Usefulness of Dual-Phase Snapshot 320-Detector Computed Tomography for the Detection of a Left Atrial Appendage Thrombus

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Summary

The diagnostic performance of 320-detector cardiac computed tomography (CCT) for the detection of thrombi in the left atrial appendage (LAA), relative to transesophageal echocardiography (TEE) as the gold standard, has not yet been evaluated. A total of 91 consecutive patients who were scheduled to undergo pulmonary vein isolation and underwent TEE and CCT were enrolled in this study. Delayed scanning on CCT was performed following early scanning, at 60 seconds after the start of the contrast injection. The radiation dose was estimated for both scans. The early scans showed a contrast medium filling defect (FD) in the LAA in 27 patients, whereas the delayed scans showed an FD in the LAA in six patients. Of these, five patients were confirmed to have a thrombus in the LAA by TEE. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 100, 74.4, 18.5, 100, and 75.8% for early scanning and 100, 98.8, 83.3, 100, and 98.9% for delayed scanning, respectively. The area under the curve for the detection of a thrombus in the LAA on the delayed scans was significantly larger than that for the detection on the early scans (0.99 versus 0.87, \( P < 0.001 \)). The estimated median radiation doses for the early and delayed scans were 2.86 and 0.42 mSv, respectively. Addition of delayed scanning to early scanning improved the diagnostic performance for the detection of a thrombus in the LAA and may obviate unnecessary TEE, with minimal additional radiation exposure.

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Key words: Cardiac computed tomography, Transesophageal echocardiogram

Atrial fibrillation (AF) is one of the most common arrhythmias related to thromboembolism\(^1\) and is characterized by the reduction of the cardiac output and uncomfortable symptoms, such as palpitation and dyspnea on exertion.\(^2\) The number of patients with AF is increasing and is expected to reach over one million in Japan by the year 2050.\(^3\) Clinically, pulmonary vein isolation (PVI) is frequently used in patients with symptomatic AF to improve their symptoms and exercise tolerance.\(^4\)

However, PVI is contraindicated in patients with a left atrial appendage (LAA) thrombus. Transesophageal echocardiography (TEE) is commonly used as the gold standard for the detection of LAA thrombi; this technique shows adequate sensitivity and specificity (83-93% and 97-100%, respectively).\(^5,6\) However, TEE is an invasive procedure, with severe complications (i.e., bronchospasm, hypoxia, complete atioventricular block, angina pectoris, and esophageal bleeding) reported in 0.18% of the cases.\(^7\) Moreover, according to one report, there was one hemorrhagic death among 10,218 patients undergoing TEE.\(^8\)

Clinical guidelines for AF ablation recommend the use of enhanced cardiac computed tomography (CCT) for the visualization of anatomical structures around the left atrium (LA) prior to the PVI procedure.\(^9\) CCT is also useful for visualizing contrast medium filling defects (FDs) in the LAA suggestive of thrombi or sluggish flow. It has been shown in previous studies that the addition of delayed scanning to CCT could be a reliable alternative to TEE for the detection of LAA thrombi.\(^9,10-14\) In these studies, 64-detector CT was used; however, the diagnostic performance of 320-detector CT is still unclear.

In addition, electrical cardioversion (ECV) for restoring the sinus rhythm is often used in patients with symptomatic persistent AF before converting to permanent AF,\(^15\) especially in patients resistant to pharmacological cardioversion. It has been reported in previous studies that ECV may impair LAA function because of atrial stunning.\(^16-19\)

The aim of this study was to clarify the diagnostic performance of CCT with delayed scanning for the detec-
tion of thrombi in the LAA and to estimate the radiation exposure associated with 320-detector CCT.

Methods

Patient population: In this study, we enrolled consecutive patients with symptomatic paroxysmal or persistent AF who were scheduled to undergo PVI from August 2016 to May 2017 at Nihon University Hospital. CCT was performed in all of the patients after TEE. After the presence of an LAA thrombus was excluded by TEE, ECV was performed in some patients to restore the sinus rhythm. Atrial stunning due to ECV would have an influence on the results of CCT; therefore, we excluded patients in whom ECV was performed.

The exclusion criteria were as follows: performing of ECV, allergy to contrast medium, and uncontrolled bronchial asthma, thyroid disease, and/or chronic kidney disease. This study and its protocol were approved by the ethics committee of Nihon University Hospital (Nihon University 20160705).

TEE procedure: All patients underwent 3D-TEE using EPIQ 7 (Philips, Amsterdam, the Netherlands) prior to CCT, without any complications. The average flow velocity (cm/second) in the LAA was measured by pulse wave Doppler in all patients. Two experienced cardiologists blinded to the CCT findings assessed the images visually for the presence of LAA thrombi.

CCT procedure: All patients underwent contrast-enhanced CCT (320-detector CT, Aquilion ONE Vision Edition; Toshiba, Tokyo, Japan) with a nonionic contrast agent (Iomerion 350; Eisai, Kamisui, Japan) administered via the right median cubital vein. If the patient’s heart rate was over 65 bpm, we administered an injection of lindolol hydrochloride (Ono Pharmaceutical, Osaka, Japan) prior to the CCT in order to reduce the patient’s heart rate. The real-time bolus tracking method was used as the CCT scanning mode. Scanning was started when the CT value of the region of interest set in the ascending aorta reached 150 HU. The exposure phases with the prospective electrocardiogram-gated technique were as follows: 75-85% for stable heart rates under 65 bpm, 35-85% for unstable heart rates under 65 bpm, 65-85% for stable heart rates of 65-75 bpm, 35-85% for unstable heart rates of 65-75 bpm, and 100% for heart rates over 75 bpm. The tube voltage for the CCT was 100 kV for patients with a body mass index (BMI) of <30 kg/m² and 120 kV for those with a BMI of ≥30 kg/m².

After the initial early scanning, the delayed scanning was started 60 seconds after the start of the contrast injection. The area of the delayed scan was 6 cm from the carina and below without table displacement at a tube voltage of 80 kV. Two experienced cardiologists blinded to the TEE findings assessed the CCT images reconstructed by multplanar reconstruction for the presence/absence of an FD in the LAA. All images were analyzed using a workstation (Ziostation2 Version 2.9.0.2; Ziosoft, Inc., Tokyo, Japan). The dose-length product (DLP) was automatically measured by the CT equipment. Radiation exposure in each patient was calculated using the following formula: estimated radiation exposure = DLP × 0.014 (mSv).

Statistics: Numerical variables are expressed as the means ± standard deviation (SD) for normally distributed distributions or as medians [interquartile ranges] for non-normally distributed variables. The normality of distribution for each parameter was tested using the Kolmogorov-Smirnov test. Categorical variables were compared using the chi-squared test, whereas the continuous variables were analyzed using Student’s t-test or Mann-Whitney U test, as appropriate. The diagnostic performance was evaluated by receiver operating characteristic curve analysis. A two-sided P-value of <0.05 was considered statistically significant. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (the R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient characteristics: A total of 91 patients were enrolled in this study, whose characteristics are shown in Table I. Of these 91 patients, 51 (56.0%) had paroxysmal AF, 27 (29.7%) had persistent AF, and 13 (14.3%) had long-standing persistent AF (AF lasting more than one year). The median interval between the TEE and CCT was three days (range: 1-15 days).

FD and thrombus in the LAA: FDs in the LAA were detected in 27 and 6 patients on the early and delayed scans, respectively. Of these, the presence of an LAA thrombus was confirmed by TEE in five patients (Table II). The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of the early and delayed scans for the detection of an LAA thrombus were as follows: 100, 74.4, 18.5, 100, and 75.8% and 100, 98.8, 83.3, 100, and 98.9%, respectively. The area under the curve (AUC) for the detection of an FD in the LAA on the delayed scans was significantly larger than that on the early scans (0.99 versus 0.87, P < 0.001).

There was only one case of discrepancy between the findings of CCT on the delayed scans and TEE. The characteristics of this case were as follows: 79-year-old female, long-standing persistent AF, enlarged left atrial dimensions as confirmed by TTE (44 mm), larger LAA size relative to the size in other cases, and LAA flow velocity low as determined by TEE (17.5 cm/second).

After the TEE and CCT, the PVI procedure was conducted in all patients without an LAA thrombus. There were no cases of cerebral stroke, systemic embolism, or severe complications during or after the procedure in these patients.

TEE Doppler findings: The median LAA flow velocity was 40.0 [29.5, 58.5] cm/second. The LAA flow velocity in patients with an FD in the LAA was significantly lower than that in those without an FD in the LAA (21.8 versus 41.5 cm/second, P < 0.001).

Radiation exposure: The median DLP for the delayed scans was significantly lower than that for the early scans (29.7 [29.3, 38.1] versus 204.0 [182.6, 386.5] mGy · cm, P < 0.001). The estimated median radiation exposure...
Representative cases: A 60-year-old male with no thrombus in the LAA detected by TEE (Figure 1A, arrow) showed an FD in the LAA in the early scans (Figure 1B, arrow). However, the FD suggestive of a thrombus in the LAA disappeared on the delayed scan (Figure 1C, arrow).

A 79-year-old female who was found to have a thrombus in the LAA by TEE (Figure 2A, arrow) showed an FD in the LAA on both early and delayed scans (Figures 2B, 2C arrows). This FD was considered as representing a thrombus in the LAA.

Discussion

The structures of the LA and pulmonary veins (PVs) are complex and variable; supernumerary PVs are observed in 16-25% of the cases on enhanced CCT.\(^\text{22,23}\) Enhanced CCT is frequently used to visualize the LA, PVs, esophagus, and the structures around them and also to detect the presence of coronary artery stenosis. CCT evaluation may help make the PVI procedure safer by avoiding complications, and an expert consensus statement\(^\text{14}\) recommends that CCT or CMR be performed prior to PVI for integrated anatomical mapping, such as using the CARTO system (Johnson & Johnson Inc., Biosense Webster, Diamond Bar, CA, USA).

TEE is an uncomfortable procedure that is associated with severe complications in a small, but definite, population of patients, which must be considered. LAA thrombi confirmed by TEE would be visualized as FDs in the LAA on CCT images, because of the insufficient mixing of contrast medium and blood in the LA. We speculated that delayed scanning may be more effective because an adequate time interval allows for enough contrast mixing in LA before scanning.

### Table I. Patient Characteristics

| Number of patients | n = 91 |
|--------------------|-------|
| Age (years)        | 67.7 ± 11.3 |
| Males              | 68 (74.7) |
| Height (cm)        | 164.3 ± 8.3 |
| Body weight (kg)   | 66.7 ± 14.9 |
| BMI (kg/m²)        | 24.3 ± 5.1 |
| AF type            |       |
| Paroxysmal AF      | 51 (56.0) |
| Persistent AF      | 27 (29.7) |
| LS-AF              | 13 (14.3) |
| HT                 | 52 (57.1) |
| DM                 | 23 (25.6) |
| History of CHF     | 8 (8.9) |
| CHADS² score       | 1.0 [1.0, 2.0] |
| CHADS²-VASc score  | 2.0 [1.0, 3.5] |
| LVEF by TTE        | 63.3 ± 11.0 |
| Moderate or severe MR | 25 (27.5) |
| LAD by TTE (mm)    | 42.0 ± 7.3 |
| Interval between TEE and CCT (days) | 3.0 [1.5, 15.0] |
| AF at the time of CCT | 40 (44.0) |
| HD                 | 7 (7.7) |
| OAC                | 85 (93.4) |

Values are represented as the mean ± SD, n (%), or median [interquartile range]. AF indicates atrial fibrillation; BMI, body mass index; CCT, cardiac computed tomography; CHADS², congestive heart failure, hypertension, age > 75 years, diabetes mellitus, prior stroke or TIA or thromboembolism; CHADS²-VASc, congestive heart failure, hypertension, age > 75 years (doubled), diabetes mellitus, prior stroke or TIA or thromboembolism (doubled), vascular disease, Age 65 to 74 years, sex category; HD, heart failure; LAD, left atrial dimension; LS-AF, long-standing persistent AF (AF lasting more than one year); LVEF, left ventricular ejection fraction; MR, mitral regurgitation; OAC, oral anticoagulant; TEE, transthoracic echocardiography; and TTE, transthoracic echocardiography.

### Table II. Relationship between CCT and TEE

| TEE          | Thrombus | No thrombus | Total |
|--------------|----------|-------------|-------|
| CCT early scan |          |             |       |
| FDs          | 5        | 22          | 27    |
| No FDs       | 0        | 64          | 64    |
| Total        | 5        | 86          | 91    |
| CCT delayed scan |       |             |       |
| FDs          | 5        | 1           | 6     |
| No FDs       | 0        | 85          | 85    |
| Total        | 5        | 86          | 91    |

CCT indicates cardiac computed tomography; TEE, transthoracic echocardiography; and FD, filling defect.

Figure 1. No thrombus detected by TEE (arrow in A). FD suggestive of a thrombus in the LAA on an early scan (arrow in B), which was no longer present in the delayed scan (arrow in C).
We showed an improvement in the diagnostic performance of CCT by the addition of delayed scanning alone to early scanning (AUC for detection of an FD in the LAA: 0.99 versus 0.87, \(P < 0.001\)). In previous studies, the usefulness of the addition of delayed scanning in 64-detector CT performed for detecting FDs in the LAA was reported.\(^{11,12,24}\) According to a meta-analysis, the diagnostic performance of delayed scanning for the detection of an FD in the LAA is actually high (the sensitivity, specificity, PPV, NPV, and accuracy were 100, 99, 92, 100, and 99\%, respectively).\(^{14}\) In the present study, we evaluated, for the first time, the diagnostic performance of delayed scanning in 320-detector CT for the detection of FDs in the LAA in a Japanese prospective population. Our study revealed that the diagnostic performance of the delayed scan was comparable to that reported by the aforementioned meta-analysis.

ECV to restore the sinus rhythm in patients with symptomatic AF is clinically useful for relieving a patient’s chest discomfort before PVI; however, ECV decreases the LAA flow velocity due to atrial stunning, which was confirmed by TEE.\(^{17-19}\) Therefore, we excluded patients who underwent ECV before CCT in this study. No previous report has specified whether the patients had undergone ECV before the CCT or not.

The present study showed that the average LAA flow velocity in patients with FDs in the LAA was significantly lower than that in those without FDs in the LAA. Insufficient contrast filling would also cause an FD in the LAA and a false-positive diagnosis of LAA thrombus. In the present study, there was only one case of discrepancy between the results of CCT with delayed scanning, which showed an FD in the LAA, and TEE, which did not show any thrombus. This patient had long-standing persistent AF, an enlarged LA, a relatively large-sized LAA, and a low LAA flow velocity. Therefore, we should pay attention to patients with these characteristics in whom the presence of an FD in the LAA on CCT may lead to a mistaken diagnosis in the absence of a thrombus in the LAA.

Addition of delayed scanning to early scanning caused extra radiation exposure to the patients (median: 0.42 mSv) in this study. While a statistical comparison would not be appropriate, slightly higher radiation exposure by 0.5-1.3 mSv was documented in previous manuscripts dealing with 64-detector CT.\(^{9,24}\) This minimum additional radiation exposure dose in the 320-detector CT in the present study was achieved by one-rotation scan without table displacement using a wider field of view.

TEE is, for all practical purposes, the gold standard for the detection of a thrombus in the LAA. While there are variations in the reported diagnostic performance of CCT between previous studies and our present study for the detection of an FD in the LAA, all have shown a consistently high NPV. This high NPV (100\% in most reports) indicates that CCT could become an alternative modality for excluding the presence of an LAA thrombus. Particularly in patients in whom CCT shows the absence of a thrombus in the LAA before PVI, the unnecessary and uncomfortable TEE procedure can be avoided. In addition, this also decreases the cost and saves time. If an equivocal FD in the LAA is found on delayed scans, we recommend that the patient undergo the semi-invasive TEE.

In regard to the time interval between the early and delayed scans, we chose a fixed 60-second interval after the start of the contrast injection for the delayed scanning. In other reports, this interval varies from 60 to 180 seconds.\(^{14}\) A long interval between the early and delayed scanning may cause low attenuation of the contrast medium in the LAA and a decrease in the signal-to-noise ratio. We chose fixed a 60-second interval, which yielded an adequate diagnostic performance.

The low prevalence of thrombi in the LAA (5.5\%) in this study seems to be comparable to the average prevalence (3.2\%) reported in previous studies.\(^{12,25-32}\) This low prevalence of thrombi would affect the PPV; therefore, visualization of FDs in the LAA by CCT needs to be confirmed by the semi-invasive TEE.

Conclusion

Addition of delayed scanning in 320-detector CCT for the detection of a thrombus in the LAA resulted in a significantly higher diagnostic performance of the modality, as compared to early scanning only. Addition of delayed scanning in CCT is expected to help obviate the need for the unnecessary semi-invasive TEE prior to PVI, with minimal additional radiation exposure.
Disclosures
Conflicts of interest: None to declare.

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