Cerebral atherosclerosis, a major cause of ischemic stroke, can be divided into extracranial atherosclerosis (ECAS) and intracranial atherosclerosis (ICAS), and anterior and posterior circulation atherosclerosis. Although ECAS is prevalent among Caucasians, ICAS is more common among Asians. Previous studies have addressed the differences in risk factors and stroke mechanisms between ICAS and ECAS, but the results are inconsistent. Whereas some reported that hypertension, diabetes mellitus, and metabolic syndrome (MetS) are more closely associated with ICAS, this was not confirmed by others. It also remains unclear whether the risk factors and stroke mechanisms differ between anterior and posterior circulation atherosclerosis.

Previous studies examined a small number of patients at single hospitals. Most importantly, prospective studies that used detailed examinations, including advanced brain and vascular imaging, are scarce. The purpose of this study was to elucidate the differences in the risk factors and mechanisms of stroke between ICAS and ECAS, and between anterior and posterior circulation atherosclerosis. We developed a multicenter, prospective, Web-based registry on atherosclerotic strokes using diffusion-weighted magnetic resonance imaging and magnetic resonance angiography. Stroke mechanisms were categorized as artery-to-artery embolism, in situ thrombo-occlusion, local branch occlusion, or hemodynamic impairment.

Results—One thousand patients were enrolled from 9 university hospitals. Age (odds ratio [OR], 1.033; 95% confidence interval [CI], 1.018–1.049), male gender (OR, 3.399; 95% CI, 2.335–4.949), and hyperlipidemia (OR, 1.502; 95% CI, 1.117–2.018) were factors favoring ECAS (vs ICAS), whereas hypertension (OR, 1.826; 95% CI, 1.274–2.618; \( P=0.001 \)) and diabetes mellitus (OR, 1.490; 95% CI, 1.105–2.010; \( P=0.009 \)) were related to posterior (vs anterior) circulation diseases. Metabolic syndrome was a factor related to ICAS (vs ECAS) only in posterior circulation strokes (OR, 2.433; 95% CI, 1.005–5.890; \( P=0.007 \)). Stroke mechanisms included artery-to-artery embolism (59.7%), local branch occlusion (14.9%), in situ thrombo-occlusion (13.7%), hemodynamic impairment (0.9%), and mixed (10.8%). Anterior ICAS was more often associated with artery-to-artery embolism (51.8% vs 34.0%) and less often associated with local branch occlusion (12.3% vs 40.4%) than posterior ICAS (\( P<0.001 \)).

Conclusions—The prevalence of risk factors and stroke mechanisms differ between ICAS and ECAS, and between anterior and posterior circulation atherosclerosis. Prevention and management strategies may have to consider these differences. (Stroke. 2012;43:3313-3318.)

Key Words: angiogram ■ cerebrovascular disease ■ diagnosis ■ registry

Risk Factors and Stroke Mechanisms in Atherosclerotic Stroke Intracranial Compared With Extracranial and Anterior Compared With Posterior Circulation Disease

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Background and Purpose—The aim of this study was to investigate differences in risk factors and stroke mechanisms between intracranial atherosclerosis (ICAS) and extracranial atherosclerosis (ECAS) and between anterior and posterior circulation atherosclerosis.

Methods—A multicenter, prospective, Web-based registry was performed on atherosclerotic strokes using diffusion-weighted magnetic resonance imaging and magnetic resonance angiography. Stroke mechanisms were categorized as artery-to-artery embolism, in situ thrombo-occlusion, local branch occlusion, or hemodynamic impairment.

Results—One thousand patients were enrolled from 9 university hospitals. Age (odds ratio [OR], 1.033; 95% confidence interval [CI], 1.018–1.049), male gender (OR, 3.399; 95% CI, 2.335–4.949), and hyperlipidemia (OR, 1.502; 95% CI, 1.117–2.018) were factors favoring ECAS (vs ICAS), whereas hypertension (OR, 1.826; 95% CI, 1.274–2.618; \( P=0.001 \)) and diabetes mellitus (OR, 1.490; 95% CI, 1.105–2.010; \( P=0.009 \)) were related to posterior (vs anterior) circulation diseases. Metabolic syndrome was a factor related to ICAS (vs ECAS) only in posterior circulation strokes (OR, 2.433; 95% CI, 1.005–5.890; \( P=0.007 \)). Stroke mechanisms included artery-to-artery embolism (59.7%), local branch occlusion (14.9%), in situ thrombo-occlusion (13.7%), hemodynamic impairment (0.9%), and mixed (10.8%). Anterior ICAS was more often associated with artery-to-artery embolism (51.8% vs 34.0%) and less often associated with local branch occlusion (12.3% vs 40.4%) than posterior ICAS (\( P<0.001 \)).

Conclusions—The prevalence of risk factors and stroke mechanisms differ between ICAS and ECAS, and between anterior and posterior circulation atherosclerosis. Posterior ICAS seems to be closely associated with metabolic derangement and local branch occlusion. Prevention and management strategies may have to consider these differences. (Stroke. 2012;43:3313-3318.)

Key Words: angiogram ■ cerebrovascular disease ■ diagnosis ■ registry
Web-based, prospective, multicenter registry of patients throughout Korea with ischemic stroke caused by cerebral atherosclerosis diagnosed.

**Patients and Methods**

This was a prospective multicenter study that involved 9 large tertiary hospitals throughout Korea. The hospitals are institutes representing each region of Korea, approximately reflecting the size of the population (3 hospitals in Seoul, 2 in Gyeonggi-do, 2 in Gyeongsang-do, 1 in Jeolla-do, and 1 in Chungcheong-do). Each center routinely (in >90% of cases) uses diffusion-weighted magnetic resonance imaging (DWI) and magnetic resonance angiography/computed tomography angiography to evaluate acute stroke and was willing to recruit consecutive patients for this study. Each center has at least 1 experienced stroke neurologist and 1 neuroradiologist who is able to assess the diagnosis and mechanism of stroke appropriately.

Inclusion criteria included acute (<7 days after onset) ischemic stroke or transient ischemic attack that was considered to be caused by symptomatic ICAS or ECAS and evaluated by DWI and vascular imaging studies, including magnetic resonance angiography, computed tomography angiography, or conventional angiogram. We only considered acute stroke patients mainly because stroke mechanisms were assessed with the use of DWI. In addition, we wished to exclude subacute stroke patients who were referred for a particular reason (eg, stenting procedures), because the inclusion of these patients might have influenced the overall prevalence of location of cerebral atherosclerosis. Patients were excluded if they: (1) did not undergo DWI or vascular imaging work-up; (2) had normal magnetic resonance angiography, computed tomography angiography, and angiogram findings; (3) presented with embolicogenic cardiac diseases;13 (4) had complex atheroma in the ascending aorta or proximal arch;14 and (5) had miscellaneous etiologies such as arterial dissection, Moyamoya disease, or vasculitis. Electrocardiography was performed in all patients, and more extensive cardiac work-ups, such as Holter monitoring and transthoracic or transesophageal echocardiogram, were performed in selected instances, such as in young (younger than 45 years old) patients without risk factors or those with suspicious embolic infarcts but without an apparent source.

The location of atherosclerosis was based on the following classification system. Intracranial arteries included the distal (including the cavernous and petrous segments) internal carotid artery (ICA), middle cerebral artery (MCA), anterior cerebral artery, posterior cerebral artery, basilar artery, and distal (including the intradural V4 segment) vertebral artery (VA). Extracranial arteries included the proximal ICA and proximal VA (ostium, V2–3 segments). We generally considered >50% narrowing or occlusion as clinically significant arterial disease. However, this criterion was not strict and a milder degree of stenosis was included if the stroke neurologists considered the infarct location to be associated with the stenosis, and if that had been confirmed by the neuroradiologist, especially in patients with ICAS-producing local branch occlusions.15

Concomitant asymptomatic cerebral atherosclerosis, ie, any extracranial and intracranial cerebral artery atherosclerotic disease unrelated to current infarction, also was assessed. The presence and degree of vascular stenosis were decided by consensus between the primary stoke neurologist and the neuroradiologist at each hospital. The data were sent to the main center (Asan Medical Center), where controversial cases were decided by consensus between 3 stroke neurologists during regular research meetings. Stroke mechanisms also were categorized in this way. This study was approved by the local Institutional Review Board of each hospital.

**Risk Factors**

The demographic features and risk factors were recorded, including hypertension (defined as receiving medication for hypertension or blood pressure >140/90 mmHg on repeated measurements), diabetes mellitus (defined as receiving medication for diabetes mellitus, fasting blood sugar ≥126 mg/dL, or 2-hour postprandial blood sugar ≥200 mg/dL), hyperlipidemia (defined as receiving cholesterol-reducing agents or an overnight fasting cholesterol level >200 mg/dL or low-density lipoprotein ≥130 mg/dL), smoking habits (current smoker or a patient who had quit smoking <6 months previously), history of stroke, and history of coronary heart disease. The National Institutes of Health Stroke Scale score was measured at the time of admission. The diagnosis of MetS was based on criteria outlined in a report from the National Cholesterol Education Program (NCEP-III).16

**Stroke Mechanisms**

After analyzing DWI, angiographic, and clinical data, stroke mechanisms were categorized according to previous descriptions. They include the following: artery-to-artery embolism; local branch occlusion; in situ thrombo-occlusion; and hemodynamic impairment.1

**Artery-to-Artery Embolism**

DWI demonstrates infarcts distal to the stenosed vessel in the territory of the relevant artery in artery-to-artery embolism. They are usually multiple, scattered, and often associated with perfusion deficits throughout the territory of the stenosed vessel.

**Local Branch Occlusion**

In local branch occlusion, infarcts are localized to an area adjacent to the stenosed vessel. This is attributable to the occlusion of the orifice of ≥1 perforators that supply the regions presumably associated with local thrombus formation.

**In Situ Thrombo-occlusion**

In situ thrombo-occlusion involves infarcts that extensively involve the entire or most of the stenosed arterial territory. However, border-zone areas are frequently spared because of collaterals.

**Hemodynamic Impairment**

With hemodynamic impairment, the infarcts are located in border-zone areas, usually are linear in shape, and are associated with perfusion deficits distal to the severely stenosed or occluded vessel. Symptoms should be closely associated with the patient’s relevant clinical history of hemodynamically disturbing conditions, such as recent bleeding, severe anemia, dehydration, and exhaustion.

**Statistical Analysis**

Differences between categorical variables were evaluated using Pearson χ² test. Differences between continuous variables were evaluated using the Student t test. Multivariate logistic regression analyses were performed to determine the different prevalence of risk factors for ECAS compared with ICAS, anterior circulation compared with posterior circulation stroke, anterior ECAS compared with posterior ICAS, posterior ECAS compared with posterior ICAS, and single ICAS compared with multiple ICAS. The variables tested in logistic regression models were those with P<0.1 by univariate analysis. All statistical analyses were performed using SPSS software for Windows (version 18.0; SPSS). P<0.05 was considered statistically significant.

**Results**

**General Features and Locations of Atherosclerosis**

The general characteristics of the enrolled patients are summarized in Table 1. Of the 1000 patients, there were 647 men and 353 women (mean age, 66.6±10.9 years; range, 23–93 years). Important risk factors included hypertension in 72.5% of patients, followed by diabetes mellitus (35.6%) and cigarette smoking (34.2%). Of the 1000 enrolled patients, symptomatic atherosclerosis was located most frequently in MCA (340), followed...
by ICA (293; proximal, 231; distal 62), VA (101; proximal, 37; distal, 64), basilar artery (83), multiple vessels (75), posterior cerebral artery (57), and anterior cerebral artery (51) (Figure). Six-hundred eighty-eight patients had ICAS, 271 had ECAS, and 41 had both (tandem lesions). Seven-hundred fifty-six patients had symptomatic atherosclerosis in anterior circulation and 264 had symptomatic atherosclerosis in posterior circulation. Four-hundred eighty-four patients had concomitant asymptomatic cerebral atherosclerosis. Patients with ICAS more often had concomitant asymptomatic ICAS, whereas those with symptomatic ECAS tended to present with asymptomatic ECAS ($P<0.001$) (Table 1).

**Differences Between ICAS and ECAS Patients**

The characteristics and risk factors were compared between ICAS and ECAS. As shown in Table 1, patients with ICAS were more often young, female, and had MetS, whereas patients with ECAS were more closely associated with cigarette smoking and hyperlipidemia. Multiple logistic regression analysis identified age (odds ratio [OR], 1.033; 95% confidence interval [CI], 1.018–1.049; $P<0.001$), male gender (OR, 3.399; 95% CI, 2.335–4.949; $P<0.001$), and hyperlipidemia (OR, 1.502; 95% CI, 1.117–2.018; $P=0.007$) as factors more prevalent in ECAS than in ICAS. The results were identical to those obtained when we investigated differences in the risk factors between symptomatic MCA and proximal ICA (data not shown).

When patients with single ICAS were compared with those having multiple ICAS, the latter were older and more often had hypertension, diabetes, cigarette smoking, MetS, and history of stroke (Supplementary Table I). Multiple regression analysis showed that age (OR, 1.024; 95% CI, 1.008–1.040; $P=0.002$), MetS (OR, 1.802; 95% CI, 1.275–2.548; $P=0.001$), and history of stroke (OR, 2.125; 95% CI, 1.467–3.079; $P<0.001$) were factors more prevalent in multiple ICAS. However, there were no factors differentiating single ECAS from multiple ECAS.

**Differences Between Anterior and Posterior Circulation Disorders**

As shown in Table 2, posterior circulation atherosclerosis was more often associated with hypertension, diabetes, and MetS, whereas anterior circulation diseases were more closely associated with cigarette smoking and alcohol consumption. Multiple logistic regression analysis revealed

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**Table 1. Characteristics of Patients With Intracranial Atherosclerosis and Those With Extracranial Atherosclerosis**

<table>
<thead>
<tr>
<th></th>
<th>All (n=1000)</th>
<th>ICAS (n=688)</th>
<th>ECAS (n=271)</th>
<th>ICAS and ECAS (n=41)</th>
<th>$P^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean±SD (y)</td>
<td>66.63±10.92</td>
<td>65.92±11.50</td>
<td>68.08±9.42</td>
<td>69.02±8.79</td>
<td>0.003</td>
</tr>
<tr>
<td>Male</td>
<td>647 (64.7)</td>
<td>400 (58.1)</td>
<td>219 (80.8)</td>
<td>28 (68.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>725 (72.5)</td>
<td>499 (72.5)</td>
<td>194 (71.6)</td>
<td>32 (78.0)</td>
<td>0.810</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>356 (35.6)</td>
<td>244 (35.5)</td>
<td>97 (35.8)</td>
<td>15 (36.6)</td>
<td>0.940</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>342 (34.2)</td>
<td>218 (31.7)</td>
<td>110 (40.6)</td>
<td>14 (34.1)</td>
<td>0.010</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>182 (18.2)</td>
<td>118 (17.2)</td>
<td>55 (20.3)</td>
<td>9 (22.0)</td>
<td>0.264</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>483 (48.3)</td>
<td>313 (45.5)</td>
<td>144 (53.1)</td>
<td>26 (63.4)</td>
<td>0.037</td>
</tr>
<tr>
<td>History of stroke</td>
<td>249 (24.9)</td>
<td>158 (23.0)</td>
<td>79 (29.2)</td>
<td>12 (29.3)</td>
<td>0.047</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>293 (29.3)</td>
<td>215 (31.3)</td>
<td>64 (23.6)</td>
<td>14 (34.1)</td>
<td>0.022</td>
</tr>
<tr>
<td>Family history of stroke</td>
<td>142 (14.2)</td>
<td>97 (14.1)</td>
<td>40 (14.8)</td>
<td>5 (12.2)</td>
<td>0.838</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>64 (6.4)</td>
<td>37 (5.4)</td>
<td>22 (8.1)</td>
<td>5 (12.2)</td>
<td>0.135</td>
</tr>
<tr>
<td>Asymptomatic ICAS</td>
<td>278 (27.8)</td>
<td>230 (33.4)</td>
<td>36 (13.3)</td>
<td>12 (29.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Asymptomatic ECAS</td>
<td>125 (12.5)</td>
<td>52 (7.6)</td>
<td>68 (25.1)</td>
<td>5 (12.2)</td>
<td></td>
</tr>
<tr>
<td>Asymptomatic ICAS and ECAS</td>
<td>81 (8.1)</td>
<td>43 (6.3)</td>
<td>34 (12.5)</td>
<td>4 (9.8)</td>
<td></td>
</tr>
</tbody>
</table>

ECAS indicates extracranial atherosclerosis; ICAS, intracranial atherosclerosis; SD indicates standard deviation.

Values are N (%), unless otherwise noted.

*Values were compared between ICAS and ECAS patients.
hypertension (OR, 1.826; 95% CI, 1.274–2.618; \( P = 0.001 \)) and diabetes mellitus (OR, 1.490; 95% CI, 1.105–2.010; \( P = 0.009 \)) were factors more prevalent in posterior circulation diseases.

We then separately compared ICAS and ECAS in each of anterior circulation diseases and posterior circulation diseases (Supplementary Tables II and III). Multiple regression analysis showed that in patients with anterior circulation diseases, ECAS was more closely associated with age (OR, 1.044; 95% CI, 1.026–1.062; \( P < 0.001 \)), male gender (OR, 5.060; 95% CI, 3.262–7.850; \( P < 0.001 \)), and hyperlipidemia (OR, 1.582; 95% CI, 1.128–2.217; \( P = 0.008 \)), whereas in patients with posterior circulation, only MetS (OR, 2.433, 95% CI, 1.005–5.890; \( P = 0.007 \)) emerged to be more prevalent in ICAS than in ECAS.

Stroke mechanisms also differed between anterior circulation disease and posterior circulation diseases. Although artery-to-artery embolism was the most common stroke mechanism in both groups, local branch occlusion was a relatively more important mechanism in posterior circulation diseases. The results were the same when only ICAS patients were analyzed.

**Discussion**

This is the first prospective, multicenter study that investigates the location of symptomatic cerebral atherosclerotic diseases in Korea. We found that ICAS is more prevalent than ECAS, with an approximate ratio of 7:3, confirming the previous notion that ICAS is a more important cause of stroke than ECAS in Asian populations. MCA atherosclerosis was the most important cause of strokes associated with large artery disease. However, proximal ICA was the second most common. With increases in the prevalence of proximal ICA in Korea and other Asian countries,\(^{17,18}\) this ratio may change in the future.

**Table 2. Characteristics of Patients With Anterior Circulation and Those With Posterior Circulation Atherosclerotic Diseases**

<table>
<thead>
<tr>
<th></th>
<th>Anterior (n=736)</th>
<th>Posterior (n=264)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean±SD (y)</td>
<td>66.62±11.11</td>
<td>66.65±10.38</td>
<td>0.972</td>
</tr>
<tr>
<td>Male</td>
<td>478 (64.9)</td>
<td>169 (64.0)</td>
<td>0.822</td>
</tr>
<tr>
<td>Hypertension</td>
<td>508 (69.0)</td>
<td>217 (82.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>238 (32.3)</td>
<td>117 (44.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>266 (36.1)</td>
<td>76 (28.8)</td>
<td>0.034</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>147 (20.0)</td>
<td>35 (13.3)</td>
<td>0.162</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>354 (48.1)</td>
<td>129 (48.9)</td>
<td>0.866</td>
</tr>
<tr>
<td>History of stroke</td>
<td>192 (26.1)</td>
<td>57 (21.6)</td>
<td>0.159</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>203 (27.6)</td>
<td>90 (34.1)</td>
<td>0.049</td>
</tr>
<tr>
<td>Family history of stroke</td>
<td>98 (13.3)</td>
<td>44 (16.7)</td>
<td>0.183</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>45 (6.1)</td>
<td>19 (7.2)</td>
<td>0.558</td>
</tr>
</tbody>
</table>

SD indicates standard deviation. Values are N (%), unless otherwise noted.

hypertension (OR, 1.826; 95% CI, 1.274–2.618; \( P = 0.001 \)) and diabetes mellitus (OR, 1.490; 95% CI, 1.105–2.010; \( P = 0.009 \)) were factors more prevalent in posterior circulation diseases.

We then separately compared ICAS and ECAS in each of anterior circulation diseases and posterior circulation diseases (Supplementary Tables II and III). Multiple regression analysis showed that in patients with anterior circulation diseases, ECAS was more closely associated with age (OR, 1.044; 95% CI, 1.026–1.062; \( P < 0.001 \)), male gender (OR, 5.060; 95% CI, 3.262–7.850; \( P < 0.001 \)), and hyperlipidemia (OR, 1.582; 95% CI, 1.128–2.217; \( P = 0.008 \)), whereas in patients with posterior circulation, only MetS (OR, 2.433, 95% CI, 1.005–5.890; \( P = 0.007 \)) emerged to be more prevalent in ICAS than in ECAS.

**Table 3. Stroke Mechanisms Associated With Each Symptomatic Vessel (n=925*)**

<table>
<thead>
<tr>
<th></th>
<th>Artery-to-Artery Embolism</th>
<th>In Situ Thrombo-occlusion</th>
<th>Local Branch Occlusion</th>
<th>Hemodynamic Impairment</th>
<th>Mixed</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACA</td>
<td>20 (39.2)</td>
<td>24 (47.1)</td>
<td>1 (2.0)</td>
<td>0</td>
<td>6 (11.7)</td>
<td>51</td>
</tr>
<tr>
<td>MCA</td>
<td>172 (50.6)</td>
<td>67 (19.7)</td>
<td>53 (15.6)</td>
<td>3 (0.9)</td>
<td>45 (13.2)</td>
<td>340</td>
</tr>
<tr>
<td>Distal ICA</td>
<td>43 (69.4)</td>
<td>5 (8.1)</td>
<td>1 (1.6)</td>
<td>2 (3.2)</td>
<td>11 (17.7)</td>
<td>62</td>
</tr>
<tr>
<td>PCA</td>
<td>21 (36.8)</td>
<td>16 (28.1)</td>
<td>13 (22.8)</td>
<td>0</td>
<td>7 (12.3)</td>
<td>57</td>
</tr>
<tr>
<td>BA</td>
<td>14 (16.9)</td>
<td>6 (7.2)</td>
<td>53 (63.9)</td>
<td>0</td>
<td>10 (12.0)</td>
<td>83</td>
</tr>
<tr>
<td>Distal VA</td>
<td>34 (53.1)</td>
<td>7 (10.9)</td>
<td>17 (26.6)</td>
<td>0</td>
<td>6 (9.4)</td>
<td>64</td>
</tr>
<tr>
<td>Proximal ICA</td>
<td>214 (92.6)</td>
<td>2 (0.9)</td>
<td>0</td>
<td>3 (1.3)</td>
<td>12 (5.2)</td>
<td>231</td>
</tr>
<tr>
<td>Proximal VA</td>
<td>34 (91.9)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3 (8.1)</td>
<td>37</td>
</tr>
<tr>
<td>ICAS</td>
<td>304 (46.3)</td>
<td>125 (19.0)</td>
<td>138 (21.0)</td>
<td>5 (0.8)</td>
<td>85 (12.9)</td>
<td>657</td>
</tr>
<tr>
<td>ECAS</td>
<td>248 (92.5)</td>
<td>2 (0.7)</td>
<td>0</td>
<td>3 (1.1)</td>
<td>15 (5.6)</td>
<td>268</td>
</tr>
<tr>
<td>Anterior</td>
<td>449 (65.5)</td>
<td>98 (14.3)</td>
<td>56 (8.2)</td>
<td>8 (1.2)</td>
<td>74 (10.8)</td>
<td>685</td>
</tr>
<tr>
<td>Posterior ICA</td>
<td>103 (42.9)</td>
<td>29 (12.1)</td>
<td>82 (34.2)</td>
<td>0</td>
<td>26 (10.8)</td>
<td>240</td>
</tr>
<tr>
<td>Anterior ICAS</td>
<td>235 (51.8)</td>
<td>96 (21.1)</td>
<td>56 (12.3)</td>
<td>5 (1.1)</td>
<td>62 (13.7)</td>
<td>454</td>
</tr>
<tr>
<td>Posterior ICAS</td>
<td>69 (34.0)</td>
<td>29 (14.3)</td>
<td>82 (40.4)</td>
<td>0</td>
<td>23 (11.3)</td>
<td>203</td>
</tr>
</tbody>
</table>

ACA indicates anterior cerebral artery; BA, basilar artery; ECAS, extracranial atherosclerosis; ICA, internal carotid artery; ICAS, intracranial atherosclerosis; MCA, middle cerebral artery; PCA, posterior cerebral artery; VA, vertebral artery.

Values are N (%).

*Patients with multiple symptomatic vascular lesions (n=75) are excluded.
The differences in prevalence of risk factors between ICAS and ECAS are still unclear. Whereas advanced hypertension and diabetes mellitus are considered more significant risk factors for ICAS compared with ECAS, this was not confirmed in our study. We found that only young age and female gender were more prevalent in ICAS, whereas hyperlipidemia was more closely associated with ECAS; this finding is consistent with a previous single-center study conducted in Korea. MetS has been reported as a factor preferentially related to ICAS in smaller single-center Asian studies. In our study, although MetS was more common in ICAS than in ECAS patients, the significance was lost when adjusted for other factors. The number of MetS components was not different between ICAS and ECAS (data not shown). However, MetS was more prevalent in multiple (vs single) ICAS. Therefore, MetS may be a factor that aggravates ICAS, rather than a factor that differentiates the location of atherosclerosis. Nevertheless, as discussed subsequently, MetS was more prevalent in ICAS than in ECAS patients when only posterior circulation stroke was analyzed. Interestingly, we found that symptomatic ICAS was preferentially accompanied by asymptomatic ICAS, whereas ECAS was closely associated with concomitant asymptomatic ECAS. Therefore, although the risk factors that discriminate the location of atherosclerosis are not fully understood, they seem to exert similar influence on contralateral cerebral vessels as well.

We also found that there are differences in prevalence of risk factors between anterior and posterior circulation strokes: hypertension and diabetes were significantly more common in the latter than in the former. The results were identical when only the patients with ICAS were analyzed, but not when those with ECAS were analyzed. Our data agree with previous studies showing that diabetes mellitus or hypertension is more often present in patients with posterior than with anterior circulation stroke, but our data are at odds with those of a recent study using warfarin–aspirin symptomatic intracranial disease data that showed that posterior circulation ICAS is more closely associated with older age and female gender, but not with diabetes mellitus. The difference in results may be explained by ethnic differences, exclusion of smaller vessel (eg, posterior cerebral artery) atherosclerosis, and different criteria of ICAS (ie, using severe [>50%] stenosis that was detected only on conventional angiography) in the cited study. We also found that among patients with anterior circulation stroke, ECAS was more closely associated with age, male gender, and hyperlipidemia than ICAS, as in stroke patients in general, whereas MetS emerged to be related to ICAS in patients with posterior circulation diseases.

Our data collectively suggest that posterior circulation ICAS may be more vulnerable to the atherosclerotic effects of metabolic derangement. Therefore, the previous inconsistent results regarding the different prevalence of risk factors between ICAS and ECAS may, in part, be related to the different proportions of posterior circulation diseases included in their studies. It is noteworthy that posterior circulation stroke was more prevalent in Asian than in European stroke registry studies. Future studies are required to elucidate why posterior circulation ICAS is particularly related to metabolic risk factors.

We also found that stroke mechanisms differ according to the location of cerebral atherosclerosis. Because perforators are directly branched out of ICAS, it is understandable that ICAS produces strokes more often by way of local branch occlusion. In addition, in situ thrombo-occlusion is more common in patients with ICAS, probably because of relatively sufficient collateral circulation through the posterior communicating artery, anterior communicating artery, and external carotid artery in patients with ECAS. However, artery-to-artery embolism was the dominant stroke mechanism in ECAS, both in patients with anterior (proximal ICA) and posterior (proximal VA) circulation diseases. Nevertheless, stroke mechanisms still differed in apparently similar intracranial vessels. For instance, although artery-to-artery embolism was the most frequent stroke mechanism in patients with MCA disease, local branch occlusion was the most important mechanism associated with basilar artery disease. In general, artery-to-artery embolism was more prevalent in anterior circulation ICAS, whereas local branch occlusion was more common in posterior circulation ICAS. This difference may be attributable to smaller and shorter perforating vessels arising from posterior circulation arteries that may be more vulnerable to occlusion in the presence of parental artery athrothrombosis. Alternatively, because posterior circulation ICAS is more closely associated with metabolic risk factors, such as hypertension, diabetes, and MetS, perforators already may be atherosclerotic and thus more vulnerable to occlusion in the presence of parental artery disease. Whatever the explanation, our data seem to be in line with previous results showing that infarcts occurring in the brain stem supplied by paramedian-penetrating branches are 3- to 4-times more common in diabetic patients than in nondiabetic patients.

There are several limitations of this study. First, because the results are based on a registry from a large tertiary hospital located in urban areas, selection bias may be present. However, this bias may not be great because a recent survey indicated that >90% of the population of Korea lives in urban areas, and acute stroke patients usually are directly admitted to large hospitals. Therefore, the participating hospitals can be regarded as the typical setting of stroke care. Second, although we adapted a similar policy for cardiac evaluation, the extensiveness of the investigation depended on the individual investigators at each hospital and was not completely regulated.

Despite these limitations, our study showed that the prevalence of risk factors, metabolic burdens, and stroke mechanisms differ between ICAS and ECAS, and between anterior and posterior circulation diseases. In the prevention and management of stroke, one may have to consider these differences. Antiatherosclerotic medications such as statins may be considered more seriously for posterior circulation ICAS, whereas dual antiplatelets may be administered in anterior circulation strokes producing embolization. Further studies are needed for better understanding of differences in the weight of risk factors, mechanisms, and appropriate treatment strategies in patients with cerebral atherosclerosis in different location.

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Disclosures

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Risk Factors and Stroke Mechanisms in Atherosclerotic Stroke: Intracranial Compared With Extracranial and Anterior Compared With Posterior Circulation Disease
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