Atherothrombotic Middle Cerebral Artery Territory Infarction
Topographic Diversity With Common Occurrence of Concomitant Small Cortical and Subcortical Infarcts

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Background and Purpose— MRI has superior capabilities for the detection of cerebral infarcts compared with CT. CT was used to locate infarcts in most previous studies of atherothrombotic middle cerebral artery (MCA) territory infarcts. Thus, there was a possibility of missing concomitant small infarcts. More accurate identification of topographic lesions in MCA territory with MRI may help to establish the pathogenesis of stroke. The present study determines topographic patterns, distribution of vascular lesions, and probable mechanisms.

Methods—Forty-two patients with MCA territory infarcts on routine MRI and no major cause of cardioembolism were studied with conventional angiography or MR angiography.

Results—The topographic patterns seen on MRI were subdivided into 4 groups: cortical border-zone infarcts (n = 6), pial territory infarcts without insular infarct (n = 3), pial territory infarcts with insular infarct (n = 14), and large subcortical infarcts (n = 19). Of 6 patients with cortical border-zone infarcts, 4 had concomitant small cortical or subcortical multiple lesions. Angiography showed intrinsic MCA disease in 4 patients. Of 3 patients with pial territory infarcts without insular infarct, 2 also had small multiple centrum ovale lesions. All had intrinsic MCA disease. Pial territory infarcts with partial or whole insular lesions were present in 10 and 4 patients, respectively. Five patients had additional multiple cortical or subcortical lesions. Ten patients had intrinsic MCA disease. Of the 19 patients with large subcortical infarcts, 12 had centrum ovale infarcts, and 4 had both basal ganglia and centrum ovale lesions. Ten had concomitant small cortical or subcortical lesions. Six patients had intrinsic MCA disease.

Conclusions—Similar vascular lesions induce different topographic patterns in MCA territory infarction, which are related to individual vascular variability, degree of primary and secondary collateralization, and pathogenesis of infarcts. Our study indicates that concomitant small cortical or subcortical lesions are also commonly associated findings in diverse patterns of MCA territory infarction, which can mostly be explained by probable embolic mechanism. (Stroke. 2000;31:2055-2061.)

Key Words: angiography, magnetic resonance • cerebral embolism • magnetic resonance imaging • middle cerebral artery

M ost middle cerebral artery (MCA) territory infarcts have been attributed to embolism from the heart or internal carotid artery (ICA), poor perfusion due to ICA occlusion, intracranial MCA occlusive disease, or intrinsic disease in the lenticulostriate penetrating vessels.

Previous studies1,2 indicated racial differences in atherothrombotic occlusive diseases of the anterior cerebral circulation. Specifically, extracranial atherosclerosis is more common in whites, whereas intracranial atherosclerosis is more frequent in blacks, Chinese, and Japanese. However, how the common intracranial atherosclerotic vascular lesions are associated with topographic patterns of infarcts has not been studied sufficiently.

MRI of the brain has superior capabilities for the detection of cerebral infarction compared with CT.3 Furthermore, fluid-attenuated inversion recovery (FLAIR) sequences offer advantages in detection of acute infarcts affecting the cortical ribbon because cortical infarcts can be hard to detect given the similarly high signal of cortical gray matter and adjacent cerebrospinal fluid and the complex convolutional geometry of the surface of the brain.4 CT was used to locate infarcts in most previous studies of MCA territory infarcts,5-14 and thus

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there was a possibility of missing concomitant small infarcts, which might in part influence the interpretation of stroke mechanisms.

We speculate that accurate identification of topographic lesions in MCA territory infarcts may help to ascertain the underlying vascular pathophysiologic mechanisms. In this Korean population study, we attempted to delineate the topographic patterns of infarcts, to describe distribution of vascular lesions, and to suggest probable mechanisms of atherothrombotic MCA territory infarcts with fast spin-echo imaging, FLAIR imaging, and angiography.

Subjects and Methods
From September 1998 to November 1999, we prospectively collected data from patients with MCA territory infarction at Kyungpook National University Hospital. Of these patients, we selected 42 patients with acute stroke in whom (1) MRI showed appropriate lesions in MCA territory and (2) transfemoral conventional angiography or MR angiography (MRA) was performed. MRI was performed within 2 weeks of the onset of symptoms (mean, 2.5 days; range, 1 to 11 days). None received thrombolytic treatment. The diagnosis of infarcts in the MCA distribution was made with the use of previously published templates. All patients had been diagnosed by fast spin-echo and FLAIR imaging. All the MRAs were obtained on a 1.5-T machine (GE, Signa, Advantage). Two sets of MRA were performed separately at the cervical carotid and the circle of Willis. The time-of-flight angiography principle for imaging was used. The magnetization transfer contrast technique was applied in the study of the circle of Willis for better resolution, contrast-to-noise ratio, and background suppression. We used the same criteria for vascular risk factors as in our previous study: hypertension, diabetes mellitus, hypercholesterolemia, and smoking. Because we attempted to focus on the atherosclerotic vascular lesion, patients were excluded who had a known cardiac source of embolism such as a recent myocardial infarction (<3 weeks), known atrial fibrillation with or without mural thrombus, mitral stenosis or prosthetic valve, dilated cardiomyopathy, sick sinus syndrome, acute bacterial endocarditis, or patent foramen ovale. All patients had electrocardiography and transthoracic echocardiography. Patients with coagulopathy such as thrombocytopenia, polycythemia, disseminated intravascular coagulation, and systemic lupus were excluded. We also excluded patients with evidence of or suspected fibromuscular dysplasia, arteritis, and arterial dissection.

MCA territory lesions on MRI were classified as cortical border-zone infarcts, in which main lesions involving cerebral cortex and immediately subcortical white matter were localized in territories between the anterior cerebral artery and the MCA or between the MCA and posterior cerebral artery; pial territory infarcts without insular infarct, in which main lesions were localized in the superficial (pial) branches territory of the MCA without involving insular cortex; pial territory infarcts with insular infarct (with or without subcortical infarct), in which main lesions involved pial branches territory including insular cortex; and predominantly subcortical infarcts, in which main lesions involved basal ganglia or centrum ovale. Patients with an isolated small subcortical infarct (<1.5 cm in diameter) were excluded. Cortical border-zone infarcts were included in this study because there is considerable variation in the supply zones of the major intracranial artery, and recent studies show that areas classically thought to be in a cortical-border-zone region can indeed be in the territory of a peripheral branch artery of the major intracranial artery. None of the patients in our study had documented systemic hypotension or iatrogenic acute lowering of the blood pressure. The adequacy of the collateral circulatory pathways is the primary determinant of regional cerebral perfusion pressure during hemodynamic compromise state. In addition, insular cortex is located furthest from leptomeningeal collateral supplies. Therefore, topographic involvement of the insula may suggest a tenuous state of collateral supplies. In this regard, we subdivided pial territory infarcts into the aforementioned 2 patterns according to the presence of insular infarct.

We used the previously suggested methods for measuring arterial stenosis on MRA or conventional angiography. The measurements of stenosis on MRA were computed directly on the maximum intensity projection views. Collapsed views were also taken into account in the evaluation of steno-occlusion of the intracranial carotid artery tributary. Results that were >50% were considered significant stenosis.

The patients’ MRI findings were copied from the original film (T2-weighted axial and FLAIR images) by one of the authors who was blinded to the angiographic findings. Angiographic results were schematically drawn by a neuroradiologist who was blinded to the MRI findings.

Results
General Features
The study included 26 men and 16 women, aged 36 to 86 years (mean age, 62 years). Hypertension was present in 24 patients, diabetes mellitus in 7 patients, hypercholesterolemia in 16 patients, and smoking in 22 patients. Twenty-six patients had left-sided MCA territory lesions, and 16 patients had right-sided lesions. Seven patients had preceding transient ischemic attacks (TIAs) within 1 week of the onset of symptoms, 3 had a TIA within 2 weeks, and 1 had a remote TIA 1 year ago. All patients had no history of a focal neurological deficit lasting >24 hours. Nineteen patients had progressive or fluctuating courses. Higher cortical function abnormalities were present in 31 patients (hemineglect in 5, anosognosia in 2, aphasia in 21, and finger agnosia and right-left disorientation in 4 patients).

Topographic Patterns of Infarcts
The patients’ MRI findings and angiographic results were combined and are presented in Figures 1 through 4.

Cortical Border-Zone Infarcts
Six patients had cortical border-zone infarcts (patients 1 through 6; Figure 1). In this group, posterior border-zone
Infarcts were seen in 2 patients. These 2 patients also had multiple small cortical and centrum ovale infarcts. Four patients had both anterior and posterior border-zone infarcts simultaneously. Of these 4 patients, patient 1 also had 2 small cortical infarcts, and patient 5 had multiple small centrum ovale infarcts.

One patient had a focal intracranial ICA stenosis, and 1 had an extracranial ICA stenosis. Three had focal stenosis of MCA main trunk, and 1 had a diffuse stenosis of MCA main trunk.

Pial Territory Infarcts Without Insular Infarct
Three patients had pial territory infarcts without insular infarct (patients 7 through 9, Figure 2). In this group, the infarcts involved territory of pial branches of the MCA while sparing the insular cortex. Two patients also had small multiple centrum ovale infarcts. One patient showed a diffuse stenosis of MCA main trunk. One had an occlusion of the lower division of the MCA, and 1 had lesions of both upper and lower divisions (a combination of occlusion and stenosis).

Pial Territory Infarcts With Insular Infarct
Fourteen patients had pial territory infarcts with insular infarct (patients 10 through 23; Figure 3). In this group, insular cortex was involved as partial or whole infarcts according to the extent of insular lesions. Whole insular infarcts involved the entire insular cortex between anterior peri-insular sulcus and inferior peri-insular sulcus on axial MRI. Pial territory infarcts with partial insular lesion were seen in 10 patients. Of these 10 patients, 4 patients also had multiple small subcortical white matter lesions. Basal ganglia was involved in 1 patient. Pial territory infarcts with whole insular lesion were seen in 4 patients. One patient also had a basal ganglia lesion. Multiple small cortical lesions were seen in 1 patient.

A diffuse stenosis of MCA main trunk was seen in 1 patient. Of the 4 patients who showed extracranial ICA stenosis, 2 had tandem ICA + MCA lesions. Distal MCA main trunk occlusions were seen in 3 patients. Lower division occlusions were seen in 4 patients. Of the 2 patients who had upper division lesions, 1 had a stenosis and the other had an occlusion.

Predominantly Subcortical Infarcts
Nineteen patients had subcortical infarcts (patients 24 through 42; Figure 4). In this group, centrum ovale infarcts were seen in 12 patients. Of these 12 patients, 3 patients had additional small multiple cortical infarcts, 1 patient had multiple small centrum ovale infarcts and an isolated cortical infarct, and 2 patients had a small insular infarct simultaneously. Basal ganglia infarcts were seen in 3 patients, of whom 1 had additional multiple cortical infarcts. Four pa-
Patients had both basal ganglia and centrum ovale infarcts. Of these, 3 patients showed multiple discrete basal ganglia or centrum ovale lesions.

Seven patients had extracranial ICA steno-occlusive lesions that extended to intracranial ICA in 4 patients and to MCA main trunk (tandem ICA+MCA) in 2 patients. One patient had additional common carotid artery stenosis. Of the 6 patients who had intracranial ICA lesions, 4 had tandem ICA+MCA lesions. Three patients had focal or diffuse MCA main trunk stenosis. One patient had a stenosis of the upper division of the MCA. Two patients had both upper and lower division lesions that were a combination of stenosis and occlusion.

**Frequency of Cortical and Subcortical Lesions in the Contralateral Hemisphere**

Small cortical and subcortical lesions in contralateral MCA territory were found in 6 patients (14.3%). Two patients had an isolated centrum ovale lesion. One had a cortical lesion, and 1 had a cortical plus centrum ovale lesion. One had multiple small centrum ovale lesions that were associated with extracranial ICA stenosis. One had a basal ganglia lesion that was associated with MCA upper division stenosis. Comparison of frequency of concomitant small cortical and subcortical lesions between ipsilateral (21/42) and contralateral (6/42) hemisphere showed significant predominance of the lesions in the diseased MCA territory over contralateral hemisphere ($P=0.00045$, $\chi^2$ test).

**Discussion**

Previous topographic studies of MCA infarcts$^{5–14}$ were analyzed for the most part with CT. Thus, there was a possibility of missing concomitant small infarcts such as small cortical lesions, which might in part influence the interpretation of stroke mechanisms. MRI with FLAIR sequences and appropriate investigation of vascular lesions in this study led us to identify the topographic patterns of the MCA territory infarcts more accurately and to infer the probable mechanisms underlying the stroke.

Although previous studies$^{1–2}$ have shown that intracranial large-artery atherosclerosis was found more commonly in Asians than in whites, there have been few systematic studies on the frequency of intracranial disease in acute stroke patients. A recent study$^{21}$ showed that intracranial occlusive disease is the most commonly found vascular lesion in Chinese acute stroke patients with symptoms in the carotid artery territory. The finding that intracranial large-artery disease was seen in 30 patients (71%) in our study corroborates this racial difference.
In this study cortical border-zone infarcts were seen in 6 patients. The border-zone, or watershed, regions between major cerebral arteries are susceptible to ischemia and infarction. Bilateral watershed infarction is common after profound systemic hypotension resulting from cardiac arrest or from other causes. Unilateral infarction within border-zone regions occurs with atherosclerotic disease, of which MCA disease is most frequent. Although the number of patients with border-zone infarcts was small, most had atherosclerotic MCA disease in our study. This finding suggests that the extent of cerebrovascular investigation should include intracranial large vessels in patients with the pattern of border-zone infarcts.

Most of the recent studies assumed that the mechanism of infarcts in border-zone areas was hemodynamic on the basis of the topography of the infarcts. Bogousslavsky and Regli found a 75% frequency of high-grade ipsilateral carotid artery stenosis or occlusion associated with a hemodynamically significant cardiopathy, increased hematocrit, or acute hypotension in patients with unilateral watershed infarcts and concluded that hemodynamic causes predominate over embolic mechanisms in these patients. Subcortical lesions in patients with low-flow infarcts were characterized by circumscribed chainlike or confluent hypodense areas in the white matter representing the core of a hemodynamically induced infarction. Notably, 3 patients (patients 2, 3, and 5) had concomitant multilocal chainlike lesions in our study, supporting the view that border-zone infarcts can be induced by hemodynamic mechanisms related to low perfusion in distal field regions.

Anatomic dissections in experimental animals and human patients have shown microemboli within small vessels within arterial boundary zones. At necropsy, border-zone infarct with cholesterol emboli within small border-zone arteries has been found in patients after cardiac surgery and after artery-to-artery embolism. A recent study showed that embolism, either cardiac or from the parent carotid artery, is the predominant stroke mechanism in unilateral posterior border-zone infarcts, not distal field perfusion failure. Although there are numerous arterial anastomoses for each gyrus of cerebral cortex that may play a role in preventing cortical infarctions, intracortical arterial anastomoses are not acknowledged by all. Therefore, it is possible that occlusion of a small cortical artery causes a small cortical infarct. We speculate that concomitant multiple small cortical infarcts in this group (such as patients 1 and 2) could be explained by multiple artery-to-artery embolisms. Thus, the mechanism underlying border-zone infarction in this study is probably explained by a combination of 2 interrelated processes: local hemodynamic compromise and embolism.

Pial territory infarcts without insular infarct were seen in 3 patients in our study. The extent of pial territory infarcts probably depends on the status of the primary and secondary collateral supply. All had intrinsic MCA disease. Mechanism for this pattern of stroke is presumed to be direct territorial obstruction and artery-to-artery embolism. Emboli have been documented distal to an MCA stenosis. The occurrence of multiple, small infarcts, linked closely in time but dispersed widely in the brain, raises the possibility of an embolic mechanism. Patients with multiple regions of increased signal intensity on diffusion-weighted imaging harbored an identifiable cause of stroke, most often embolic. Therefore, it seems that the topographic pattern of infarcts as seen in patient 7 could be due to artery-to-artery embolism.

Pial territory infarcts with insular infarct were seen in 14 patients. Arterial contributions to the insula originated entirely from the MCA, predominantly via the superior division. There were also separate, dedicated, arterial feeders (terminal vessels) to the insula, of which most arose from the MCA branch to the central sulcus. In this study pial territory infarcts with partial or whole insular lesion were seen in 10 patients and 4 patients, respectively. Predominant diffusion-weighted imaging lesions affecting the insular region and appropriate occlusive MRA lesions were consistent with the expected maximal hypoperfusion furthest from collateral supplies. We speculate that the extent of insular lesions depends on the arterial distribution pattern of the superior and inferior divisions of the MCA to the insula and the degree of leptomeningeal collateral supply. Hypoperfusion due to intrinsic MCA disease is a likely mechanism in most patients with pial territory infarcts with insular infarct, although concomitant distal embolization cannot be ruled out in patients with multiple small white matter lesions. Artery-to-artery embolism is a presumed mechanism in patients with an isolated extracranial ICA stenosis or with both extracranial ICA stenosis and distal MCA occlusion.

In our study predominantly subcortical infarcts were seen in 19 patients. The centrum ovale, which is the central white substance of the cerebral hemispheres, is supplied by long medullary arteries that perforate it and course toward the upper part of the lateral ventricle. These medullary branches usually have single territories and do not interdigitate. Large centrum ovale infarcts were explained by a hemodynamic mechanism associated with ipsilateral carotid disease, although artery-to-artery embolism could not be ruled out in some patients with severe carotid disease. Twelve patients had centrum ovale infarcts in our study that could be explained by a local hemodynamic failure due to occlusive disease of the MCA and ICA, of which about half were intracranial large-artery disease. The involvement of the MCA in this group is in contrast with the previous finding that MCA occlusive disease never induced centrum ovale infarcts, which were usually associated with ICA occlusive disease. The cortical surface appears to be spared because of sustained flow past the area of the stenosis as well as blood supply from the primary and secondary collateral pathway. Notably, 6 of the patients with centrum ovale infarcts also had concomitant small cortical infarcts suggesting distal embolizations, which might be related to impaired clearance of emboli in the region of decreased blood flow, as suggested by previous authors.

When one considers the well-recognized interindividual variation in vascular territories, it is difficult to distinguish infarction affecting the internal border-zone (internal watershed) region from infarction limited to the deeper portions of the territory of the white matter medullary arteries. Therefore, it should be pointed out that, although we used the previously published template to locate centrum ovale...
infarcts, there is a possibility of mistaking internal border-zone infarcts for centrum ovale infarcts in some cases of our study.

Three patients had large striatocapsular infarction associated with intrinsic MCA disease in our study. This infarction was caused by occlusion of multiple penetrating vessel ostia and direct territorial obstruction. Anatomical observation of a probable embolic mechanism. Studies with CT, were common in our study, which can explain why basal ganglia infarcts occur even when the occlusive lesion is in the proximal upper division of the MCA, as in 1 of our patients. Concomitant multiple cortical lesions in 1 patient were presumed to be caused by distal embolization.

Infarction involving both centrum ovale and basal ganglia was seen in 4 patients. Centrum ovale infarcts could be explained by a hemodynamic mechanism in these patients. Since the paraventricular white matter of the corona radiata is the terminal supply zone of the lenticulostriate arteries, ischemia resulting from a hemodynamically significant carotid lesion might be expected to involve this area more extensively than the deeper gray matter. Thus, we speculate that discrete lesions of basal ganglia in 2 patients with ICA occlusion might be caused by multiple embolisms rather than hemodynamic compromise.

Several limitations of our study deserve mention. Although we used MRI and angiography to determine topographic patterns and vascular lesions in this study, the observed images were but a snapshot of a complex dynamic state with evolution based on the individual’s unique anatomic and vascular constraints, as well as the responsible pathophysiological cause. Therefore, the results of our study may not reflect the likely site of arterial occlusion and severity of stenosis, the locus of maximal hyperperfusion, and pathogenesis within minutes of infarction onset. Additionally, it should be pointed out that we are not sure whether nonvisualization of the MCA on MRA represents thrombus propagation to the MCA from the lesioned ICA or just reflects reduced distal blood flow due to the occluded ICA. Furthermore, we have not employed a diffusion-weighted imaging study in which all concurrent and acute lesions may be identified by apparent diffusion coefficient signal and may plausibly be attributed to the same vascular process. Thus, the concomitant infarcts we observe could be remote in time and different in mechanism than the index MCA infarcts. However, considering that all patients in this study had no remote symptoms of ischemia lasting >24 hours, that most preceding TIAs occurred recently, and that concomitant small cortical and subcortical infarcts were found more commonly in the diseased MCA territory than in the contralateral hemisphere, we speculate that the concomitant lesions are more likely to be caused by the same vascular process.

Our study indicates that similar vascular lesions induce different topographic patterns in MCA territory infarction, which are related to individual vascular variability in supply zones, degree of primary and secondary collateralization, and pathogenesis of infarcts. Concomitant small cortical or subcortical lesions, which might have been missed in previous studies with CT, were common in our study, which can mostly be explained by a probable embolic mechanism. Understanding of these patterns of MCA infarcts may have implications for therapy in the acute phase of stroke and for secondary prevention.

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