Right–Left Propensity and Lesion Patterns Between Cardiogenic and Aortogenic Cerebral Embolisms

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Background and Purpose—Based on thrombus location and nature and anatomic features of aorta and cerebral arteries, we hypothesized that cardiogenic embolisms (CE) and aortogenic embolisms (AE) might have different right–left propensity and lesion patterns.

Methods—We retrospectively reviewed patients with acute ischemic stroke with high-risk CE sources or moderate or severe aortic atherosclerotic plaques on transesophageal echocardiography. Lesion side and patterns on diffusion-weighted imaging were compared between CE and AE.

Results—CE was identified in 123 and AE in 63. In multivariate analysis, right-sided lesions and corticosubcortical infarcts were independently associated with CE, and left-sided lesions and pial infarcts were independently associated with AE.

Conclusions—CE and AE have different radiological characteristics, as shown by the right–left propensity and lesion patterns of cerebral infarcts. (Stroke. 2011;42:00-00.)

Key Words: acute cerebral infarction ■ aortic atherosclerosis ■ cardioembolism ■ magnetic resonance imaging

The majority of cryptogenic strokes have infarct patterns compatible with embolic features, suggesting they were caused by cardiogenic (CE) or aortogenic (AE) embolisms. Although several studies have focused on the lesion patterns in cardiogenic and aortogenic infarctions,1,2 their radiological differences remain largely unknown.

The direction of cerebral embolization may be affected by anatomic and rheological characteristics of the aortic segment and the location of thrombi.3 In addition, CE and AE have distinct pathological mechanisms of thrombus formation in terms of fibrin-rich and platelet-rich thrombi.4 Thus, we hypothesized that right–left propensity and lesion patterns of cerebral infarcts might differ between CE and AE.

Methods

We retrospectively assessed all patients with stroke admitted to the Stroke Center at Asan Medical Center, Seoul, South Korea, between November 1, 2002, and October 30, 2008. Patients were screened if they had an acute symptomatic stroke identified on diffusion-weighted imaging and if transesophageal echocardiography was performed during admission to include those with definitive isolated high-risk CE or AE. CE was defined if there were high-risk cardioembolic sources according to SSS-TOAST classification.5 AE was defined if there was a moderate or severe degree of atherosclerotic plaques (≥4 mm thick) with or without complex plaques (eg, mobile debris, ulcerating plaques) in the ascending aorta or aortic arch.6 Patients with low- or uncertain risk of CE, a mild degree of aortic atherosclerosis, or combined CE and AE were excluded from this study. The study was approved by the Institutional Review Board of our center. Patient informed consent was not required due to the retrospective design.

Lesion side and patterns on diffusion-weighted imaging were determined blinded to stroke etiology. Right-sided lesions were defined as those in the territories of right innominate artery and right posterior inferior cerebellar artery, whereas left-sided lesions were defined as those in the territories of left common carotid artery and left posterior inferior cerebellar artery. We excluded patients with infarcts in the territories of anterior inferior cerebellar, basilar, and posterior cerebral arteries, because these lesions could occur by embolization through either side of vertebral arteries. In addition, anatomic variations (common trunk of anterior cerebral arteries or fetal-type posterior cerebral artery) were considered when determining the side of the index lesions. Diffusion-weighted imaging lesions in each patient were classified into 1 of 8 patterns: 4 single and 4 multiple patterns (Table).

Clinical and imaging characteristics were compared between the CE and AE groups using Student t test, Mann–Whitney U test, or χ² or Fisher exact tests as appropriate. Multiple logistic regression analysis was used to determine independent factors of CE and AE.
Results
Of a total of 545 patients who had acute symptomatic stroke and underwent transesophageal echocardiography, 186 patients met the eligibility criteria of this study: 97 (52.2%) were men, and the median age was 66 years (range, 20 to 89 years). CE was diagnosed in 123 patients and AE in 63. The most common etiology of CE was atrial fibrillation (96 [60.4%]) followed by rheumatic valve disease (21 [13.2%]). Of the 63 patients with AE, 38 (60.3%) had a severe and 25 (39.7%) had a moderate degree of aortic atherosclerosis. Patients with AE were older \( (P=0.003) \) and had diabetes mellitus \( (P=0.012) \) and hypercholesterolemia \( (P=0.012) \) more frequently than patients with CE.

Patients with CE were more likely to have right-sided lesions, whereas patients with AE more frequently had left-sided lesions. Of the lesion patterns, corticosubcortical infarcts were more frequently associated with CE and pial infarcts were more often associated with AE (Table; Figure). The frequency of multiple lesions was similar between CE \( (46.3\%) \) and AE \( (50.8\%) \).

In multivariate analysis, right-sided lesions \( (OR, 2.74; 95\% CI, 1.34 \text{ to } 5.58) \), corticosubcortical infarcts \( (OR, 2.35; 95\% CI, 1.09 \text{ to } 5.09) \), and female \( (OR, 2.15; 95\% CI, 1.03 \text{ to } 4.47) \) were independently associated with CE. In contrast, left-sided lesions \( (OR, 2.77; 95\% CI, 1.39 \text{ to } 5.53) \), pial infarcts \( (OR, 3.0; 95\% CI, 1.05 \text{ to } 8.62) \), age \( (OR, 1.07; 95\% CI, 1.03 \text{ to } 1.1) \), and diabetes \( (OR, 2.53; 95\% CI, 1.10 \text{ to } 5.79) \) were independently associated with AE.

Discussion
To our knowledge, this study is the first to compare the radiological characteristics of CE and AE.

Several mechanisms may explain the differing right–left propensity of cerebral infarcts between CE and AE. First, the innominate artery supplying the right brain has the largest caliber and heads upward and parallel to the direction of ascending aorta, whereas the left carotid artery arises perpendicular to the aortic arch. Consequently, cardiogenic emboli may flow more frequently into the right hemisphere. Second, aortic plaques are more commonly observed in the distal aortic arch than in the ascending aorta, and thereby aortic plaques and superimposed thrombus may easily obliterate left carotid or vertebral arteries, resulting in left-sided strokes. Nevertheless, we found that approximately one third of patients with AE had right-sided lesions. Emboli from aortic plaques may move backward into the right hemisphere because the aorta has normally turbulent flows in the diastolic stage.

We also found that CE was associated with large corticosubcortical infarcts, whereas AE was associated with pial infarcts. AE is thought to be due to plaque rupture and to the embolization of platelet-rich small thrombi similar to the stroke mechanism in internal carotid artery stenosis. In contrast, CE is thought to be due primarily to the stasis-related formation of thrombi within the cardiac chamber and the subsequent dislodgement of large-sized thrombi.

This study had several limitations. The study design was retrospective. Although our center has a standardized stroke work-up protocol, transesophageal echocardiography was performed in selected patients. Transesophageal echocardiography may underestimate atherosclerosis in the more proximal aortic arch and ascending aorta owing to imaging in the far field and interference by air in the trachea and bronchus.
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Disclosures
None.

References


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**Supplemental Methods**

Other exclusion criteria included: (1) intracranial and extracranial arterial stenosis (>50%) corresponding to the index stroke; (2) small vessel occlusion; (3) no DWI lesions; (4) hematological abnormalities or coagulopathies; (5) cancer-associated strokes; (6) other miscellaneous causes of stroke (e.g., dissection, Takayasu’s arteritis); and (7) undetermined causes despite complete diagnostic evaluation.

The topography of ischemic lesions was determined using published templates.\(^1\) Cortico-subcortical infarcts were defined as large infarcts involving the cortical and subcortical areas. Perforating artery infarcts included striatocapsular infarcts, with large PAIs defined as lesions of diameter ≥2 cm. Pial infarcts were defined as infarcts occurring in the territories supplied by the branches of the major intracranial vessels. Border-zone infarcts included anterior and posterior cortical BZ and internal BZ.\(^2\)

Transsthoracic (TTE) and transesophageal echocardiography (TEE) were performed by experienced cardiologists who had no information about the underlying causes of stroke. The cardiac valves, interventricular septum, ventricular wall motion, and ejection fraction were examined by TTE. The left atrial appendage and atrium, the atrial septum, and the aorta were evaluated by TEE. Atherosclerosis was defined as irregular intimal thickening with increased echogenicity. Because the ascending aorta and the proximal aortic arch were the regions most likely to be sources of cerebral emboli, we recorded all plaques in these two regions.

**Supplemental Results**

Of total 545 patients who had acute symptomatic stroke and underwent TEE, 339 patients were excluded: 124 with corresponding large artery disease, 15 with small vessel occlusive disease, 56 with two or more stroke etiologies, 112 with undetermined stroke etiology, 18 with other miscellaneous causes of stroke, and 14 with no DWI lesion. An additional 20 patients were excluded because the side of the index lesion could not be determined (e.g., anterior inferior cerebellar artery infarcts).

The most common etiology of CE was atrial fibrillation (n=96, 60.4%), followed by rheumatic valve disease (n=21, 13.2%), prosthetic/mechanical valve (n=12, 7.6%), symptomatic congestive heart failure with <30% of ejection fraction (n=9, 5.7%), infective endocarditis (n=5), dilated cardiomyopathy (n=4), left atrial appendage thrombus (n=4), chronic myocardial infarction with <28% of ejection fraction (n=2), sick sinus syndrome (n=2), papillary fibroelastoma (n=2), left ventricular thrombus (n=1), and left ventricular myxoma (n=1).

We compared clinical and imaging variables between high-risk CE patients with and without TEE performance. During the study period 541 patients had high-risk CE sources: 195 (36.0%) patients underwent TEE while 346 (64.0%) did not undergo TEE. Between the high-risk CE patients who underwent and did not undergo TEE, gender and stroke risk factors were not different. However, younger, milder (low NIHSS scores), and first-ever stroke patients underwent TEE more frequently than older, severe, and recurrent stroke patients. Of the 195 patients who underwent TEE, 72 patients were further excluded from this study because of combined aortic atherosclerosis, no DWI lesions, or undetermined lesion side. Between 123 CE patients enrolled in this study and high-risk CE patients without TEE, there was no difference in terms of lesion laterality.

We also performed univariate and multivariate analyses with lesion laterality entered into the model as a dichotomous variable (right and left, with bilateral lesions distributed into both groups) instead of a trichotomous variable (right, left, bilateral). Both univariate and multivariate analyses with dichotomous lesion side showed same results as the analyses with trichotomous lesion side.
**Supplemental Figure**

**Figure.** Diagram showing the anatomy of aorta, aortic plaques, and blood flows. Aortic plaques (blue area) are more common and severe in the distal aortic arch. The black arrows indicate blood flow from the heart, whereas the red arrows indicate the direction of blood flow and possible courses of cardiogenic emboli.

A = ascending aorta; B = aortic arch; C = descending aorta; 1 = innominate artery; 2 = right subclavian artery; 3 = right carotid artery; 4 = left carotid artery; 5 = left subclavian artery
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Abstract 10

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Key Words: acute cerebral infarction ■ aortic atherosclerosis ■ cardioembolism ■ magnetic resonance imaging

배경과 목적
혈전의 위치와 성상, 그리고 대동맥 및 대뇌동맥의 해부학적 특징에 근거하여, 저자들은 심장성동맥절(cardiogenic embolism, CE)과 대동맥성동맥절(aortogenic embolism, AE)이 서로 다른 좌우 폐향과 병변 양상을 가질 것으로 가설을 세웠다.

방법
저자들은 식도경유 심장초음파검사(transesophageal echocardiography)에서 고위험의 CE 환이나 증상이 동반한 대동맥 자라장폐쇄를 가진 급성 혈청증(ischemic stroke) 환자를 후향적으로 조사하였다. 확산강조영상에서 병변의 위치와 양상을 CE와 AE에서 비교하였다.

결과
CE가 123명, AE가 63명 있었다. 다변량 분석에서 우측 병변과 피질피질후방경색(corticosubcortical infarct)은 CE와, 좌측 병변과 연막경색(pial infarct)은 AE와 독립적으로 연관이 있었다.

결론
CE와 AE는 병변의 좌우 폐향과 병변 양상 등에서 나타난 바와 같이, 서로 다른 양상의학적 특징을 가진다.

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Figure. Right-sided corticosubcortical lesion in a patient with CE (A) and left-sided pial infarcts in a patient with AE (B). CE indicates cardiogenic embolism; AE, aortogenic embolism.