Radiology

Thrombus in the Left Atrial Appendage in Stroke Patients:
Detection with Cardiac CT Angiography—A Preliminary Report[1]

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Purpose: To assess the diagnostic performance of 64-section cardiac computed tomographic (CT) angiography for detection of left atrial appendage (LAA) thrombi in stroke patients by using transesophageal echocardiography (TEE) as the reference standard.

Materials and Methods: This study was approved by the institutional review board. Records were reviewed from 101 consecutive patients who had experienced a recent stroke (onset within the previous 1 month) from a suspected cardioembolic source and who had undergone both 64-section cardiac CT angiography and TEE within 1 week. The numbers of thrombi in the LAA detected with cardiac CT angiography and with TEE were recorded, and the agreement between thrombus detection with CT and with TEE was assessed by using κ statistics.

Results: Eight thrombi in the LAA were detected with TEE, and 12 were detected with cardiac CT angiography. With TEE used as the reference standard, the overall sensitivity, specificity, and accuracy of 64-section cardiac CT angiography for detecting thrombi were 100% (95% confidence interval [CI]: 63%, 100%), 95% (95% CI: 90%, 99%), and 96% (95% CI: 92%, 100%), respectively. The concordance between LAA thrombus detection with 64-section cardiac CT angiography and with TEE was high: 89 patients with no thrombus at CT or TEE; eight patients with thrombus at both CT and TEE; and four patients with thrombus at CT but not at TEE (overall κ = 0.779 [95% CI: 0.571, 0.987]).

Conclusion: Sixty-four–section cardiac CT angiography is a noninvasive and sensitive modality for detecting thrombi in the LAA of stroke patients. Although TEE is currently considered the reference standard modality for detecting LAA thrombi, 64-section cardiac CT angiography has the potential to become a useful modality for detection of intracardiac thrombus.

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Cardiogenic emboli have been estimated to be the causative factor in 20%–40% of all stroke cases (1). Therefore, identification of a cardiac source of embolism in stroke patients is important for proper therapeutic management. The left atrial appendage (LAA) is an important location of thrombus formation and subsequent cardioembolic events, especially in association with dysrhythmias, such as atrial fibrillation (2,3).

Transesophageal echocardiography (TEE) is considered the reference standard modality for detecting LAA thrombi, with a sensitivity of almost 100% and a specificity of almost 99% (3–5). TEE offers high-resolution images of the left atrium, its appendage, and the thoracic aorta for evaluation of left atrial blood stasis and aortic atherosclerosis. Although TEE is widely available and portable, it requires special skills for proper performance and interpretation. In addition, TEE is a semi-invasive test, usually performed with the use of conscious sedation.

In current clinical practice, there is a need for a less-invasive modality that can help to assess the cardiovascular system of patients who have had an embolic stroke. Computed tomography (CT) is a well-established but rarely used technique for imaging intracardiac thrombi (6–11). For the detection of an intracardiac thrombus, CT has the advantage of being able to provide images of uniform sections of the heart, thus allowing the possible detection of a thrombus in the cardiac chambers, including the LAA. Multidetector CT provides high-quality noninvasive images of the heart, great vessels, and coronary vasculature. The current 64-section scanners allow rapid scanning of the cardiac anatomy, require minimal patient cooperation (short breath hold),

and have improved image quality (better spatial and temporal resolution) and high diagnostic accuracy (12–14). Sixty-four–section cardiac CT angiography, with subsecond rotation times and a dedicated cardiac reconstruction algorithm, allows the acquisition of three-dimensional data for the heart, enabling detailed visualization of not only the coronary arteries but also other cardiac structures, such as the LAA.

We assessed the diagnostic performance of 64-section cardiac CT angiography for the detection of LAA thrombi in stroke patients. TEE was used as the reference standard.

Materials and Methods

Patient Selection

This retrospective study was approved by our institutional review board. By performing a computerized search of medical and radiologic records from May 2006 to June 2007, we found 158 patients who had been admitted to our hospital who had had a recent episode of stroke (with stroke onset within the previous 1 month) and had undergone TEE evaluation for suspicion of cardioembolic stroke. TEE was performed within 2 weeks of the initial stroke except in cases of decreased consciousness, impending brain herniation, poor systemic conditions, tracheal intubation, or failure to introduce an esophageal transducer. Of these 158 patients, 101 patients who had more than two risk factors for coronary artery disease also underwent 64-section cardiac CT angiography. These 101 patients made up our study population. All examinations were performed within a 1-week interval. We included all stroke subtypes, from both the anterior and the posterior circulation. All patients underwent brain CT or brain magnetic resonance (MR) imaging to characterize

the stroke and to exclude hemorrhages and other causes.

The study population consisted of 63 men (mean age, 69 years; range, 45–81 years) and 38 women (mean age, 64 years; range, 51–85 years). The mean age of all 101 patients was 67 years. Baseline clinical characteristics, including systemic hypertension, hyperlipidemia, diabetes mellitus, and smoking habits, were determined from medical records and routine laboratory data.

Cardiac CT Angiography

Cardiac CT angiography was performed with a 64-section helical CT scanner (Sensation 64; Siemens Medical Solutions, Forchheim, Germany) in the craniocaudal direction during a single breath hold. The heart rate of the patient was measured before the examination. In patients with a heart rate greater than 65 beats per minute, a β-blocker (40 mg of propranolol hydrochloride [Pranol; Dae Woong, Seoul, Korea]) was administered orally 1–2 hours before examination to reduce the heart rate. For each patient, electrocardiograms were recorded simultaneously. The mean heart rate (± standard deviation) was 62 beats per minute ± 12 (range, 52–92 beats per minute) during CT. The scan parameters were as follows: 330-msec gantry rotation time, 120 kV, 800 mAs, 0.6-mm

Advance in Knowledge

- The overall sensitivity, specificity, and accuracy of 64-section cardiac CT angiography for detecting left atrial appendage thrombi in stroke patients were 100%, 95%, and 96%, respectively.

Implication for Patient Care

- Cardiac CT angiography has the potential to become a useful modality for detection and follow-up of intracardiac thrombi.

section collimation, 1-mm section width, and 3.3-mm table feed per rotation. A contrast solution composed of 60–90 mL of nonionic contrast agent (370 mg of iodine per milliliter; iopamidol [Iopamiro; Bracco, Milan, Italy]), followed by 50 mL of a saline chaser solution, was administered intravenously at a rate of 5 mL/sec with a power injector (Envision CT; Medrad, Indianola, Pa).

Image reconstruction was performed on the scanner's workstation by using commercially available software (Syngo, Somaris/5; Siemens Medical Solutions). For image reconstruction, segmented adaptive cardiac volume reconstruction based on a half-rotation reconstruction technique was used, which provided a heart rate–dependent temporal resolution between 83 and 165 msec from a 330-msec gantry rotation. This was based on retrospective electrocardiographic triggering. The reconstruction parameters were as follows: 0.6-mm section thickness, 0.4-mm increments, 512 × 512–pixel image matrix, medium smooth kernel, and 18- to 20-cm field of view. The image settings were sent to the workstation (Wizard; Siemens Medical Solutions). For evaluation of intracardiac thrombus, we used the scanner's standard software to reformat the curved multiplanar reconstruction images with a 2-mm section thickness without a gap along the curved line of the long axis of the LAA (Fig 1). The total radiation dose was calculated to be approximately 8–10 mSv, depending on the scan range and the patient's body weight.

TEE Examination

TEE was performed by an experienced cardiologist (C.Y.S., with 5 years of experience with TEE) with a 5-MHz phased-array transducer attached to the tip of a commercially available gastroscope (Acuson; Siemens, Mountain View, Calif). Patients received mild local pharyngeal anesthesia immediately before the gastroscope was inserted. TEE was performed while the patient was in the supine left lateral decubitus position. For each patient, all images were recorded as movie images on digital videotape in real time for display and evaluation. Images of the left atrium and the LAA were evaluated in both the horizontal (0-degree) plane and the plane obtained by rotating the imaging sector from 0 to 180 degrees during continuous visualization of the LAA.

Image Analysis

Two experienced radiologists (Y.J.K. and B.W.C., with 5 years and 8 years of experience with cardiac CT, respectively) collectively and retrospectively reviewed the cardiac CT angiographic images of the 101 patients independently. Differences in the radiologists' assessments were resolved by consensus. The image quality of all cardiac CT angiographic images was acceptable for the evaluation of the coronary arteries and intracardiac abnormalities. Each reader was blinded to the results of other examinations and to clinical data.

For CT, we defined a thrombus as a filling defect with an oval or convex shape. Blood stasis was defined as a typical triangular filling defect at the ventral side of the LAA, which appeared as fluid–fluid levels. For TEE, a thrombus was defined as a well-circumscribed, uniformly consistent echogenic mass with texture different from that of the LAA wall.

At TEE, the echo pattern known as "spontaneous echo contrast" was characterized by dynamic clouds of echoes curling up slowly into a circular or spiral shape within the LAA cavity. On the basis of its appearance and density, the severity of the spontaneous echo pattern was prospectively classified into four grades: (a) none, the phenomenon was not present; (b) mild, there was minimal echogenicity that was only transiently detectable with optimal gain
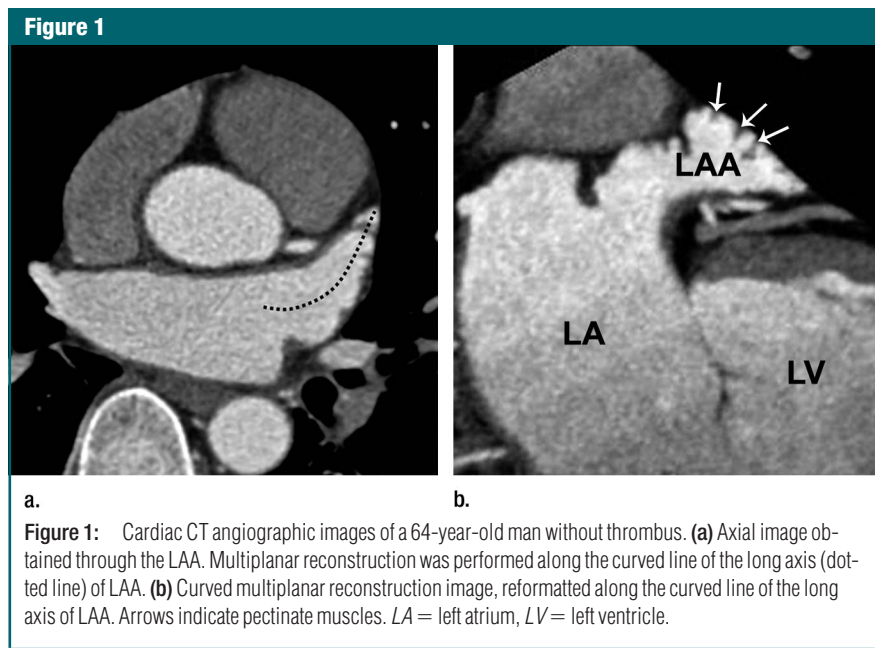
Figure 1

a.
b.

Figure 1: Cardiac CT angiographic images of a 64-year-old man without thrombus. **(a)** Axial image obtained through the LAA. Multiplanar reconstruction was performed along the curved line of the long axis (dotted line) of LAA. **(b)** Curved multiplanar reconstruction image, reformatted along the curved line of the long axis of LAA. Arrows indicate pectinate muscles. *LA* = left atrium, *LV* = left ventricle.

Table 1

Clinical Characteristics of 101 Stroke Patients

Characteristic	No. of Patients
Stroke subtype	
Anterior circulation	63 (62)
Posterior circulation	32 (32)
Both	6 (6)
Hypertension	69 (68)
Hyperlipidemia	13 (13)
Diabetes mellitus	31 (31)
Smoking	23 (23)
Old cerebrovascular accident	10 (10)
Atrial fibrillation	21 (21)

Note.—Data in parentheses are percentages.

settings during the cardiac cycle; *(c)* moderate, a dense swirling pattern of echoes during the entire cardiac cycle; and *(d)* severe, an intense echogenicity and slow swirling pattern in the LAA, usually with similar echogenicity in the main cavity. Size measurements of the thrombi were based on the largest long and short axes on the CT images and two-dimensional TEE planes.

Statistical Analysis

With TEE used as the reference standard, the sensitivity, specificity, and accuracy of 64-section cardiac CT angiography for detecting thrombi in the LAA were calculated; 95% confidence intervals (CIs) were calculated by using the method of exact binomial tail areas (15). Significant differences in the mean size of the thrombi measured with cardiac CT angiography and with TEE were assessed by using a paired *t* test. Agreement between the detection of thrombi with CT and with TEE was assessed by using κ statistics, and the κ values are presented with their respective 95% CIs. The associations between thrombus and blood stasis detected at CT and *(a)* the grade of spontaneous echo contrast and *(b)* atrial fibrillation were assessed with the Cochran-Armitage test for the detection of trends. *P* values less than .05 were considered to represent significant differences. All statistical analyses were performed with commercially available software (SAS, version 9.1 [SAS Institute, Cary, NC]; or SPSS, version 10.0 [SPSS, Chicago, Ill]).
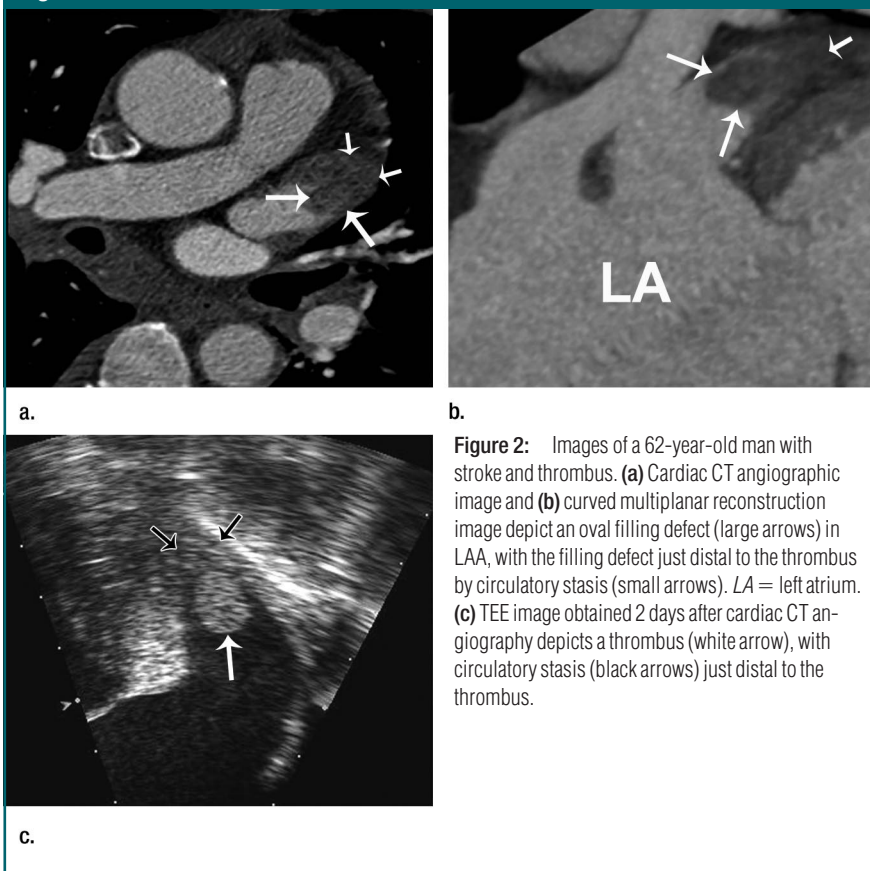
Results

The image quality of all cardiac CT angiographic examinations was considered acceptable for the evaluation of the coronary arteries and intracardiac abnormalities. The clinical characteristics of the 101 patients are summarized in Table 1. Twenty-one of the 101 patients (21%) were in atrial fibrillation at the time of their stroke.

With TEE, eight thrombi were depicted, all located in the LAA. With cardiac CT angiography, 19 filling defects were depicted in the LAA. Among these 19 lesions, 12 filling defects were diagnosed as thrombus and seven as blood stasis (Figs 2, 3). Of the 12 filling defects diagnosed as thrombus with cardiac CT angiography, four were not diagnosed as true thrombi with TEE (Fig 4). The overall sensitivity, specificity, and accuracy of 64-section cardiac CT angiography for the detection of thrombus in the

Figure 2

a.

b.

c.

Figure 2: Images of a 62-year-old man with stroke and thrombus. **(a)** Cardiac CT angiographic image and **(b)** curved multiplanar reconstruction image depict an oval filling defect (large arrows) in LAA, with the filling defect just distal to the thrombus by circulatory stasis (small arrows). *LA* = left atrium. **(c)** TEE image obtained 2 days after cardiac CT angiography depicts a thrombus (white arrow), with circulatory stasis (black arrows) just distal to the thrombus.
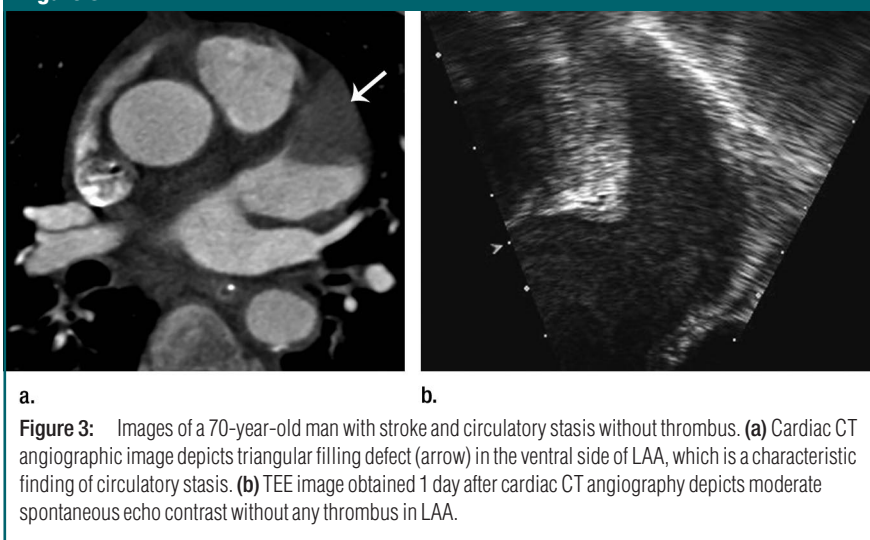
Figure 3

a.

b.

Figure 3: Images of a 70-year-old man with stroke and circulatory stasis without thrombus. **(a)** Cardiac CT angiographic image depicts triangular filling defect (arrow) in the ventral side of LAA, which is a characteristic finding of circulatory stasis. **(b)** TEE image obtained 1 day after cardiac CT angiography depicts moderate spontaneous echo contrast without any thrombus in LAA.

Figure 4

a.   b.   c.

Figure 4: Images of a 69-year-old man with stroke and false-positive finding of thrombus at cardiac CT angiography. **(a)** Cardiac CT angiographic image and **(b)** curved multiplanar reconstruction image depict a small round filling defect (arrows) in LAA. *LA* = left atrium. **(c)** TEE image obtained 3 days after cardiac CT angiography depicts moderate spontaneous echo contrast without any thrombus in LAA.

LAA were 100% (95% CI: 63%, 100%), 95% (95% CI: 90%, 99%), and 96% (95% CI: 92%, 100%), respectively.

In the eight cases in which thrombi were depicted with both cardiac CT angiography and TEE, the mean size of the thrombi was 1.55 cm^2 (range, 0.84–2.55 cm^2) with cardiac CT angiography and was 1.18 cm^2 (range, 0.72–1.82 cm^2) with TEE (P = .012). The mean size of the thrombus was 23% larger (0.37 cm^2; range, 0.12–0.73 cm^2) when detected with CT than with TEE. The size of presumed thrombi at CT that were not depicted with TEE ranged from 0.56 to 0.64 cm^2.

The concordance between detection of thrombus in the LAA with 64-section cardiac CT angiography and with TEE was high: 89 patients with no thrombus seen at CT or TEE; eight patients with thrombus seen at both CT and TEE; and four patients with thrombus seen at CT but not TEE (overall κ = 0.779 [95% CI]: 0.571, 0.987). In no patient was thrombus detected at TEE but not at cardiac CT angiography.

Thrombus and blood stasis were more likely to be diagnosed with cardiac CT angiography in patients who had a moderate or severe grade of spontaneous echo contrast (P < .01). Of the four filling defects that were seen with CT and were not depicted as a thrombus with TEE, spontaneous echo contrast was categorized as severe in two cases and as moderate in

two cases. Of the eight filling defects diagnosed correctly as thrombus with CT, spontaneous echo contrast was categorized as severe in four cases and as moderate in two cases and was not present in two cases. Of the seven filling defects diagnosed as blood stasis with CT, spontaneous echo contrast was categorized as severe in three cases and as moderate in three cases and was not present in one case (Table 2).

Thrombus and blood stasis diagnosed at cardiac CT angiography were more likely to be found in patients with atrial fibrillation (P < .01). Of the 19 patients with filling defects diagnosed as thrombus or blood stasis at CT, 17 patients (89%) had atrial fibrillation. Only two patients with filling defects diagnosed as thrombus with both modalities had no atrial fibrillation and no demonstrable spontaneous echo contrast at TEE. Of the 82 patients without throm-

bus, only four (5%) had atrial fibrillation (Table 3).

Discussion

Our study demonstrates that 64-section cardiac CT angiography is a noninvasive and sensitive modality for detecting thrombi in the LAA of stroke patients. Thrombi of the left atrium and LAA are common causes of stroke. Because these thrombi are treatable sources of emboli, their detection may affect patient care. Although TEE is a relatively invasive technique, it is the reference standard for evaluating patients suspected of having intracardiac thrombi. However, TEE has several pitfalls associated with its use for detecting left atrial or LAA thrombus, including false-negative results caused by poor images of the left atrium or LAA, small

Table 2

Associations among Thrombus, Blood Stasis, and Spontaneous Echo Contrast Grade

CT Finding	TEE		Spontaneous Echo Contrast			
	Thrombus	No Thrombus	None	Mild	Moderate	Severe
Thrombus	8	4	2	0	4	6
Blood stasis	0	7	1	0	3	3
No thrombus	0	82	72	8	2	0

Note.—Data are numbers of patients.

thrombi, closely adherent mural thrombi, and newly formed thrombi (16).

CT is a sensitive tool for detecting intracardiac thrombus. In several studies, investigators have reported that intracardiac thrombi can be detected with CT (6–11). Tomoda et al (6) reported that the overall sensitivity and specificity of CT for the detection of left atrial thrombi in 56 patients were 100% and 91%, respectively, compared with 60% and 86%, respectively, for two-dimensional echocardiography. However, the configuration of the various cardiac structures determined with CT can be influenced by the effects of cardiac movements. Therefore, a small intracardiac thrombus is difficult to diagnose because of motion artifacts. Multidetector CT has several advantages compared with single-section helical CT, including a faster scanning time and a higher z-axis resolution, which results in a high-quality real-time three-dimensional image with fewer misregistration artifacts. Because of the higher z-axis resolution of the high-quality real-time three-dimensional images of multidetector CT, multiplanar reconstruction images offer great potential for the evaluation of intracardiac structures.

Cardiac MR imaging is also an appealing modality with which to evaluate a patient suspected of having had an embolic stroke (17). Cardiac MR imaging can adequately image potential sources of emboli, such as left ventricular thrombi, cardiac masses, aortic plaques, or LAA thrombi. The advantages of cardiac MR imaging, compared with cardiac CT angiography, are the absence of radiation exposure and the avoidance of iodinated contrast media.

However, cardiac MR imaging also has several disadvantages compared with CT: The examination time is much longer, cardiac MR imaging is much more expensive, and it cannot be performed in patients with implanted metallic devices.

For the accurate diagnosis of LAA thrombi, differentiation of a small thrombus from pectinate muscle is essential. For that purpose, the anatomy of the LAA must be evaluated with careful analysis of serial contiguous sections. In our experience, serial reformatted images along the curved line of the long axis of the LAA provide detailed morphologic features of the LAA. In addition, we believe that the curved reformations in multiple planes are helpful for differentiating between the continuity of the pectinate muscle and the discontinuity of the thrombus.

Another pitfall in the diagnosis of thrombus is circulatory stasis. In several studies, investigators have demonstrated that circulatory stasis can cause a filling defect, mimicking a thrombus (10,11). Nakanishi et al (10) demonstrated that in addition to a thrombus, circulatory stasis can produce a filling defect on early phase images and that ventral and triangular filling defects could be characteristic of circulatory stasis. They reported that differentiating between thrombi and circulatory stasis is possible only with late phase images.

In our study, cardiac CT angiography was sensitive and was comparable to TEE in detecting an LAA thrombus. The eight thrombi diagnosed with TEE were all also detected with cardiac CT angiography. Of the seven filling defects diagnosed correctly as blood stasis at

cardiac CT angiography, all showed typical triangular filling defects on the ventral side of the LAA, which is a characteristic finding of circulatory stasis. However, in our study, we found four false-positive filling defects at cardiac CT angiography that were diagnosed as blood stasis with TEE. For the four filling defects diagnosed with cardiac CT angiography but not with TEE, spontaneous echo contrast was categorized as severe in two cases and as moderate in two cases. This finding suggests that because of the various LAA structures (in particular, multilobed LAA or prominent pectinate muscle), blood stasis can also cause oval or convex filling defects in the LAA, mimicking a thrombus.

In our study, the thrombus was 23% larger when depicted with CT than with TEE. A thrombus is often associated with circulatory stasis, which also causes a filling defect. Therefore, in those cases, measuring the exact boundary of the thrombus is difficult. This finding suggests that the thrombus is overestimated with single-phase CT images.

Spontaneous echo contrast in the left atrium and the LAA is caused by local blood stasis, which is associated with a high incidence of thrombus formation and thromboembolic events (18,19). LAA dysfunction, which is associated with atrial fibrillation from various causes, is also commonly accompanied by spontaneous echo contrast (20,21). Fatkin et al (19) reported that substantial LAA dysfunction is similarly associated with formation of LAA thrombus and that the degree of LAA spontaneous echo contrast is negatively associated with LAA blood flow velocities. Our results obtained with cardiac CT angiography were similar to those from previous studies. In our study, of 19 filling defects diagnosed as either thrombus or blood stasis at CT, 16 filling detects (84%) were graded as moderate or severe spontaneous echo contrast. Moreover, of the 19 patients with filling defects diagnosed as thrombus or blood stasis at CT, 17 (89%) had atrial fibrillation.

Our study had several limitations. First, the total number of thrombi was

Table 3

Associations among Thrombus, Blood Stasis, and Atrial Fibrillation

CT Finding	TEE		Atrial Fibrillation	
	Thrombus	No Thrombus	Yes	No
Thrombus	8	4	10	2
Blood stasis	0	7	7	0
No thrombus	0	82	4	78

Note.—Data are numbers of patients.

too small to allow us to generalize the results. Second, we did not analyze late phase images, which are important for the differentiation between thrombus and blood stasis. Even though we can observe a clear filling defect in the LAA cavity, a single scan in the early phase can lead to false-positive results. This must be considered when CT images are interpreted. Third, the cardiac CT angiographic images were reviewed independently by two radiologists. However, differences in assessment were resolved by consensus. The fourth limitation is radiation exposure. In our study, the total radiation dose was calculated to be approximately 8–10 mSv. Because strokes typically affect elderly patients, we believe that the radiation dose is not a major risk factor in most patients and is acceptable for intracardiac thrombus detection in stroke patients. Finally, we used TEE as a reference standard, and as a result, we may have missed some cases of thrombus.

Sixty-four–section cardiac CT angiography is a noninvasive and sensitive modality for detecting thrombus in the LAA of stroke patients. With advances in CT technology, we believe that cardiac CT angiography will play an increasingly important role in the detection and follow-up of intracardiac thrombus.

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