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Cardiac Computed Tomographic Angiography for Detection of Cardiac Sources of Embolism in Stroke Patients

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Background and Purpose—We assessed the diagnostic performance of 2-phase 64-slice cardiac computed tomographic angiography (CCTA) for the detection of a cardiac source of embolism in stroke patients using transesophageal echocardiography (TEE) as the reference standard.

Methods—We selected 137 patients who had experienced a recent episode of stroke and had undergone both 2-phase 64-slice CCTA and TEE within a period of 5 days. A potential cardiac source of embolism detected at both CCTA and TEE was recorded, and echocardiographic findings were categorized into high- and medium-risk sources based on the TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification.

Results—Of 137 patients, 100 abnormal findings in 91 patients were found on TEE, and 46 patients had no abnormal finding on TEE. The overall sensitivity, specificity, positive predictive value, and negative predictive value of the 64-slice CCTA for detecting cardiac sources of embolism were 89% (95% CI, 82%, 95%), 100% (95% CI, 90%, 100%), 100% (95% CI, 95%, 100%), and 81% (95% CI, 70%, 92%), respectively. TEE detected a total of 47 high-risk sources of embolism, whereas CT detected 44 lesions. For medium-risk sources of cardiac embolic stroke, TEE detected a total of 53 abnormal findings, whereas CT detected 44 abnormal findings. Of 53 lesions, there were 8 false-negative results on CT (5 patent foramen ovale and 3 atrial septal aneurysm).

Conclusions—Two-phase 64-slice CCTA is a noninvasive and useful modality for detecting high-risk cardiac sources of embolism in stroke patients. (Stroke. 2009;40:2073-2078.)

Key Words: cardiac computed tomographic angiography ■ embolism ■ stroke ■ transesophageal echocardiography

Cardiogenic emboli have been estimated to be the causative factor in 20% to 40% of all stroke cases. Therefore, identification of a cardiac source of embolism in stroke patients is important for proper therapeutic management.

Currently, transesophageal echocardiography (TEE) is considered the reference standard method for the detection of potential sources of cerebral embolism. TEE offers high-resolution images of the left atrium (LA) and its appendage as well as the thoracic aorta for the evaluation of left atrial blood stasis and aortic atherosclerosis. Although TEE is widely available, it is a semi-invasive test, usually performed under conscious sedation.

Recently introduced 64-slice cardiac computed tomographic angiography (CCTA) with subsecond rotation times and a dedicated cardiac reconstruction algorithm can acquire 3-dimensional data of the heart, enabling detailed visualization of not only the coronary arteries but also other cardiac structures such as the left atrial appendage (LAA), myocardium, valves, and septa. By previous reports, CT has shown its diagnostic capability in the detection of intracardiac thrombi and patent foramen ovale (PFO).

The aim of this study was to assess the diagnostic performance of 2-phase 64-slice CCTA for the detection of a cardiac source of an embolism in stroke patients using TEE as the reference standard.

Materials and Methods

Patient Selection
Our Institutional Review Board approved this study, and patients were provided with informed consent. From January 2008 to July 2008, 331 consecutive patients were admitted to our hospital for a recent stroke (onset within the previous 7 days) and prospectively enrolled in the current study. Of these patients, 248 patients underwent TEE for suspected cardioembolic stroke within 1 week of the initial stroke, except in patients (n = 83) with decreased consciousness, impending brain herniation, poor systemic conditions, tracheal intubations, or failure in receiving an esophageal transducer. Of these, 142 patients, who had >2 risk factors for coronary artery disease were prospectively enrolled to perform 2-phase CCTA for...
evaluation of coronary artery disease and potential cardiac embolic sources. Five patients who had contrast agent allergy (n=2), renal dysfunction (n=1), or failed to provide an informed consent (n=2) were excluded. Finally, the remaining 137 patients with >2 risk factors for coronary artery disease were included. All examinations were performed within a 5-day interval (mean, 2.8 days). All patients underwent brain CT or brain MRI to characterize the stroke and to exclude hemorrhages and other causes. The patients consisted of 91 men and 46 women, aged from 37 to 85 years (mean age, 61 years).

Baseline clinical characteristics, including systemic hypertension, hyperlipidemia, diabetes mellitus, and smoking habits, were determined from medical records and routine laboratory data.

Subtypes of ischemic stroke were classified according to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification system. Whereas the TOAST classification does not define how to categorize a patient with aortic atheromas, which is a significant cause of stroke, atheroma ≥4 mm in the ascending aorta and aortic arch was classified as cardioembolism in this study. The stroke subtypes of 331 patients were stroke of undetermined etiology (n=6, 2%), cardioembolism (n=97, 29%), large artery atheroma (n=122, 40%), and stroke of undetermined etiology (n=6, 2%).

**CCTA Examination**

We performed 2-phase CCTA using a 64-slice helical CT (Sensation 64; Siemens Medical Solutions). The scan protocol included both an early-phase scan to evaluate the coronary arteries, and cardioembolic sources (eg, intracardiac thrombus, intracardiac shunt), and a late-phase scan to differentiate between a thrombus and circulatory stasis and to evaluate aortic atheromas. The mean laboratory testing of all patients after 2-phase CCTA examinations.

A β-blocker (40 mg propranolol hydrochloride; Pranol; Dae Woong) was administered orally to reduce the heart rate 1 to 2 hours before examination in patients with a heart rate >65 beats per minute. The mean heart rate was 61±12 beats per minute (range, 51–87 bpm) during the CT examination. Contrast solution, composed of 75 mL of nonionic contrast agent (370 iodine mg/mL; Iopamiro; Bracco) chased by a 50-mL saline solution was administered intravenously at a rate of 5 mL/sec using a power injector (Envision CT; Medrad).

Early-phase scanning was started with a time delay determined by the bolus-tracking technique using a region of interest in the ascending aorta to monitor a threshold of 100 Hounsfield units. The following echocardiographic abnormalities were considered a possible cardiac source of embolism: LA or LAA thrombus, left ventricle thrombus, cardiac tumors, valve vegetation, infective en-
were seen in the left-side cardiac chambers within 3 cardiac cycles of the main cavity. PFO was considered to be present if any microbubbles were transiently detectable with optimal gain settings transiently none, the absence of this phenomenon; mild, minimal echogenicity as compared to the valve. SEC was characterized by dynamic clouds of echoes curling slowly in a circular or spiral shape within the LAA as compared to the valve. SEC was defined as a filling defect that appeared as a triangular shape in the LAA only on early-phase images but was absent on late-phase images. PFO was defined as the presence of a contrast jet from the contrast-filled LA to the saline-filled right atrium (RA) toward the inferior vena cava (IVC) with a channel-like appearance of the interarterial septum.\textsuperscript{11,12} Atrial septal defect was defined as the presence of a contrast jet from contrast-filled LA to the saline-filled right atrium perpendicular to the septum without the channel-like appearance of an interarterial septum. ASA was defined as an abnormally bulging of the interatrial septum with an excursion of $\geq 10$ mm and a base span $\leq 15$ mm.\textsuperscript{15} Sessile aortic atheroma was considered to be a discrete, nonmobile lesion $\geq 4$ mm in the ascending aorta, or the aortic arch.\textsuperscript{16}

In TEE, a thrombus was defined as a well-circumscribed, uniformly consistent, echo-reflective mass of a different texture from the LA or LAA wall. Valvular vegetations were diagnosed as echo densities on the mitral or aortic valves that had independent motion the LA or LAA wall. Valvular vegetations were diagnosed as echo-reflective mass of a different texture from the LA or LAA wall. Valvular vegetations were diagnosed as echo densities on the mitral or aortic valves that had independent motion the LA or LAA wall. Valvular vegetations were diagnosed as echo-reflective mass of a different texture from the LA or LAA wall. Valvular vegetations were diagnosed as echo densities on the mitral or aortic valves that had independent motion. Echocardiographic findings were categorized into high- and medium-risk sources based on their relative propensities for causing embolism according to the TOAST classification system.\textsuperscript{13,14}

Continuous variables were expressed as mean (SD) and were compared between 2 groups with the Student \( t \) test for independent samples. For all imaging modalities, we recorded the number of the detected cardiac sources of embolism. Using TEE as the reference standard, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of CCTA for detecting cardiac sources of embolism were calculated; 95\% CI were calculated by using the method of exact binomial tail areas.\textsuperscript{17} The analysis was performed on a per-lesion and per-patient basis. On a per-patients analysis, patients with both high- and medium-risk sources were categorized as high-risk sources.

All statistical analyses were performed with SPSS software (Version 10.0; Statistical Package for the Social Sciences).

### Results

The image quality of all CCTA examinations was considered acceptable for the evaluation of intracardiac abnormalities. However, there were some nonassessable segments for eval-

<table>
<thead>
<tr>
<th>Cardiac Sources</th>
<th>All Lesions</th>
<th>All Patients</th>
<th>High-Risk Lesions</th>
<th>High-Risk Patients</th>
<th>Medium-Risk Lesions</th>
<th>Medium-Risk Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>True-positive</td>
<td>89</td>
<td>85</td>
<td>44</td>
<td>45</td>
<td>45</td>
<td>40</td>
</tr>
<tr>
<td>False-negative</td>
<td>46</td>
<td>46</td>
<td>46</td>
<td>46</td>
<td>46</td>
<td>46</td>
</tr>
<tr>
<td>False-positive</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>False-negative</td>
<td>11</td>
<td>6</td>
<td>3</td>
<td>2</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>89</td>
<td>93</td>
<td>94</td>
<td>96</td>
<td>83</td>
<td>91</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>81</td>
<td>88</td>
<td>94</td>
<td>96</td>
<td>84</td>
<td>92</td>
</tr>
</tbody>
</table>

\*In a per-patient analysis, patients with both high- and medium-risk sources were categorized as high-risk sources.
In 91 patients were found on TEE. Furthermore, 10 patients had atrial fibrillation (AF). Of these 137 patients, 100 abnormal findings except for those in AF. Fifty-seven patients (42%) were in AF at the time of their stroke. AF was more commonly observed in patients with an abnormal finding on TEE.

The potential cardiac sources of embolism detected by TEE and CT are summarized in Table 2. On TEE, 100 abnormal findings were detected in 91 patients, whereas 89 abnormal findings were detected in 91 patients by CT, including 11 false-negative results (Table 2). Using TEE as the reference standard, the overall sensitivity, specificity, PPV, and NPV of the 64-slice CCTA for detecting cardiac sources of embolism were 89% (95% CI, 82%, 95%), 100% (95% CI, 90%, 100%), 100% (95% CI, 95%, 100%), and 81% (95% CI, 70%, 92%), respectively (Table 3).

In a per-patient analysis, 91 stroke patients had at least 1 abnormal finding on TEE. Of these 91 patients, 6 patients had missed cardiac embolic sources with CT. Therefore, using TEE as the reference standard, the overall sensitivity, specificity, PPV, and NPV of the 64-slice CCTA for detecting cardiac sources of embolism were 93% (95% CI, 87%, 99%), 100% (95% CI, 90%, 100%), 100% (95% CI, 95%, 100%), and 88% (95% CI, 78%, 98%), respectively (Table 3).

For the detection of high-risk sources for cardiac embolic stroke, TEE detected a total of 47 abnormal findings, whereas CT detected 45 abnormal findings (Table 2). Using TEE as the reference standard, the overall sensitivity, specificity, PPV, and NPV of the 64-slice CCTA for detecting medium-risk cardiac sources of embolism were 83% (95% CI, 71%, 94%), 100% (95% CI, 90%, 100%), 100% (95% CI, 90%, 100%) and 84% (95% CI, 73%, 95%), respectively (Table 3).

In a per-patient analysis, 44 patients had medium-risk sources on TEE. Of these 44 patients, 4 patients had missed cardiac embolic sources with CT. Using TEE as the reference standard, the overall sensitivity, specificity, PPV, and NPV of the 64-slice CCTA for detecting medium-risk cardiac sources of embolism were 91% (95% CI, 81%, 100%), 100% (95% CI, 90%, 100%), 100% (95% CI, 89%, 100%), and 92% (95% CI, 83%, 100%), respectively (Table 3).

On TEE, there was a total of 15 SEC, and all were correctly detected by 2-phase 64-slice CCTA. By CT, all SEC detected on TEE showed typical finding of a filling defect that appeared as a triangular shape in the LAA only on early-phase imaging.
images but was absent on late-phase images (Figure 2). Of the 15 filling defects diagnosed correctly as circulatory stasis without thrombus by CT, SEC was categorized as severe in 6 cases, moderate in 7 cases, and mild in 2 cases. TEE detected a total of 19 PFO and 3 atrial septal defects. Fifteen of 19 patients had PFO diagnosed by the showing of microbubbles on the left-side cardiac chambers within 3 cardiac cycles of the maximum right atrium opacification after agitated saline injection, whereas 4 of 19 cases were diagnosed by a showing of a turbulent color jet within the interarterial septum on Doppler TEE, even though no microbubbles were seen. On CT, LA to right atrium contrast jet toward the inferior vena cava was found in 14 patients, and contrast jet perpendicular to the septum was found in 3 patients (Figure 3). All 3 atrial septal defects were correctly diagnosed by CT. However, of the 19 PFO, 14 lesions were correctly diagnosed by CT (73%, 14 of 19). Four PFO were combined with ASA, and 3 of 4 lesions were correctly diagnosed by CT. Of the 11 ASA, 8 lesions were correctly diagnosed by CT (73%, 8 of 11; Figure 4).

Discussion

This study demonstrates that 2-phase 64-slice CCTA is a useful modality for the detection of cardiac sources of embolism in stroke patients. The diagnostic performance for the detection of high-risk cardiac sources of embolism by 2-phase 64-slice CCTA was excellent and comparable to TEE.

In our study, we categorized cardiac sources of embolism detected on TEE into high- and medium-risk sources according to the TOAST classification systems. The TOAST classification system defines high- and medium-risk cardiac sources based on their relative propensities for causing an embolism. For high-risk embolic sources, antiocoagulation is an indication for therapeutic management; however, medium-risk sources have more modest or undefined risks and little randomized comparative evidence to guide management. Therefore, in determining the effectiveness of therapeutic management, the detection of high-risk cardiac sources is more important.

In our study, 2-phase CCTA showed high sensitivity (94%) and high specificity (100%) in the detection of high-risk cardiac sources as compared with TEE. The highly accurate diagnostic performance strongly suggests that 2-phase CCTA could be useful in the detection of high-risk cardiac sources of embolism in stroke patients. Although there were 3 false-negative results, the 12 thrombi diagnosed by TEE were all correctly diagnosed by CCTA.

For the detection of medium-risk sources, the diagnostic yield of CT was lower compared to TEE, especially for diagnosing PFO. Recently, there have been a few reports on the multi-detector row CT findings of a PFO that were channel-like appearances of the interarterial septum and left-to-right interatrial shunt. In our study, LA to right atrium contrast jet toward the inferior vena cava was found in 14 patients on CT, and all these patients had PFO diagnosed with TEE. We believe that the lower sensitivity for diagnosing PFO by CT is caused by the fundamentally different principles for diagnosing PFO between TEE and CT. TEE diagnoses of PFO were made by detecting momentary right-to-left shunts with a provocative maneuver, whereas CT diagnoses were made by detecting a left-to-right shunt in the resting state. Therefore, in diagnosing PFO, CT has its limitation in that although routine cardiac CT during the resting state can anatomically detect PFO, it fails to analyze the functional aspects of PFO by pointing out the clinically significant cases. For example, PFO with high membrane mobility and right-to-left shunting at rest are more associated with cryptogenic stroke.
In our study, the diagnostic yield of CT for detection of thrombus, aortic atheroma, and SEC were high, which can be anatomically detected by CT. However, the diagnostic yield for detection of PFO or ASA was lower by CT as compared to TEE, which need provocative maneuver for their diagnosis. This result suggests that CT can have limitation in the detection of cardioembolic sources, especially in younger stroke patients, because it is known that the incidence of PFO, ASA, or a combination of both are higher in younger stroke patients or with cryptogenic stroke.19,20 For many cardiac risk sources of embolism, referred to as medium-risk sources, the optimal choice of therapy is not clear. At present, there is not enough evidence in the literature to recommend anticoagulation therapy over aspirin in patients with medium-risk factors; therefore, TEE does not provide therapeutic gains in terms of medical treatment.21–24 Furthermore, the diagnostic performance of the CCTA for detecting medium-risk sources was improved in a per-patient analysis. In that respect, we believe that 2-phase CCTA can be used as a screening test for detecting potential cardiac sources of embolism in selected stroke patients before TEE, because it has high diagnostic accuracy in the detection of high-risk cardiac sources of embolism and is a noninvasive modality. Our study had several limitations. First, we did not perform CCTA studies in all stroke patients who underwent TEE. For CCTA indication, we selected patients who had >2 risk factors for coronary artery disease. This would potentially yield an older stroke population with increased likelihood that CCTA would identify high-risk sources of embolism, such as aortic plaques. It is known that the prevalence of medium-risk sources would be expected to be higher in a younger population.19,20 Therefore, the frequencies of some cardiac sources of embolism, particularly those that are dependent on echocardiographic studies, could be underestimated and the overall results could be affected. Second, we did not perform the 2 examinations on the same day. All examinations were performed within a 5-day interval to evaluate for intracardiac sources of embolism. A further limitation was radiation exposure. Although we performed 2-phase imaging, we used prospective ECG gating and lowered the mAs to 200 for the late-phase imaging to reduce the radiation dose. Therefore, the additional radiation dose for late-phase imaging was small.

Conclusion

Two-phase 64-slice CCTA is a useful modality for detecting potential cardiac sources of embolism in stroke patients. In addition, 2-phase CCTA exhibits excellent diagnostic performance in the detection of high-risk cardiac sources of embolism, which have absolute indications for oral anticoagulation therapy.

Disclosures

None.

References