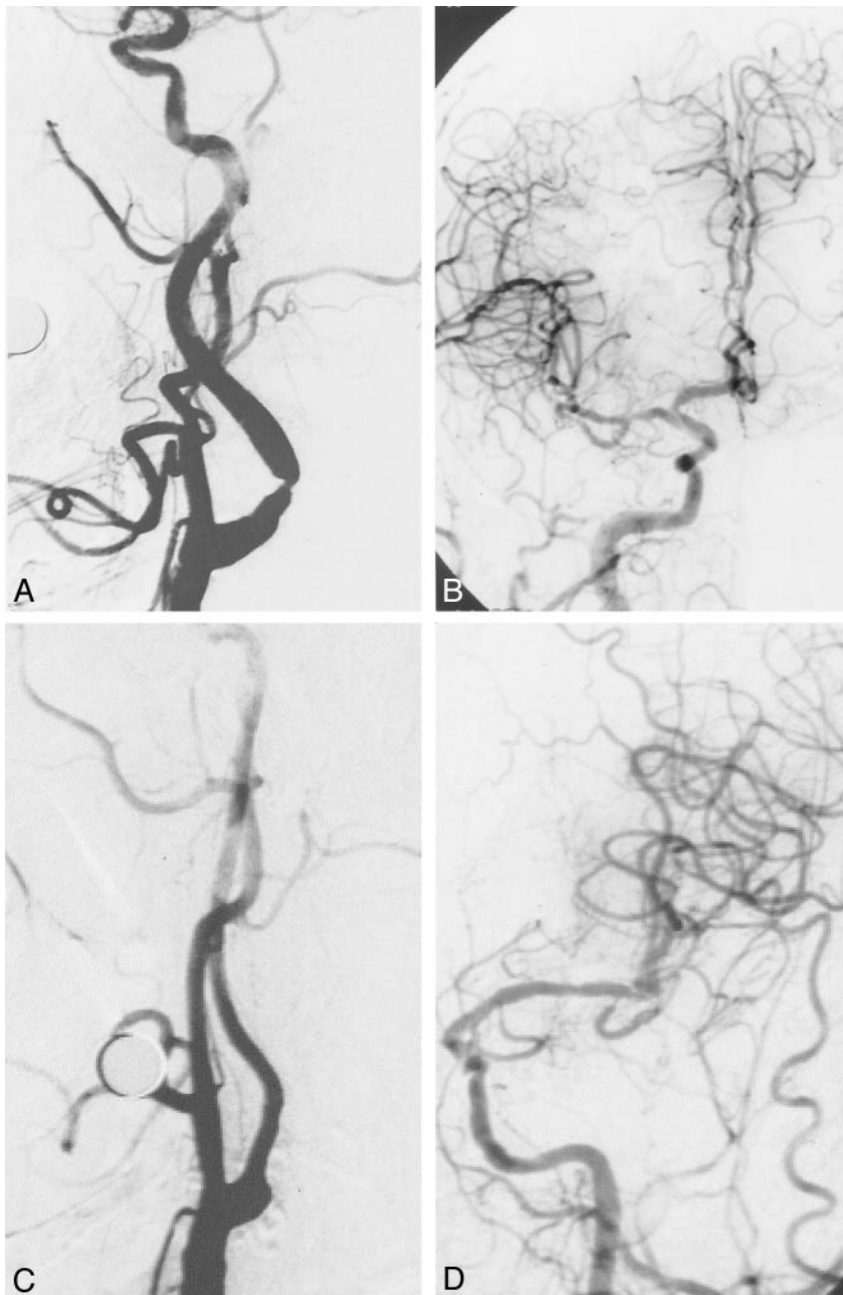


FIG 1. A 66-year-old male patient presented with unstable angina. He had mild right hemiparesis due to a stroke 8 years before, and he had a 2-month history of transient left hemiparesis. His risk factors included diabetes mellitus and hypertension.

A, Lateral right common carotid arteriogram shows severe stenosis in the proximal cervical segment of the right internal carotid artery.

B, Anteroposterior view shows no significant stenosis in the intracranial vessels except for mild luminal irregularities.

C and D, Left common carotid arteriograms shows mild narrowing of the carotid bulb portion without significant stenosis in the intracranial vessels.

(51%) were extracranial. The extracranial internal carotid artery ( $n = 22$ ) was the most common location of severe stenosis.

### Discussion

The pathogenesis of the trend toward more intracranial occlusive lesions 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 origin of the

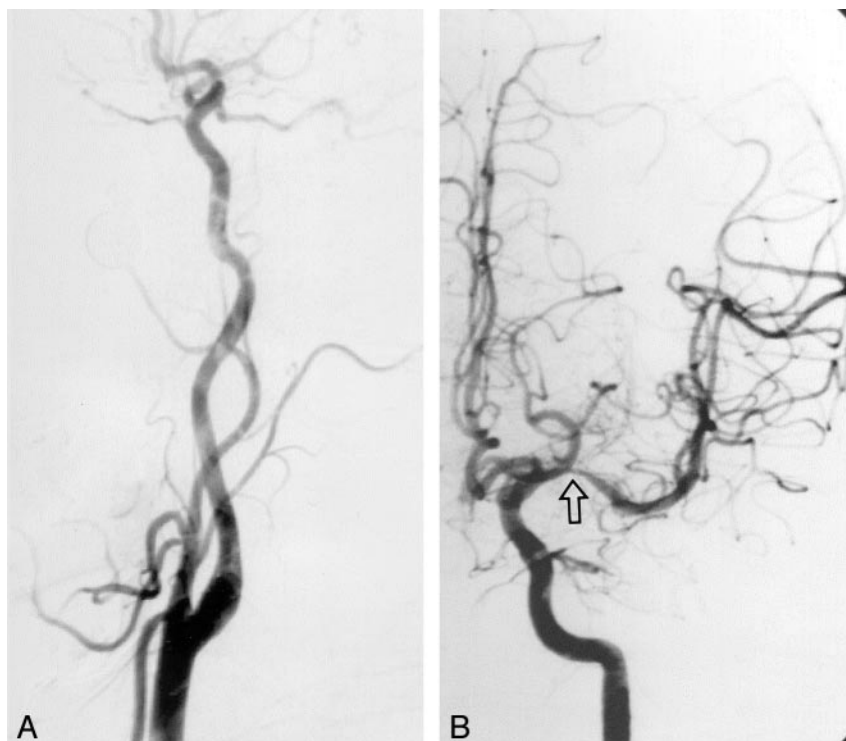
internal carotid artery, whereas diabetes mellitus is more often noted in patients with intracranial arterial disease (13, 14). An analysis of risk factors from the Oslo study (15) has shown that blood pressure and, to a lesser extent, the serum lipid levels are important risk factors for intracranial atherosclerosis. Compared with extracranial stenoses, intracranial stenoses do not correlate as well with the typical atherosclerotic risk factors for peripheral and coronary vascular disease; that is, male sex and hypercholesterolemia (4, 14). Compared with those with nonatherosclerotic disease, patients with intracranial disease were significantly younger and had an increased frequency of hypercholesterolemia and insulin-dependent diabetes (4). The greater prevalence of diabetes and hypercholesterolemia among blacks and Hispanics from north-



FIG 2. A 43-year-old male patient presented with repeated right hemiparesis due to a transient ischemic attack. He had a 15 pack-year smoking history.

A, Left carotid bulb is normal.

B, Intracranial angiogram shows severe stenosis (arrow) of the left M1 segment corresponding to the patient's symptoms.



ern Manhattan accounted for much of the increased frequency of intracranial atherosclerotic stroke. Although white race, male sex, and coronary heart disease and/or hypercholesterolemia have not been definitely correlated as causative factors until now, these are more commonly associated with occlusive disease of the extracranial arteries. In contrast, in 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 (4, 5, 8, 14).

Although the Framingham study indicated that diabetes mellitus was an independent risk factor for cerebral infarction (14, 16), whether diabetes mellitus affects the distribution of atherosclerosis in cerebral arteries has yet to be fully elucidated. Risk-factor studies based on racial differences reveal different vessel involvement in diabetes mellitus (14). Diabetes mellitus, age, and hypercholesterolemia seem to be associated with atherosclerosis of the extracranial internal carotid artery, and hypertension may play a role in the development of middle cerebral artery occlusion in Japanese patients with an atherothrombotic lesion (17–20). Gorelick et al (21) investigated racial differences in the distribution of posterior circulation occlusive disease and found that distal basilar atherosclerotic lesions and diabetes mellitus were more common in blacks than in whites.

Our study shows that severe stenosis in the Korean patients were intracranial in 52% and extracranial in 48%. Intracranial distribution of severe stenoses is thus more common in Koreans than in whites (4, 5, 7, 8), but it is less common than in the Chinese (5, 9). This difference is more definite and statistically significant when a 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 (7, 9–12, 17).

Methods used to analyze the location and degree of carotid stenosis differed among the various studies we reviewed. Kieffer et al (7) compared angiographic findings in 77 white patients and Japanese patients (ratio, 42:35), but they did not mention the exact anatomic border between the intra- and extracranial internal carotid arteries. Feldmann et al (5) 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 (9) did not include the internal carotid arterial portion through the skull base because they analyzed the distribution of stenosis in the intracranial vessels and that in the extracranial carotid arteries separately in 114 consecutive human autopsies. Gorelick et al (8) analyzed the angiographic findings and risk factors in 71 black patients and white patients. They classified the extracranial vessels up to the internal carotid siphon and regarded the stenosis as severe when it was greater than 75%. Among 438 patients of the Northern Manhattan stroke study (4), 73 patients with atherosclerotic stroke were assigned to extracranial and/or intracranial categories on the basis of extracranial duplex and transcranial Doppler findings or angiographic results, without definite anatomic division.

In this study, we divided the intra- and extracranial

TABLE 1: Distribution of severe ( $\geq 70\%$ ) stenosis

Location	No. of Lesions
Intracranial arteries	203 (52)
Anterior circulation	114
M1	58
A1	24
ICA	15
M2	10
A2	6
ACHA	1
Posterior circulation	89
VA	27
P1-3	23
PICA	14
BA	12
VBJ	7
AICA	4
P4	1
SCA	1
Extracranial arteries	186 (48)
Anterior circulation	117
ICA	116
CCA	1
Posterior circulation	69
VA	61
SA	8
Total	389

Note.—Data in parentheses are percentages. M1 indicates the horizontal segment of middle cerebral artery; A1, horizontal segment of anterior cerebral artery; ICA, internal carotid artery; M2, vertical segment of middle cerebral artery; A2, vertical segment of anterior cerebral artery; ACHA, anterior choroidal artery; VA, vertebral artery; P1-3, area from precommunicating segment to the quadrigeminal segment of posterior cerebral artery; PICA, posterior inferior cerebellar artery; BA = basilar artery; VBJ, vertebrobasilar junction; AICA, anterior inferior cerebellar artery; P4 = cortical branch of posterior cerebral artery; SCA, superior cerebellar artery; CCA, common carotid artery; SA, subclavian artery.

vessels at the point where the internal carotid artery passes the inner dura just below the origin of the ophthalmic artery, as Gorelick et al did (8). We also defined the border in the posterior circulation where the vertebral artery passes the dura at the level of the foramen magnum. The reason why we applied 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 because of the risk of vascular rupture, the therapeutic strategy for stenosis is applied differently when angioplasty or stent placement is considered. In addition, the branches of the internal carotid artery up to the level of the inner dura are only minor contributing factors when an occlusion is present in the extracranial portion of the internal carotid artery.

The higher incidence of intracranial atherosclerotic arterial stenosis in our study may be more significant than that of other studies because our investigation included fewer internal carotid arteries than that of Feldmann et al (5), who regarded the intracranial vessels beginning at the starting point of the carotid siphon. Our study focused on the stenoses of more

TABLE 2: Distribution of severe ( $\geq 70\%$ ) stenosis, single versus multiple stenosis

Group and Location	No. of Lesions
Single stenosis	56
Intracranial	37 (66)
M1	16
PICA	7
VA	4
P1-3	4
M2	2
A2	1
ACHA	1
BA	1
AICA	1
Extracranial	19 (34)
ICA	14
VA	4
SA	1
Multiple stenosis	333
Intracranial	166 (50)
M1	42
A1	24
VA	23
P1-3	19
ICA	15
BA	11
M2	8
A2	5
VBJ	7
PICA	7
AICA	3
P4	1
SCA	1
Extracranial	167 (50)
ICA	102
VA	57
SA	7
CCA	1

Note.—Data in parentheses are percentages. Abbreviations are defined in the footnote for Table 1.

than 70% because symptomatic stenosis greater than 70% is clinically significant and because it can be treated effectively with endarterectomy (22). Also, cerebral infarction is more common in asymptomatic patients with a stenosis of more than 75% than in those with a less severe stenosis (23).

Being hospital- and angiography-based, our study differs from consecutive human autopsy studies (9) and cohort studies (4). Nevertheless, the significant difference in the distribution of severe stenosis in atherosclerotic patients probably affects the Korean population because we included consecutive patients from a single large referral center in the capital city.

## Conclusion

Intracranial atherosclerotic stenosis was more common than extracranial lesions in our Korean patients. This finding is in contrast with those of previously reported studies in white patients. Furthermore, single and severe stenosis has an increasing tendency toward intracranial involvement.

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