Trial of ORG 10172 in Acute Stroke Treatment (TOAST) Classification and Vascular Territory of Ischemic Stroke Lesions Diagnosed by Diffusion-Weighted Imaging

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Background—The association between the location and the mechanism of a stroke lesion remains unclear. A diffusion-weighted imaging study may help resolve this lack of clarity.

Methods and Results—We studied a consecutive series of 2702 acute ischemic stroke patients whose stroke lesions were confirmed by diffusion-weighted imaging and who underwent a thorough etiological investigation. The vascular territory in which an ischemic lesion was situated was identified using standard anatomic maps of the dominant arterial territories. Stroke subtype was based on the Trial of ORG 10172 in Acute Stroke Treatment, or TOAST, classification. Large-artery atherosclerosis (37.3%) was the most common stroke subtype, and middle cerebral artery (49.6%) was the most frequently involved territory. Large-artery atherosclerosis was the most common subtype for anterior cerebral, middle cerebral, vertebral, and anterior and posterior inferior cerebellar artery territory infarctions. Small vessel occlusion was the leading subtype in basilar and posterior cerebral artery territories. Cardioembolism was the leading cause in superior cerebellar artery territory. Compared with carotid territory stroke, vertebrobasilar territory stroke was more likely to be caused by small vessel occlusion (21.4% versus 30.1%, P<0.001) and less likely to be caused by cardioembolism (23.2% versus 13.8%, P<0.001). Multiple-vascular-territory infarction was frequently caused by cardioembolism (44.2%) in carotid territory and by large-artery atherosclerosis (52.1%) in vertebrobasilar territory.

Conclusions—Information on vascular territory of a stroke lesion may be helpful in timely investigation and accurate diagnosis of stroke etiology. (J Am Heart Assoc. 2014;3:e001119 doi: 10.1161/JAHA.114.001119)

Key Words: cerebral infarction • diffusion magnetic resonance imaging • etiology • location

The etiology of ischemic stroke affects prognosis and outcome. Clinical practice guidelines recommend different treatments according to stroke mechanism. Consequently, timely and accurate diagnosis of stroke mechanism is required. Supplementation of clinical features with information on infarction patterns and vascular territories obtained from initial brain images may enable individualization of the diagnostic workup and diagnosis of stroke mechanism.

In the late 1980s, a study using brain computed tomography (CT) data from the Lausanne stroke registry reported a particular stroke mechanism affecting a particular vascular territory. In 2000, a similar study was performed using brain CT and magnetic resonance imaging data obtained from the Besançon stroke registry. These 2 studies agreed that stroke mechanisms were different among vascular territories but disagreed as to the pattern of the dependence.

Advances in neuroimaging techniques have made diffusion-weighted imaging (DWI) a commonly used imaging modality for acute ischemic stroke, leading to significant improvement in the sensitivity and specificity of diagnosis and reduction of interrater variability.

A few magnetic resonance imaging–based studies have reported a particular stroke mechanism affecting a particular vascular territory. However, no DWI-based study has
investigated the global relationships between vascular territories in which stroke lesions occur and stroke mechanisms, and these relationships have not been reported for Asian populations, for which stroke mechanisms may be different from those in Western countries. In this study, the Trial of ORG 10172 in Acute Stroke Treatment, or TOAST, classification of stroke subtypes was adopted and related to the vascular territories of acute ischemic lesions detected by DWI in ischemic stroke patients. In addition, we intended to provide practical information about the distribution of stroke mechanisms according to invaded vascular territories.

Methods

Based on a prospective stroke registry database, acute ischemic stroke patients admitted to Seoul National University Bundang Hospital between January 2004 and November 2009 within 7 days of symptom onset were identified and analyzed for this study. Patients who did not undergo DWI or angiographic evaluation or who showed no acute lesion on DWI were excluded. Demographics, risk factors for stroke, etiology workups, stroke subtypes, vascular territories of acute ischemic lesions, and other stroke characteristics were obtained directly from the registry database or by review of electronic medical records. The institutional review board approved the study, despite the absence of patient consent, due to its retrospective nature and minimal risk to participants.

Stroke subtypes were classified into 5 categories based on etiology, using the TOAST classification: (1) large-artery atherosclerosis (LAA), (2) small vessel occlusion (SVO), (3) cardioembolism (CE), (4) stroke of other determined etiology, and (5) stroke of undetermined etiology. We modified the definition of SVO as a lesion diameter of less than 20 mm and located in a subcortical area or brainstem on DWI. The “undetermined etiology” category included 3 heterogeneous groups: “two or more causes,” “negative evaluation,” and “incomplete evaluation.” Negative evaluation was defined as no likely etiology despite extensive evaluation. Evaluation for cardioembolic source was regarded as extensive when 24-hour Holter monitoring, transthoracic echocardiography, and transesophageal echocardiography were performed. For some uncooperative patients, cardiac multidetector CT substituted for transesophageal echocardiography. Extent of diagnostic workup and stroke subtypes were determined primarily by stroke neurologists in charge of patients, and stroke subtypes were confirmed at a weekly stroke registry meeting.

The vascular territories and topographic localization of ischemic lesions were determined by a stroke neurologist (S.H.P.) on the basis of a neuroradiologist’s (J.H.K.) formal reading and review of DWI results with reference to the anatomic maps of the dominant arterial territories proposed by Tatu et al. The carotid territory included the middle cerebral artery (MCA) territory, the anterior cerebral artery (ACA) territory, the internal carotid artery (ICA) territory, and the border zone territory. The ICA territory was diagnosed when the anterior choroidal artery or the entire ICA territory was involved. The border zone territory consisted of the anterior watershed area (between the superficial territory of the ACA and the MCA), the posterior watershed area (between the superficial territory of the MCA and the posterior cerebral artery), and the subcortical watershed area (between the deep and superficial territory of the MCA). Ischemic lesions in posterior cerebral artery, basilar artery, vertebral artery, superior cerebellar artery, anterior inferior cerebellar artery, and posterior inferior cerebellar artery (PICA) were categorized as occurring in vertebrobasilar territory. Noncontiguous lesions observed by DWI to be in 2 or more vascular territories were classified as involving multiple territories, but uninterrupted lesions visible in contiguous vascular territories were not.

Statistical Methods

Pearson chi-square tests or Fisher’s exact tests were used for categorical variables, and Kruskal–Wallis tests were used for continuous variables. All statistical analyses were performed with SPSS (version 21.0; IBM Inc), and a 2-sided P<0.05 was considered the minimal level of statistical significance.

Results

During the study period, 2798 patients were hospitalized within 7 days of stroke onset. After excluding 44 due to unavailability of DWI or absence of ischemic lesion in DWI and another 52 who lacked an angiographic evaluation, 2702 patients were enrolled for this study. Mean age was 67.3 years (SD, 12.5 years), and 59.2% were men. Intra- and extracranial magnetic resonance angiography was performed in 98.7%. Cardiac evaluation was done in 91.5%, transthoracic echocardiography was done in 87.5%, 24-hour Holter monitoring was performed in 41.5%, transesophageal echocardiography was used in 20.5%, and cardiac multidetector CT was used in 17.1%. Risk-factor profiles and initial stroke severity exhibited dependence on the vascular territory in which the lesion occurred. A history of stroke and transient ischemic attack was more common in patients who had ischemic lesions in basilar artery and multiple territories. Atrial fibrillation was more prevalent in patients who had lesions in the ICA and superior cerebellar artery territories. Patients with lesions in the PICA territory had relatively milder
Table 1. Baseline Characteristics According to Vascular Territory of Acute Ischemic Lesions

|                  | ACA (n=49) | MCA (n=1341) | ICA (n=33) | PCA (n=230) | VA (n=71) | BA (n=305) | PICA (n=144) | AI/CA (n=8) | SCA (n=10) | BZ (n=79) | Multiple (n=432) | Total (n=2702) | P Value |
|------------------|------------|--------------|------------|-------------|-----------|------------|-------------|------------|------------|----------|-----------------|----------------|---------|
| Age, mean±SD     | 68.6±11.9  | 67.3±12.8    | 70.6±13.7  | 66.6±12.9   | 61.5±13.3 | 67.8±10.9  | 64.0±11.6   | 67.8±9.7   | 71.0±8.5   | 66.7±12.2 | 68.8±12.3       | 67.3±12.5       | <0.001  |
| Male             | 55.1       | 57.9         | 45.5       | 56.1         | 81.7      | 58.0       | 66.7        | 37.5       | 40.0       | 64.6     | 61.3            | 59.3           | 0.088   |
| History of stroke| 10.2       | 21.6         | 15.2       | 16.1         | 15.5      | 24.3       | 17.4        | 12.5       | 0.0        | 20.3     | 25.2            | 21.2           | 0.033   |
| History of TIA   | 6.1        | 5.3          | 3.0        | 3.0          | 5.6       | 6.2        | 3.5         | 0.0        | 0.0        | 3.8      | 5.8             | 5.1            | 0.831   |
| Hypertension     | 75.5       | 60.6         | 69.7       | 63.5         | 53.5      | 71.1       | 54.2        | 75.0       | 70.0       | 60.8     | 64.4            | 62.6           | 0.007   |
| Diabetes mellitus| 28.6       | 25.1         | 45.5       | 30.9         | 38.0      | 40.3       | 24.3        | 75.0       | 30.0       | 34.2     | 33.1            | 29.6           | <0.001  |
| Hyperlipidemia   | 20.4       | 16.9         | 3.0        | 16.5         | 22.5      | 19.0       | 22.2        | 37.5       | 10.0       | 16.5     | 15.5            | 17.2           | 0.204   |
| Smoking status   | 30.6       | 36.7         | 33.3       | 37.8         | 54.9      | 36.4       | 38.9        | 12.5       | 20.0       | 50.6     | 40.3            | 38.0           | 0.019   |
| Atrial fibrillation| 10.2      | 18.2         | 39.4       | 12.6         | 4.2       | 4.9        | 9.0         | 12.5       | 50.0       | 3.8      | 20.8            | 15.6           | <0.001  |
| Initial NIHSS, median (IQR) | 3.0 (1.0 to 6.0) | 4.0 (2.0 to 9.0) | 13.0 (6.0 to 19.5) | 2.5 (1.0 to 5.0) | 3.0 (1.0 to 4.0) | 4.0 (2.0 to 5.0) | 1.0 (0.0 to 3.0) | 2.5 (0.3 to 3.8) | 3.0 (0.0 to 4.0) | 5.0 (2.0 to 9.0) | 5.0 (2.0 to 12.0) | 4.0 (2.0 to 8.0) | <0.001 |
| Thrombolytic treatment* | 12.2   | 14.0         | 27.3       | 3.0          | 0.0       | 3.9        | 2.1         | 0.0        | 10.0       | 12.7     | 17.6            | 7.5            | <0.001  |

Values are percentages of patients, unless otherwise noted. ACA indicates anterior cerebral artery; AICA, anterior inferior cerebellar artery; BA, basilar artery; BZ, border zone infarction; ICA, internal carotid artery; IQR, interquartile range; MCA, middle cerebral artery; Multiple, multiple-territory infarction; NIHSS, National Institutes of Health stroke scale; PCA, posterior cerebral artery; PICA, posterior inferior cerebellar artery; SCA, superior cerebellar artery; TIA, transient ischemic attack; VA, vertebral artery.

*Thrombolytic treatment: intravenous thrombolysis, intra-arterial thrombolysis, or both.
strokes, and those with lesions in the ICA territory had the most severe strokes. Baseline characteristics of the study subjects and the extent of diagnostic investigation according to the vascular territory of the acute ischemic lesion are summarized in Tables 1 and 2, respectively.

The MCA was the most frequently involved territory (49.6%), followed by basilar artery (11.3%) and posterior cerebral artery (8.5%). The most common stroke subtype in the whole study population was LAA (37.3%), followed by SVO (22.9%) and CE (20.6%) (Table 3). Among the 439 subjects with undetermined etiology (16.2% of the whole study population), negative evaluation was most common (68.3% of the subjects with undetermined etiology).

Table 2. Extent of Diagnostic Evaluation According to Vascular Territory of Acute Ischemic Lesions

| Mechanism                  | ACA (n=49) | MCA (n=1341) | ICA (n=33) | PCA (n=230) | VA (n=71) | BA (n=305) | PICA (n=144) | AICA (n=8) | SCA (n=10) | BZ (n=79) | Multiple (n=432) | Total (n=2702) | P Value |
|----------------------------|------------|--------------|------------|------------|-----------|------------|--------------|------------|------------|-----------|-----------------|-----------------|---------|
| DWI                        | 100        | 100          | 100        | 100        | 100       | 100        | 100          | 100        | 100        | 100       | 100              | 100             | 0.437   |
| Other brain MRI sequences† | 98.0       | 99.0         | 97.0       | 97.4       | 100       | 99.7       | 97.9         | 100        | 98.7       | 98.8      | 98.9             | 0.437           |
| Brain MRA†                 | 100        | 98.6         | 100        | 98.3       | 100       | 100        | 98.6         | 100        | 100        | 100       | 100              | 100             | 0.334   |
| Conventional angiography   | 12.2       | 23.6         | 42.4       | 10.0       | 23.9      | 14.4       | 20.1         | 100        | 50.6       | 31.3      | 23.1             | -0.001          |
| Transcranial Doppler       | 83.7       | 77.6         | 45.5       | 82.6       | 83.1      | 86.2       | 79.9         | 87.5       | 90.0       | 84.8      | 72.9             | 78.5            | -0.001  |
| Brain SPECT                | 12.2       | 15.7         | 9.1        | 10.9       | 14.1      | 10.2       | 9.7          | 100        | 48.1       | 15.0      | 14.9             | -0.001          |
| Electrocardiogram          | 100        | 100          | 100        | 100        | 100       | 100        | 100          | 100        | 100        | 100       | 100              | 100             | -0.001  |
| Transthoracic echocardiogram| 87.8       | 87.9         | 57.6       | 94.3       | 85.9      | 88.2       | 91.7         | 100        | 89.9       | 82.2      | 87.5             | <0.001          |
| Transesophageal echocardiogram| 42.9      | 20.4         | 12.1       | 28.3       | 8.5       | 9.8        | 20.8         | 37.5       | 100        | 13.9      | 25.9             | 20.5            | <0.001  |
| Cardiac MDCT               | 24.5       | 19.1         | 15.2       | 14.8       | 9.9       | 11.5       | 13.2         | 12.5       | 20.0       | 8.9       | 19.2             | 17.1            | 0.110   |
| 24-h Holter monitoring     | 59.2       | 41.1         | 24.2       | 40.0       | 35.2      | 36.4       | 47.9         | 62.5       | 30.0       | 39.2      | 45.4             | 41.5            | 0.130   |
| Extensive embolic source evaluation†| 42.9     | 22.5         | 12.1       | 22.6       | 8.5       | 14.4       | 20.8         | 37.5       | 10.0       | 10.1      | 26.4             | 21.7            | <0.001  |

Values are percentages of patients. ACA indicates anterior cerebral artery; AICA, anterior inferior cerebellar artery; BA, basilar artery; BZ, border zone infarction; DWI, diffusion-weighted imaging; ICA, internal carotid artery; MCA, middle cerebral artery; MDCT, multidetector computed tomography; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; Multiple, multiple territory infarction; PCA, posterior cerebral artery; PICA, posterior inferior cerebellar artery; SCA, superior cerebellar artery; SPECT, single-photon emission computed tomography; VA, vertebral artery.

*Axial T1, T2, gradient echo, enhanced T1, and enhanced fluid attenuation inversion recovery image.
†MRA: intracranial and extracranial neck vessels.
‡Extensive embolic source evaluation comprised 24-h Holter monitoring, transthoracic echocardiography, and transthoracic echocardiogram (or cardiac MDCT) during hospital stay.

Table 3. Comparison of Stroke Subtypes Between Carotid and Vertebrobasilar Territory Infarctions

| Mechanism     | Carotid (n=1606) | Vertebobasilar (n=914) | Both (n=182) | Total (n=2702) | P Value |
|---------------|------------------|------------------------|------------|---------------|---------|
| LAA           | 37.6             | 40.0                   | 21.4       | 37.3          | <0.001  |
| SVO           | 21.4             | 30.1                   | 0.0        | 22.9          | <0.001  |
| CE            | 23.2             | 13.8                   | 32.4       | 20.6          | <0.001  |
| OD            | 1.9              | 3.7                    | 8.2        | 2.9           | <0.001  |
| Two or more   | 3.9              | 2.4                    | 4.9        | 3.4           | 0.081   |
| Negative      | 10.8             | 8.3                    | 28         | 11.1          | <0.001  |
| Incomplete    | 1.4              | 1.6                    | 4.9        | 1.7           | 0.002   |

Values are percentages of patients. CE indicates cardioembolism; Incomplete, incomplete evaluation; LAA, large-artery atherosclerosis; Negative, negative evaluation; OD, other determined etiology; SVO, small vessel occlusion; Two or more, two or more causes identified.

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Among carotid, vertebrobasilar, and dual-territory infarctions (P<0.001 on Pearson’s chi-square test).

LAA was the leading subtype in border zone infarction as well as in ACA, vertebral artery, PICA, ICA, anterior inferior cerebellar artery, MCA, and multiple territory infarctions. The proportion was highest in border zone infarction (89.9%), followed by ACA territory infarction (65.3%) (Table 4). SVO was the most common subtype in basilar artery and posterior cerebral artery territory infarctions. CE was most frequent in superior cerebellar artery territory infarction (60%). Stroke of other determined etiology was uncommon, but its proportion was highest in vertebral artery territory infarction (11.3%), followed by multiple territory infarction (6.9%). In vertebral artery territory infarction, all patients with stroke of other determined etiology had arterial dissection; in PICA territory infarction, 80% of patients with other determined etiology had arterial dissection. Negative evaluation was most frequently observed in multiple-territory infarction (21.3%), followed by ACA (18.4%) and PICA (15.3%) territory infarction. In cerebellar infarction, CE was the most common subtype of superior cerebellar artery territory stroke and LAA was the leading subtype of anterior inferior cerebellar artery and PICA territory stroke (Table 4). The difference in stroke mechanisms among vascular territories was statistically significant (P<0.001 on Fisher’s exact test).

TOAST subtype was dependent on multiplicity of lesion territory (Table 5). Compared with infarction confined to a single vascular territory, CE and negative evaluation were more common and LAA and SVO were less common in multiple-vascular-territory infarction. Carotid territory and vertebrobasilar strokes had similar patterns except that LAA accounted for 52% of multiple-territory infarctions in vertebrobasilar artery

### Table 4. Stroke Subtypes According to Vascular Territory of Acute Ischemic Lesions

| Mechanism     | ACA (n=49) | MCA (n=1341) | ICA (n=33) | PCA (n=230) | VA (n=71) | BA (n=305) | PICA (n=144) | AICA (n=8) | SCA (n=10) | BZ (n=79) | Multiple (n=432) | P Value* |
|---------------|------------|--------------|------------|-------------|-----------|------------|--------------|------------|-------------|-----------|----------------|----------|
| LAA           | 65.3       | 34.2         | 51.5       | 28.7        | 60.6      | 30.2       | 59.0         | 50.0       | 10.0        | 89.9      | 32.4          | <0.001   |
| SVO           | 0.0        | 25.6         | 0.0        | 36.1        | 18.3      | 58.7       | 0.0          | 0.0        | 0.0         | 0.0       | 0.0            | <0.001   |
| CE            | 10.2       | 22.8         | 33.3       | 19.1        | 8.5       | 3.9        | 15.3         | 25.0       | 60.0        | 5.1       | 32.2          | <0.001   |
| OD            | 2.0        | 1.7          | 0.0        | 3.0         | 11.3      | 1.0        | 4.2          | 0.0        | 0.0         | 1.3       | 6.9            | <0.001   |
| Two or more   | 4.1        | 3.9          | 3.0        | 3.5         | 0.0       | 3.0        | 0.7          | 0.0        | 0.0         | 1.3       | 4.4            | 0.456    |
| Negative      | 18.4       | 10.4         | 6.1        | 9.6         | 1.4       | 3.0        | 15.3         | 0.0        | 10.0        | 2.5       | 21.3          | <0.001   |
| Incomplete    | 0.0        | 1.4          | 6.1        | 0.0         | 0.0       | 0.3        | 5.6          | 25.0       | 20.0        | 0.0       | 2.8            | <0.001   |

Values are percentage of patients. ACA indicates anterior cerebral artery; AICA, anterior inferior cerebellar artery; BA, basilar artery; BZ, border zone infarction; CE, cardioembolism; ICA, internal carotid artery; Incomplete, incomplete evaluation; LAA, large-artery atherosclerosis; MCA, middle cerebral artery; Multiple, multiple-territory infarction; Negative, negative evaluation; OD, other determined etiology; PCA, posterior cerebral artery; PICA, posterior inferior cerebellar artery; SCA, superior cerebellar artery; SVO, small vessel occlusion; Two or more, two or more causes identified; VA, vertebral artery.

*P values were obtained from comparisons of vascular territories according to the presence or absence of individual stroke subtypes using Pearson chi-square tests or Fisher’s exact tests, as appropriate.

### Table 5. Stroke Subtypes According to Lesion Territory Multiplicity

| Total (n=2702)       | LAA    | SVO    | CE     | OD     | Two or More | Negative | Incomplete | P Value* |
|----------------------|--------|--------|--------|--------|-------------|----------|------------|----------|
| Single vascular      | 38.2   | 27.2   | 18.4   | 2.2    | 3.3         | 9.2      | 1.5        | <0.001   |
| territory (n=2270)   |        |        |        |        |             |          |            |          |
| Multiple vascular    | 32.6   | 0.0    | 32.2   | 6.7    | 4.4         | 21.3     | 2.8        |          |
| territory (n=432)    |        |        |        |        |             |          |            |          |
| Carotid territory    | 38.5   | 22.8   | 21.7   | 1.7    | 3.7         | 10.2     | 1.4        | <0.001   |
| (n=1606)             |        |        |        |        |             |          |            |          |
| Single vascular      | 25.0   | 0.0    | 44.2   | 4.8    | 5.8         | 19.2     | 1.0        |          |
| territory (n=1502)   |        |        |        |        |             |          |            |          |
| Multiple vascular    | 52.1   | 0.0    | 23.3   | 6.2    | 2.7         | 14.4     | 1.4        | <0.001   |
| territory (n=914)    |        |        |        |        |             |          |            |          |
| Single vascular      | 37.8   | 35.8   | 12.0   | 3.3    | 2.3         | 7.2      | 1.7        |          |
| territory (n=768)    |        |        |        |        |             |          |            |          |
| Multiple vascular    | 52.1   | 0.0    | 23.3   | 6.2    | 2.7         | 14.4     | 1.4        |          |
| territory (n=146)    |        |        |        |        |             |          |            |          |

Values are percentages of patients. CE indicates cardioembolism; Incomplete, incomplete evaluation; LAA, large-artery atherosclerosis; Negative, negative evaluation; OD, other determined etiology; SVO, small vessel occlusion; Two or more, two or more causes identified.

*P values were obtained from comparisons of vascular territory multiplicity according and distribution of stroke subtypes using Pearson chi-square tests or Fisher’s exact tests when appropriate.
territory but only 25% of multiple-territory infarctions in carotid territory. The extent of investigation for cardioembolic source was not uniform against both vascular territory and TOAST classification. More than 40% of patients with ACA territory infarction received extensive evaluation, whereas only 8.5% of patients with vertebral artery territory infarction did (Table 2). Extensive embolic source evaluation was more frequently performed in patients with negative evaluation (40.7%) compared with those with other subtypes.

**Discussion**

In this study, 59% of the study population had acute ischemic lesions in carotid territory and 34% had acute ischemic lesions in vertebrobasilar territory. Involvement of vertebrobasilar territory was more common in our study compared with the Lausanne stroke registry (26%) and the Besançon stroke registry (14%). This can be explained by a higher frequency of small infarctions in brainstem and cerebellum and a higher detection rate of small lesions by thin-section DWI. The more frequent observation of multiple-territory infarction in our study (16%), compared with the Lausanne stroke registry (5%) and the Besançon stroke registry (10%), can also be attributed to the use of DWI. Comparisons of stroke subtypes between carotid and vertebrobasilar territories showed that CE was more common in carotid territory and SVO was more common in vertebrobasilar territory. In carotid territory, common etiologies were LAA (39%), followed by SVO (23%), and CE (22%). In contrast, carotid territory showed a higher frequency of CE (39%), followed by SVO (23%), and LAA (22%).

**Table 6. Stroke Subtypes According to Vascular Territory in This Study and the Lausanne and Besançon Stroke Registries**

| Mechanism* | ACA | MCA | ICA† | PCA | Brainstem | Cerebellum | BZ | Multiple | Total‡ |
|------------|-----|-----|------|-----|-----------|------------|----|---------|--------|
| LAA        |     |     |      |     |           |            |    |         |        |
| Our study  | 65.3| 34.2| 51.5 | 28.7| 40.1      | 48.4       | 89.9| 32.4    | 37.3   |
| Lausanne   | 50.0| 44.4| 12.5 | 35.0| 38.0      | 53.0       | 79.0| 27.0    | 43.2   |
| Besançon   | 20.0| 27.8| 34.8 | 25.9| 43.3      | 34.7       | 35.3| 31.1    | 30.5   |
| SVO        |     |     |      |     |           |            |    |         |        |
| Our study  | 0.0 | 25.6| 0.0  | 36.1| 44.4      | 0.0        | 0.0 | 0.0     | 22.9   |
| Lausanne   | 0.0 | 15.6| 0.0  | 9.0 | 25.0      | 6.0        | 0.0 | 19.0    | 13.2   |
| Besançon   | 2.9 | 1.3 | 13.9 | 0.0 | 16.5      | 0.0        | 0.9 | 2.3     | 10.0   |
| CE         |     |     |      |     |           |            |    |         |        |
| Our study  | 10.2| 22.8| 33.3 | 19.1| 5.8       | 21.9       | 5.1 | 32.2    | 20.6   |
| Lausanne   | 35.0| 18.8| 0.0  | 25.0| 6.0       | 29.0       | 9.0 | 15.0    | 20.4   |
| Besançon   | 45.7| 43.4| 22.2 | 41.0| 17.5      | 33.3       | 27.6| 30.5    | 31.0   |
| OD         |     |     |      |     |           |            |    |         |        |
| Our study  | 2.0 | 1.7 | 0.0  | 3.0 | 3.0       | 3.1        | 1.3 | 6.9     | 2.9    |
| Lausanne   | 5.0 | 7.9 | 62.5 | 13.0| 17.0      | 12.0       | 4.0 | 31.0    | 10.6   |
| Besançon   | 0.0 | 2.0 | 1.4  | 1.2 | 1.0       | 5.8        | 5.2 | 4.0     | 2.5    |
| UD         |     |     |      |     |           |            |    |         |        |
| Our study  | 22.5| 15.7| 15.2 | 13.1| 6.7       | 26.6       | 3.8 | 28.5    | 16.2   |
| Lausanne   | 10.0| 13.7| 25.0 | 18.0| 14.0      | 0.0        | 8.0 | 8.0     | 12.6   |
| Besançon   | 38.5| 25.3| 27.8 | 31.8| 21.6      | 26.1       | 31.0| 32.2    | 26.1   |

Due to differences in the ethnicity of the study population, the study time period, the modality of brain imaging, and the methods of etiologic evaluation, careful interpretation of results should be made. Values are percentages of patients. ACA indicates anterior cerebral artery; BZ, border zone infarction; CE, cardioembolism; ICA, internal carotid artery; LAA, large-artery atherosclerosis; MCA, middle cerebral artery; Multiple, multiple-territory infarction; OD, other determined etiology; PCA, posterior cerebral artery; SVO, small vessel occlusion; UD, undetermined etiology. *Mechanism: Our study used stroke subtypes using the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) to categorize stroke mechanism. The Lausanne and Besançon stroke registries used different stroke mechanism categories. Stroke mechanism categories from previous studies were modified as follows. Lausanne stroke registry: LAA, atherosclerosis with or without stenosis; SVO, hypertensive arteriolopathy; CE, embolic heart disease; OD, other determined etiology-arterial dissection and other etiologies; UD, Combined etiology-atherosclerosis with stenosis and embolic heart disease; Combined etiology-hypertensive arteriolopathy and embolic heart disease, and undetermined etiology. Besançon stroke registry: LAD, large vessel disease and atheroma with no stenosis; SVO, small vessel disease; CE, cardioembolism; OD, dissection; UD, combined, miscellaneous, and undetermined. †ICA: Definition of ICA territory infarction was different among studies: our study, when anterior choroidal artery or the entire ICA territory was involved; Lausanne stroke registry: when entire ICA territory was involved; Besançon stroke registry: when anterior choroidal artery was involved. ‡Total: Our study and the Lausanne stroke registry included only patients with visible stroke lesion in imaging studies. The Besançon stroke registry also included patients with no visible stroke lesion on imaging studies. Consequently, in the total category, the Besançon stroke registry contains data from patients without stroke lesion.
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vertebrobasilar territory, LAA was the most common (38%), followed by SVO (36%), and CE (12%). LAA was also the most common subtype in both territories in the Lausanne stroke registry; however, in the Besançon stroke registry, CE was the most common subtype (Table 6). The prevalence of atrial fibrillation was 30% in the Besançon stroke registry, 27% in the Lausanne stroke registry, and 15% in our study. This difference in risk-factor profiles may explain, at least in part, the difference in stroke subtypes.

In our study, MCA was the most frequently involved vascular territory (50% of the single vascular territory infarctions), followed by basilar artery, posterior cerebral artery, and PICA. In the Lausanne stroke registry and the Besançon stroke registry, MCA territory infarction was found in 65% and 51%, respectively. In the Lausanne stroke registry, when a stroke lesion was invisible with brain CT, electroencephalogram results were used to confirm the territory of the infarction, if superficial. Variations in the efforts to localize the vascular territory might have over- or underestimated the frequency of some territorial involvement in previous studies.

Regarding the ACA territory, our patients had less CE compared with the Lausanne and Besançon stroke registries: 10% versus 35% and 46%, respectively (Table 6). ACA infarction is usually caused by cardioembolism in studies from Western countries, whereas in a Japanese study and a Korean study, LAA was most common. The difference may reflect an ethnic difference in the distribution of cerebral atherosclerosis. The proportion of negative evaluation was highest in ACA territory infarction among single vascular-territory infarctions. Arterial dissection was suggested to be an important cause of isolated ACA territory infarction previously, but it was only 2% in our study. Lesser application of conventional angiography (12.2%) compared with other vascular territories (Table 2) may lead to the underestimation of arterial dissection as a cause of ACA territory infarction.

In reports from Western countries, LAA is the most common subtype in posterior circulation infarctions and CE is the major subtype in cerebellar infarction. In our study, LAA was also most common in vertebrobasilar territory infarction, but CE was only the third most common subtype in cerebellar infarction. The most common subtype in cerebellar infarction was LAA. CE was the most common subtype only in superior cerebellar artery territory infarction. The high prevalence of intracranial atherosclerosis in Asian populations may explain the high prevalence of LAA in cerebellar infarction.

Generally, our patients had more SVO than was shown in previous studies, and this may be attributed to the increased detection of small lacunes by DWI.

Limitations of this study should be noted. First, this was a retrospective single-center study of Korean stroke patients,

hence, the generality of the study results is limited. Second, the definition of stroke mechanism in the study was based on TOAST classification. Recently, new subtype classification systems with better reliability were proposed, although they are not yet widely used. Third, different rates of embolic source evaluation among vascular territories should be noted. Due to the retrospective nature of our study, the extent of embolic source evaluation could not be controlled. Fourth, as shown in Table 1, baseline characteristics differed between vascular territories, and this might affect the relationship between vascular territory and stroke mechanism. Adjustment for those differences was not made. Finally, we could not exclude a possibility that vascular territory may affect diagnosis of stroke subtype and then the relationship between them might be biased, although TOAST classification was originally designed independently of vascular territory.

This study has revealed significant dependence of ischemic stroke subtype on the vascular territory of the acutely imaged lesions. Localization of vascular territory of ischemic lesions that seems somewhat predictive of stroke subtype may help development of effective strategies for diagnosis of stroke subtypes in acute settings.

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Disclosures

None.

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Trial of ORG 10172 in Acute Stroke Treatment (TOAST) Classification and Vascular Territory of Ischemic Stroke Lesions Diagnosed by Diffusion-Weighted Imaging

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