

# Predictors of Spontaneous Echocardiographic Contrast Within the Left Atrial Appendage in Cardiac Computed Tomography of Patients with Atrial Fibrillation

Kotaro Ouchi (✉ [kotaro-alex@jikei.ac.jp](mailto:kotaro-alex@jikei.ac.jp))

Jikei University School of Medicine: Tokyo Jikeikai Ika Daigaku <https://orcid.org/0000-0002-0228-6845>

Toru Sakuma

Jikei University School of Medicine: Tokyo Jikeikai Ika Daigaku

Takahiro Higuchi

Jikei University School of Medicine: Tokyo Jikeikai Ika Daigaku

Jun Yoshida

Jikei University School of Medicine: Tokyo Jikeikai Ika Daigaku

Ryosuke Narui

Jikei University School of Medicine: Tokyo Jikeikai Ika Daigaku

Ayumi Nojiri

Jikei University School of Medicine: Tokyo Jikeikai Ika Daigaku

Teiichi Yamane

Jikei University School of Medicine: Tokyo Jikeikai Ika Daigaku

Hiroya Ojiri

Jikei University School of Medicine: Tokyo Jikeikai Ika Daigaku

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## Research Article

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# Abstract

## Purpose

Cardiac computed tomography (CT) depiction of the relationship between spontaneous echocardiographic contrast (SEC) and findings of the left atrial appendage (LAA) has not been reported. We evaluated predictors of SEC within the LAA using findings of cardiac CT in patients with atrial fibrillation (AF).

## Methods

We retrospectively analyzed cardiac CT findings of the LAA, including morphology, volume, and filling defects, of 641 patients who underwent Transesophageal echocardiography (TEE) prior to pulmonary vein isolation (PVI) from January 6, 2013 through December 16, 2019 at our institution. We investigated potential associated factors that might be predictors of SEC and computed a receiver operator characteristic, choosing a threshold value at which the likelihood of SEC could be predicted based on the LAA volume indexed for body size.

## Results

SEC correlated significantly with history of persistent AF ( $P < 0.001$ ; odds ratio [OR], 3.74; 95% confidence interval [CI], 1.91–7.29), LAA early filling defects ( $P = 0.003$ ; OR, 2.83; 95% CI, 1.43–5.62), LAAFV ( $P < 0.001$ ; OR, 0.97; 95% CI, 0.96–0.99), and indexed LAA volume ( $P = 0.001$ ; OR, 1.18; 95% CI, 1.07–1.30) of  $8.04 \text{ cm}^3/\text{m}^2$  or greater (sensitivity, 75.0%; specificity, 48.7%). The addition of LAAFV to indexed LAA volume increased the area under the receiver operator characteristic curve from 0.642 to 0.724 ( $P < 0.001$ ).

## Conclusion

Findings of LAA in cardiac CT might allow the noninvasive estimation of SEC and additional information for risk stratification and management of thromboembolic events in patients with AF.

## Introduction

Atrial fibrillation (AF) is the most common cause of cardiogenic embolism, and more than 90% of embolic strokes result from thrombi in the left atrial appendage (LAA) [1, 2]. The appearance of spontaneous echo contrast (SEC) in the LAA has been associated with a high risk of thromboembolic events and may represent the stage preceding thrombus formation [3, 4]. The CHADS<sub>2</sub> scoring scheme is a validated method for estimating the risk of stroke and the need for anticoagulation therapy in patients with AF [5], and LAA morphology and reduced LAA flow velocity (LAAFV) have been reported as important predictors of SEC and thrombus in the LAA and risk of stroke in these patients [6, 7]. The high spatial and temporal resolutions and multiplanar reconstruction capabilities of cardiac computed tomography (CT) allow noninvasive and detailed assessment of the cardiovascular system and good visualization of the LAA, but cardiac CT findings regarding the relationship between SEC and LAA have not been reported in

patients with AF. We therefore sought to define predictors of SEC using LAA findings in cardiac CT of patients with AF.

## Materials And Methods

Our institutional review board approved this retrospective observational study and waived the requirement for documentation of informed consent from patients. An opt-out option on our website allowed patients to decline inclusion of their data in the study.

## Patients

We identified 783 consecutive patients with AF who underwent Transesophageal echocardiography (TEE) evaluation of SEC and flow velocity in the LAA prior to percutaneous pulmonary vein isolation (PVI) at our institution between January 6, 2013 and December 16, 2019. Among these cases, we also assessed data of transthoracic echocardiography (TTE) performed within the 6 months prior to PVI and cardiac CT performed within the 3 months prior to PVI. We excluded 139 patients who did not undergo TTE and/or cardiac CT within that period and 3 patients whose CT data could not be analyzed because of image degradation caused by an artifact (one case), the absence of part of the LAA from imaging range (one case), and inability to recognize the LAA structure (one case). No patient demonstrated LAA thrombus on TEE. The final study included data of 641 patients (570 men, mean age,  $59.35 \pm 9.16$  years, age range, 26–81 years; 71 women, mean age,  $65.17 \pm 6.88$  years, age range, 44–79 years). When a patient underwent TEE more than once during the study period, we analyzed findings of only the initial TEE (Fig. 1). All patients who underwent PVI for AF routinely received anticoagulation therapies, either warfarin or non-vitamin K antagonist oral anticoagulants, prior to echocardiography and CT. For patients receiving warfarin, the international normalized ratio of prothrombin time (PT-INR) was controlled within the therapeutic range between 2 and 3 [8].

## Transesophageal Echocardiography

Transesophageal echocardiography was performed at our institution according to standard clinical procedure using one of 4 ultrasound systems: Pro Sound Alpha 10 (multiplane 5.0 MHz transducer) (Aloka, Tokyo, Japan); Pro Sound F75cv (multiplane 5.0 MHz transducer) (Hitachi, Tokyo, Japan); iE33™ (multiplane 2.0 to 8.0 MHz transducer) (Philips Healthcare, Best, The Netherlands); or EPIQ7 (multiplane 2.0 to 8.0 MHz transducer) (Philips Healthcare). All TEE examinations were performed within 3 months before the scheduled PVI procedure (interval between TEE and PVI, 0 to 10 days [mean 2.12 days] in the group with SEC and 0 to 93 days [mean 2.77 days] in the group without SEC). Lidocaine was used for local anesthesia of the hypopharynx. All patients received intravenous midazolam for conscious sedation. Multiple planes of the LAA, including a continuous view through the LAA from 0 to 180 degrees, were examined at the appropriate level within the esophagus. Detailed observations were made of all LAA structures. Flow velocity in the left atrial appendage was assessed using pulsed-wave Doppler

interrogation on TEE in the view at 0 and 90 degrees. Peak LAAFV was measured after optimally aligning the pulsed-wave Doppler signal with LAA flow using color flow imaging, with sampling done at the site where maximal flow velocities were obtained. The highest LAAFV between the two values for each patient was applied for further analysis. SEC was defined as dynamic “smoke-like” echoes characterized by a swirling motion and observed during the cardiac cycle using an optimal gain setting [9]. The observation of echo-dense material acoustically separate from the endocardium within the LAA confirmed a definite thrombus. Two echocardiographers blinded to the CT results interpreted all images.

## Transthoracic Echocardiography

Transthoracic echocardiography was performed according to standard clinical protocol. All patients underwent TTE within the 6 months prior to PVI (interval between TEE and TTE, -6 to 178 days [mean 28.97 days] in the group with SEC and -92 and 181 days [mean 27.97 days] in the group without SEC). Quantitative assessment of the left ventricular ejection fraction (LVEF) was determined using the modified Simpson’s method. Conventional TTE was performed using one of 5 ultrasound systems: Pro Sound Alpha 10 (1.5 to 4.3 MHz transducer) (Aloka, Tokyo, Japan); Pro Sound F75cv (3.0 MHz transducer) (Hitachi, Tokyo, Japan); Vivid E9 (3.3 MHz transducer) (GE Healthcare, Tokyo, Japan); Vivid 7 (3.3 MHz transducer) (GE Healthcare); or Artida™ (2.5 MHz transducer) (Canon Medical Systems, Tochigi, Japan).

## Computed Tomography

All patients underwent cardiac CT with either of 2 dual-source systems (SOMATOM® Definition Flash [SDFlash] or SOMATOM® Definition [SD], Siemens Medical Solutions, Forchheim, Germany) within the 3 months prior to PVI (interval between TEE and CT, 0 to 81 days [mean 20.22 days] in the group with SEC and -11 and 87 days [mean 20.29 days] in the group without SEC). The CT scan protocol did not call for the use of beta-adrenergic blocking agents prior to scanning. Patients were administered sublingual nitroglycerine a few minutes before CT scanning to allow simultaneous evaluation of the coronary artery. During scan acquisition, each patient received intravenous administration of contrast material (Iopamiron®, 370 mg I/mL; Bayer AG, Leverkusen, Germany). Early-phase scanning was controlled by bolus tracking in the ascending aorta and followed by injection of 30 mL of pure saline at the same speed when enhancement was achieved. Delayed-phase scanning began 60 seconds after the start of contrast material injection. The injection speed was computed using the formula: injection speed (mL/s) = body weight (kg) × 0.07 mL/s, and the volume of the iodine bolus was computed as: volume (mL) = injection speed × duration of CT data acquisition (seconds) + 5. Scan parameters were: slice collimation, 2 × 64 × 0.6 mm (SDFlash) or 2 × 32 × 0.6 mm (SD) with a z-flying focal spot; gantry rotation time, 280 ms (SDFlash) or 330 ms (SD); pitch, 0.2 to 0.5; tube voltage, 120 kVp; and tube current, 330 mAs (SDFlash) or 300 mAs (SD). Scanning ranged from the level of the carina to just below the dome of the diaphragm. We retrospectively applied electrocardiography (ECG) gating and ECG-dependent tube-current

modulation to reconstruct images. All reconstructed image data were transferred to workstations (MultiModality Workplace, Siemens), and ECG gating of data of transaxial slices (effective slice width, 0.75 mm; increment, 0.4 mm; medium-smooth convolution kernel B 36 F) permitted reconstruction of images. Reconstructed images were obtained during the 1-96% -R interval of the cardiac phase. Heart rates ranged between 39 and 148 beats per minute (bpm) (mean 64.75 bpm).

## Image Evaluation

Two radiologists with 9 and 25 years' experience in cardiovascular radiology who were blinded to the patient's history and TEE results retrospectively reviewed the CT examinations in consensus. In the present study, we classified the morphology of the LAA into 4 types according to the shape and complexity of the appendage—chicken-wing, wind-sock, cauliflower, and cactus— using 3-dimensional volume-rendered structures based on findings of a previous study [10] (Fig. 2). The chicken-wing type displays only one lobe (length > 40 mm) and demonstrates bending of less than 100 degrees in the proximal part of the LAA; the wind-sock type shows one dominant lobe (length > 40 mm) with several secondary, or even tertiary, lobes and bending that exceeds 100 degrees; the cauliflower type is characterized by its length less than 40 mm and complex internal structures; and cactus type morphology manifests a dominant central lobe (length < 40 mm) with one or more secondary lobes.

LAA early filling defect was defined as a clear low attenuating lesion representing incomplete mixing of the contrast agent and blood that appeared only on early-phase images and demonstrated complete homogenous enhancement on late-phase images [11] (Fig. 3).

We quantified the volume of the LAA from its contours as depicted in cross-sectional images obtained using SYNAPSE VINCENT® 3-dimensional analytical volume software (Fujifilm Medical Co., Tokyo, Japan) (Fig. 4). The operator contoured and filled the LAA at each slice (Figs. 4a–c, green area), and the computer added the volumes of all of the slices to calculate the LAA volume; volumes of the slices were calculated automatically by multiplying the contoured area and slice thickness in cubic centimeters (cm<sup>3</sup>) (Fig. 4d). The ostium of the LAA was defined by the plane that connected between the base of the Coumadin ridge and the proximal left circumflex artery [12]. These procedures were evaluated against the original transverse images and multiplanar reformations that included short- and long-axis views of the heart. LAA volume was indexed for body size by dividing by body surface area calculated using the DuBois formula.

One radiologist with 9 years' experience in cardiovascular radiology who was blinded to the patient's history and the results of TEE and TTE performed visual and quantitative measurement of the LAA, and two assessors independently measured the LAA volume of 100 randomly selected patients to allow examination of inter-rater reliability [13]. The inter-observer agreement regarding LAA morphology was also evaluated using Cohen's kappa [14, 15].

## Statistical analysis

We tested normal distribution for the continuous variables to describe the frequencies and distributions of these factors and used Fisher's exact test to compare categorical data between the groups with and without SEC and Wilcoxon rank sum test and Student's t-test to compare continuous data between the 2 groups. Categorical variables were presented as number and percentage of cases, and continuous variables were presented as mean ( $\pm$  standard deviation [SD]) or median (interquartile range).

We prepared multivariable logistic-regression models to estimate the incidence of SEC with potential predictors that we selected based on previous studies and clinical perspectives associated with the appearance of SEC or LAA thrombus [5–7]. Before the multivariate logistic regression analysis, we analyzed statistics using the variance inflation factor (VIF) to check for multicollinearity and selected AF type (paroxysmal/persistent), CHADS<sub>2</sub> score, LVEF, LAAFV, indexed LAA volume, LAA morphology, and LAA early filling defect as independent variables. We assessed the odds ratios (OR) for each variable with 95% confidence intervals (CI).

A CHADS<sub>2</sub> score ranging from 0 to 6 was calculated for each patient at the time of TEE, assigning one point each to congestive heart failure (CHF), hypertension, or age above 75 years and two points each to history of stroke, transient ischemic attack (TIA), or systemic embolism [5, 16].

We classified AF as either paroxysmal, defined as recurrent AF terminating spontaneously or with intervention within 7 days of onset, or persistent, defined as AF failing to self-terminate within 7 days and considered longstanding when it failed to resolve after more than 12 months [17].

We also computed a receiver operator characteristic (ROC) curve for the completed model, choosing a threshold value at which the likelihood of SEC could be predicted based on the indexed LAA volume and estimating the resulting sensitivity and specificity.

We used intraclass correlation coefficients (ICC) to calculate inter-rater reliability for measurements of LAA volume (ICC 2, 1), and based on the 95% confidence interval of the ICC estimate, we judged reliability to be poor (values below 0.5), moderate (between 0.5 and 0.75), good (between 0.75 and 0.9), and excellent (above 0.90) [18].

We used  $\kappa$ -statistics to measure inter-rater reliability regarding the assessment of LAA morphology, with values below 0.2 representing slight agreement, between 0.21 and 0.40, fair agreement, 0.41 and 0.60, moderate agreement, 0.61 and 0.80, substantial agreement, and above 0.81, almost perfect agreement [19].

A *P*-value below 0.05 was considered statistically significant.

We conducted all statistical analyses using R commander 2.7-0 (R 4.0.2; CRAN, freeware).

## Results

The baseline characteristics of the patients are summarized in Table 1. As Compared to patients without SEC, those with SEC demonstrated significantly larger mean indexed LAA volume, decreased mean LAAFV and LVEF, a trend toward greater incidence of LAA early filling defect, and greater likelihood of history of persistent AF. There was no statistically significant difference in the other variables between the 2 groups.

Table 1

Clinical variables of patients with and without spontaneous echo contrast in the left atrial appendage (LAA)

	With (n = 78)	Without (n = 563)	<i>P</i> value	
Age	60.08 (8.68)	59.99 (9.18)	0.935	
Sex			1	
	Male	70 (89.7%)	500 (88.8%)	
	Female	8 (10.3%)	63 (11.2%)	
AF type				
	Paroxysmal	13 (16.7%)	255 (45.1%)	<0.001
	Persistent	41 (52.6%)	206 (36.6%)	
	Longstanding persistent	24 (30.8%)	102 (18.1%)	
Heart failure	8 (10.3%)	42 (7.4%)	0.37	
Hypertension	38 (48.7%)	266 (47.2%)	0.81	
Diabetes mellitus	11 (14.1%)	74 (13.1%)	0.858	
Stroke	7 (9.0%)	46 (8.1%)	0.826	
Dyslipidemia	28 (35.9%)	176 (31.3%)	0.437	
Smoking	31 (39.7%)	191 (33.9%)	0.313	
BSA (m <sup>2</sup> )	1.84 (0.19)	1.82 (0.18)	0.26	
CHADS <sub>2</sub> score	1.00 [0.00, 4.00]	1.00 [0.00, 5.00]	0.479	
LVEF (%)	61.95 [34.60, 72.00]	63.50 [21.50, 85.00]	0.019	
LAAFV (cm/s)	41.46 (16.16)	55.27 (22.78)	<0.001	
LAA volume (cm <sup>3</sup> )	14.41 (5.44)	11.78 (5.03)	<0.001	
Indexed LAA volume (cm <sup>3</sup> / m <sup>2</sup> )	7.75 [2.16, 17.68]	6.03 [1.70, 19.63]	<0.001	
LAA morphology			0.819	
	Chicken-wing	31 (39.7%)	230 (40.9%)	

AF, atrial fibrillation; BSA, area of the body surface; LAAFV, left atrial appendage flow velocity; LVEF, left ventricular ejection fraction

	With (n = 78)	Without (n = 563)	<i>P</i> value
Wind-sock	34 (43.6%)	215 (38.2%)	
Cauliflower	7 (9.0%)	62 (11.0%)	
Cactus	6 (7.7%)	56 (9.9%)	
LAA early filling defect	21 (26.9%)	37 (6.5%)	<0.001

AF, atrial fibrillation; BSA, area of the body surface; LAAFV, left atrial appendage flow velocity; LVEF, left ventricular ejection fraction

The results of the multivariate analysis are listed in Table 2. A significant correlation was found between SEC and a history of persistent AF ( $P < 0.001$ ; OR, 3.74; 95% CI, 1.91–7.29), LAAFV ( $P < 0.001$ ; OR, 0.97; 95% CI, 0.96–0.99), indexed LAA volume ( $P = 0.001$ ; OR, 1.18; 95% CI, 1.07–1.30), and LAA early filling defect ( $P = 0.003$ ; OR, 2.72; 95% CI, 1.43–5.62).

Table 2

Odds ratios for spontaneous echo contrast in the left atrial appendage (LAA) in multivariate logistic regression analysis

Variables	Odds ratio (95% CI)	<i>P</i> value
Persistent AF	3.74 (1.91-7.29)	<0.001
CHADS <sub>2</sub> score	1.15 (0.87-1.51)	0.33
LAA morphology	Chicken-wing (reference)	
	Wind-sock	0.80 (0.45-1.42) 0.44
	Cauliflower	1.72 (0.66-4.68) 0.26
	Cactus	1.52 (0.53-4.37) 0.43
Indexed LAA volume (cm <sup>3</sup> / m <sup>2</sup> )	1.18 (1.07-1.30)	0.001
LAA early filling defect	2.83 (1.43-5.62)	0.003
LAAFV (cm/s)	0.97 (0.96-0.99)	<0.001
LVEF (%)	0.99 (0.96-1.02)	0.42

AF, atrial fibrillation; LAAFV, left atrial appendage flow velocity; LVEF, left ventricular ejection fraction

We generated a ROC curve to identify threshold values for indexed volume at which SEC was most likely to appear (Fig. 5a) and observed the curve's inflection points at 8.04 cm<sup>3</sup>/m<sup>2</sup> (area under the curve (AUC), 0.642; sensitivity, 75.0%, specificity, 48.7%) for indexed LAA volume. We also determined if the addition of LAAFV parameter to a logistic-regression models that included indexed LAA volume improved SEC

prediction using the DeLong method. When LAAFV was added to indexed LAA volume, the AUC increased from 0.642 to 0.724 ( $P < 0.001$ ) (Fig. 5b).

Inter-rater reliability was excellent for measurements of LAA volume (ICC 0.99 [95% CI, 0.96– 0.97]) and LAA morphology ( $\kappa$  score 0.81).

## Discussion

Our findings support persistent AF and decreased FV, increased volume, and early filling defects of the LAA as independent predictors of SEC. Our ROC curve suggested an increased likelihood of SEC when the indexed volume exceeded  $8.04 \text{ cm}^3/\text{m}^2$ . The combination of LAA volume and LAAFV significantly improved the accuracy of SEC prediction.

Decreased LAAFV, increased LAA volume and persistent AF were independent predictors of SEC. The presence of SEC in the LAA has been associated with a high risk of thromboembolic events and may be the preceding stage to thrombus formation [3, 4]. Its appearance is thought to reflect increased erythrocyte aggregation caused by low shear rate due to altered atrial flow dynamics and uncoordinated atrial systole [20, 21]. Virchow's triad of factors related to thrombus formation includes abnormal changes in blood flow, constituents, and vessel walls. SEC may fulfill the first two components for thrombogenesis [22]. Spontaneous echocardiographic contrast in patients with AF has been associated with reduced LAA ejection velocity and findings of left atrial enlargement on transesophageal echocardiography (TEE) [23, 24]. Reduced LAAFV measured during TEE is a well-established risk factor for the development of SEC and thromboembolism. Magnetic resonance imaging (MRI) studies have shown larger mean LAA volumes in patients with a history of AF and stroke than those without stroke [25]. As well in our study, increased LAA volume was independent predictors of SEC and combination of LAA volume and LAAFV strengthened the accuracy of SEC prediction. Restriction of contractile function and flow velocity within the LAA can lead to thrombus formation [26]. It is reasonable to consider that abnormal blood flow affected by persistent AF could more likely lead to the development of SEC in the LAA in the same way as the thrombus develops, and patients with persistent or permanent AF have been more likely to occur embolization than those with paroxysmal AF [27–30]. Chicken-wing LAA has been reported to have the highest LAA-emptying flow velocity and lowest risk for the development of SEC, transient ischemic attack, and stroke [6, 7]. In contrast, we did not demonstrate the type of LAA morphology as a significant predictor for SEC. LAA morphology was originally divided into four types to help in the practical planning of placement of transcatheter LAA closure devices [31], but the anatomical features of LAA are actually more complicated. More rigorous definitions for the types of LAA might be required to assess the relationship between SEC and LAA morphology.

Depiction of filling defects in the LAA is challenging in early-phase CT. It has not been fully comprehend their significance in the absence of thrombus. It has been considered that inadequate blending of the contrast medium with blood or the encumbrance of contrast filling by the bulky pectinate muscles contribute to filling defects in the LAA [32, 33]. Our results showed that the filling defects observed reflect

slow-flow states that correlate with SEC. The incidental discovery of early LAA filling defects has increased with the use of cardiac CT, and physicians should be mindful that such findings might indicate the presence of SEC.

Our findings generate several hypotheses with potential implications for clinical decision-making. Identification of predictors of SEC on cardiac CT findings might allow noninvasive estimation of the risk of SEC which is associated with risk for thromboembolism. Although CT does not permit assessment of hemodynamics and function, CT has proven a safer, faster, and less invasive tool for the visualization and measurement of the LAA than TEE, the modality commonly used to assess LAA function [34]. Current guidelines for the management of atrial fibrillation recommend the scoring of CHADS<sub>2</sub> or CHA<sub>2</sub>DS<sub>2</sub>-VASc to estimate their risk of stroke and determine whether they would benefit from anticoagulation therapy [5, 35]. However, the prediction of stroke risk can be clinically perplexing in patients with lower CHADS scores. Although, to date, no guidelines have been put forward to guide the treatment of patients with SEC, the presence of SEC in the LAA has been associated with a high risk of thromboembolic events [3, 4]. Our results did not show the CHADS<sub>2</sub> score alone to be a significant predictor of SEC, which suggests that patients with SEC could have high risk of LAA thrombus independently of CHADS<sub>2</sub> score. Various clinical factors independently of the current CHADS<sub>2</sub>/CHA<sub>2</sub>DS<sub>2</sub>-VASc scoring, including SEC could determine the risk of thromboembolic events in patients with AF. The primary limitation to detect the presence of SEC in the LAA is that it requires TEE which is semi-invasive and requires conscious sedation. We expect that in patients with cardiac CT findings that predict SEC in the LAA, subsequent TEE evaluation is needed for its definitive identification and to assess the need or benefit of anticoagulant therapy. Validation of this hypothesis will involve prospective studies of to evaluate the relationship between SEC and actual thromboembolic events.

In this study, we measured LAA volume by manual segmentation of CT data and cursor tracing and observed excellent inter-rater reliability regarding LAA volume and morphology, though results using manual methods can be highly variable and create measurement bias. Indeed, the gold standard for image segmentation is that of manual labeling by a human expert [36]. However, automated segmentation to optimize LAA volume measurement is expected to address the shortcomings of this time-consuming method.

## Limitations

Our study was limited by its retrospective and observational approach. In addition, the make-up of our study population, patients with relatively low risk of stroke (mean CHADS<sub>2</sub> score, 0.88), reflects selection bias and does not permit the adaptation of our findings to a population with high stroke risk. However, our data may indicate factors to be considered in risk stratification in patients with AF with low CHADS<sub>2</sub> scores. As well, anticoagulant therapy in patients who underwent PVI for AF led to thrombus resolution and a lower incidence of stroke. However, the use of anticoagulants does not affect the presence of SEC because it does not change red-cell aggregation [37, 38]. In this study, the specificity of threshold for the

indexed LAA volume for SEC was not high. It's because the lack of unification of the cardiac phase of the reconstructed images might affect measurement results of LAA volume, especially in patients with paroxysmal AF. The retrospective study design did not allow us to evaluate the relationship between factors associated with SEC and actual thromboembolic events, nor did it allow us to investigate correlation between cardiac phase in reconstructed images and its effect on LAA volume in patients with paroxysmal AF. Future prospective studies should address these shortcomings and examine these relationships.

## Conclusions

We observed LAA findings of cardiac CT including increased volume and early filling defects as independent predictors of SEC in patients with AF. Cardiac CT findings might allow the noninvasive estimation of SEC and additional information for risk stratification and management of thromboembolic events in patients with AF.

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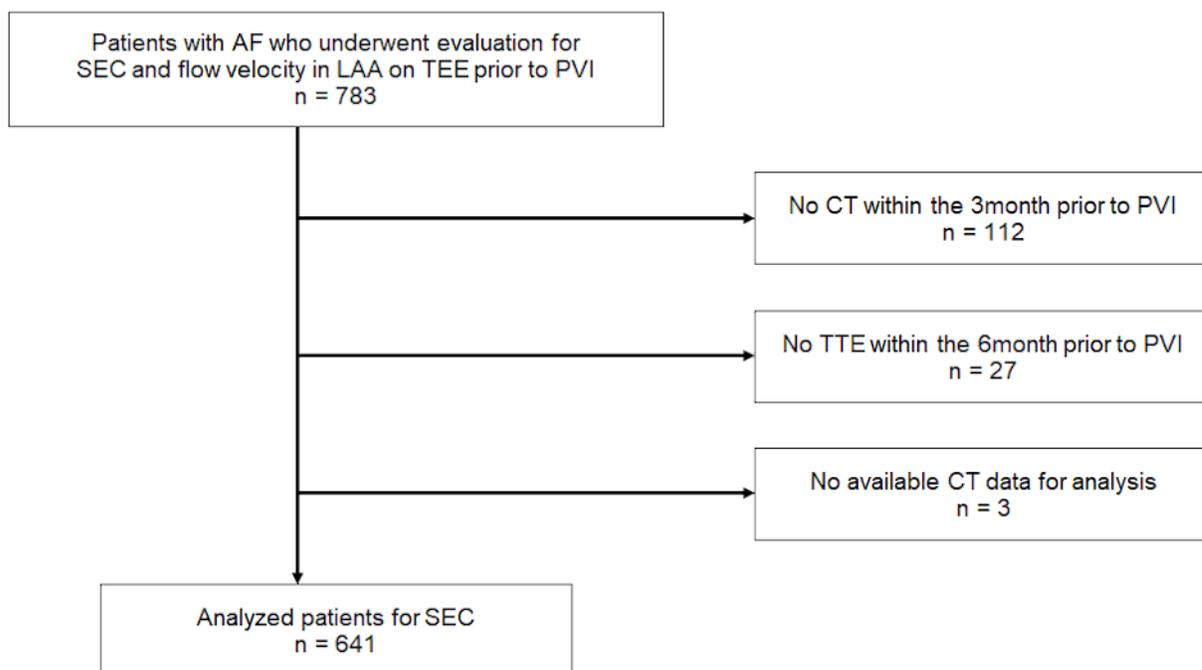
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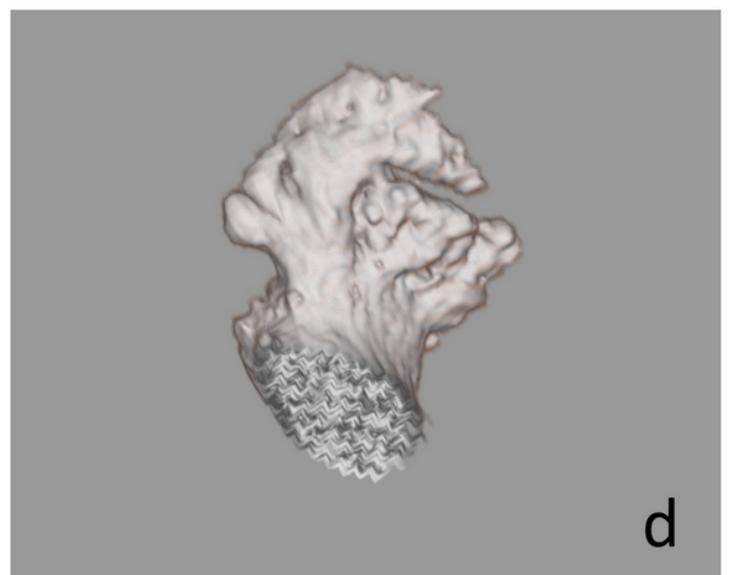
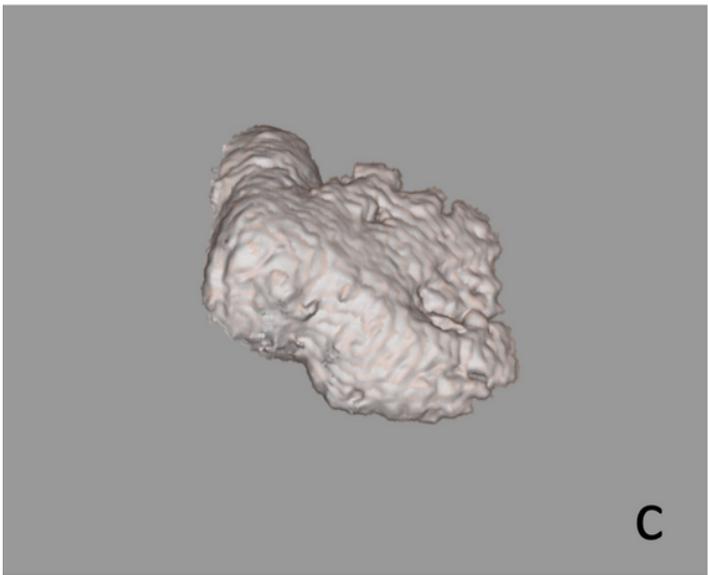
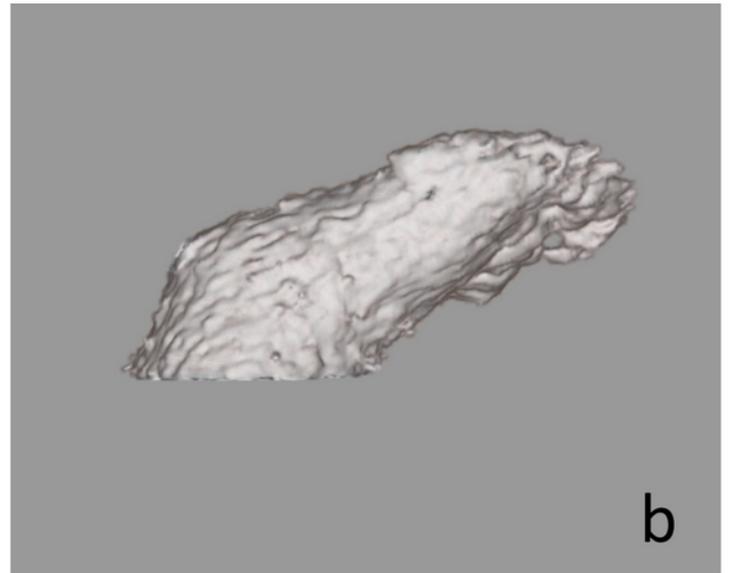
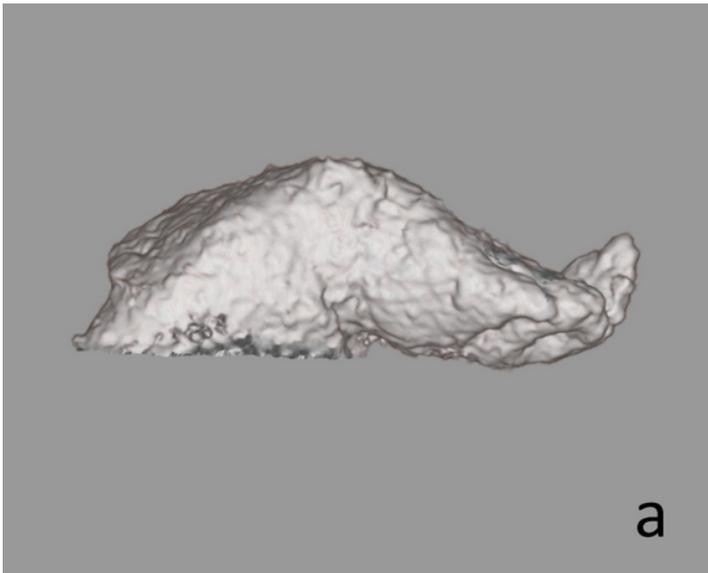
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## Figures



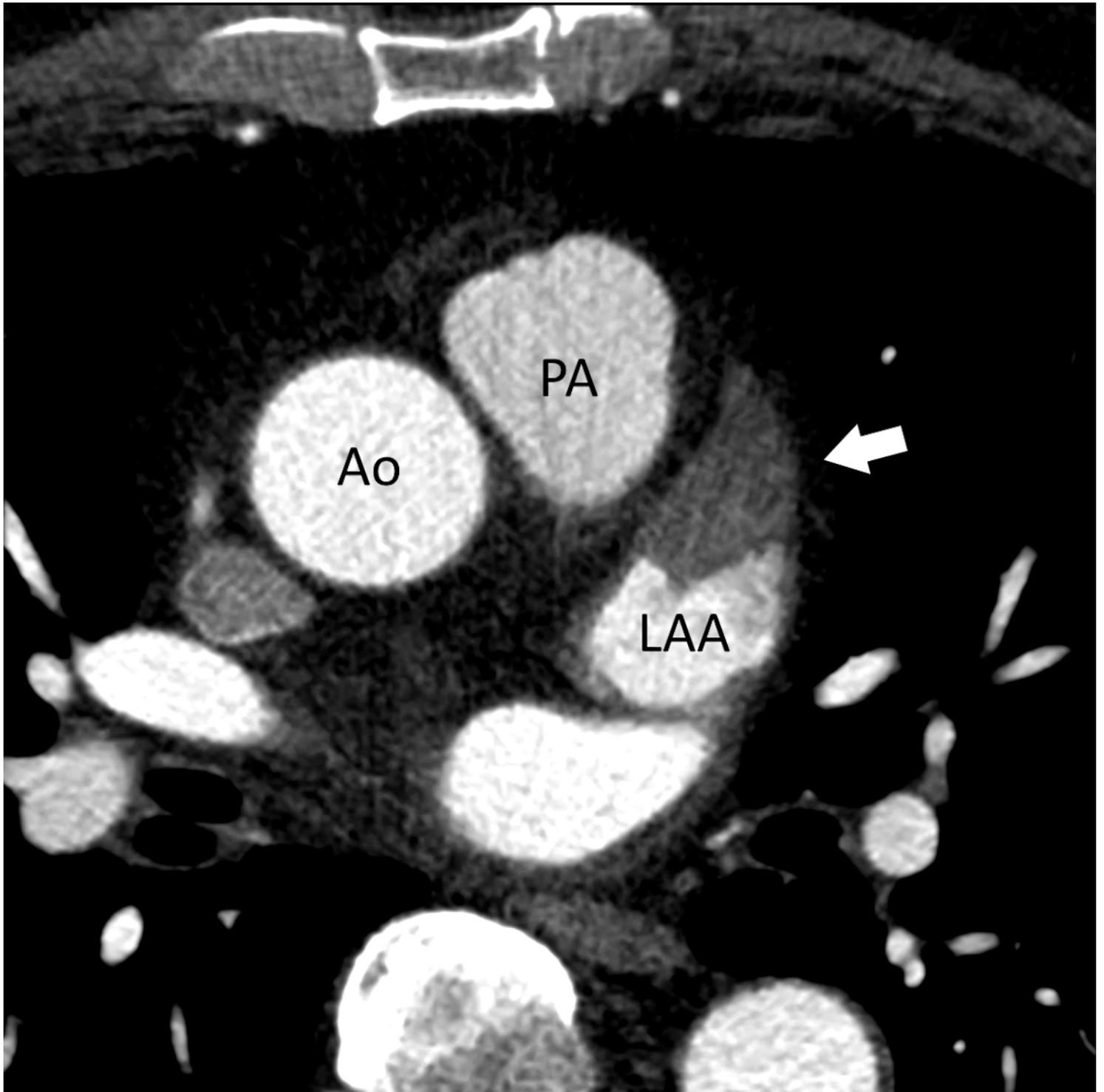
**Figure 1**

Flowchart for all participants. AF, atrial fibrillation; CT, computed tomography; LAA, left atrial appendage; PVI, pulmonary vein isolation; SEC, spontaneous echo contrast; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography



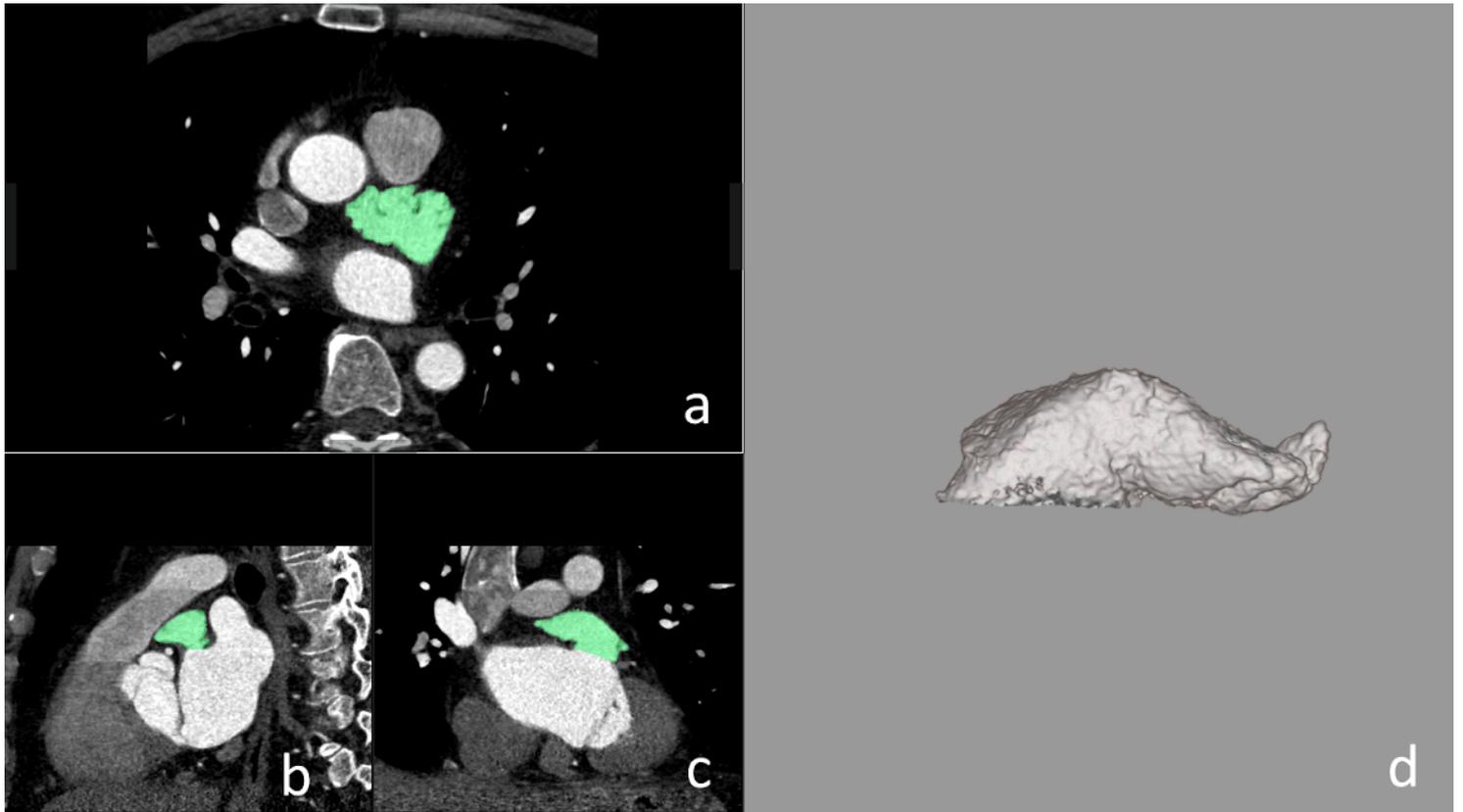
**Figure 2**

Typical examples of the 4 morphology types of the left atrial appendage: (a) Chicken wing, (b) Wind sock, (c) Cauliflower, and (d) Cactus



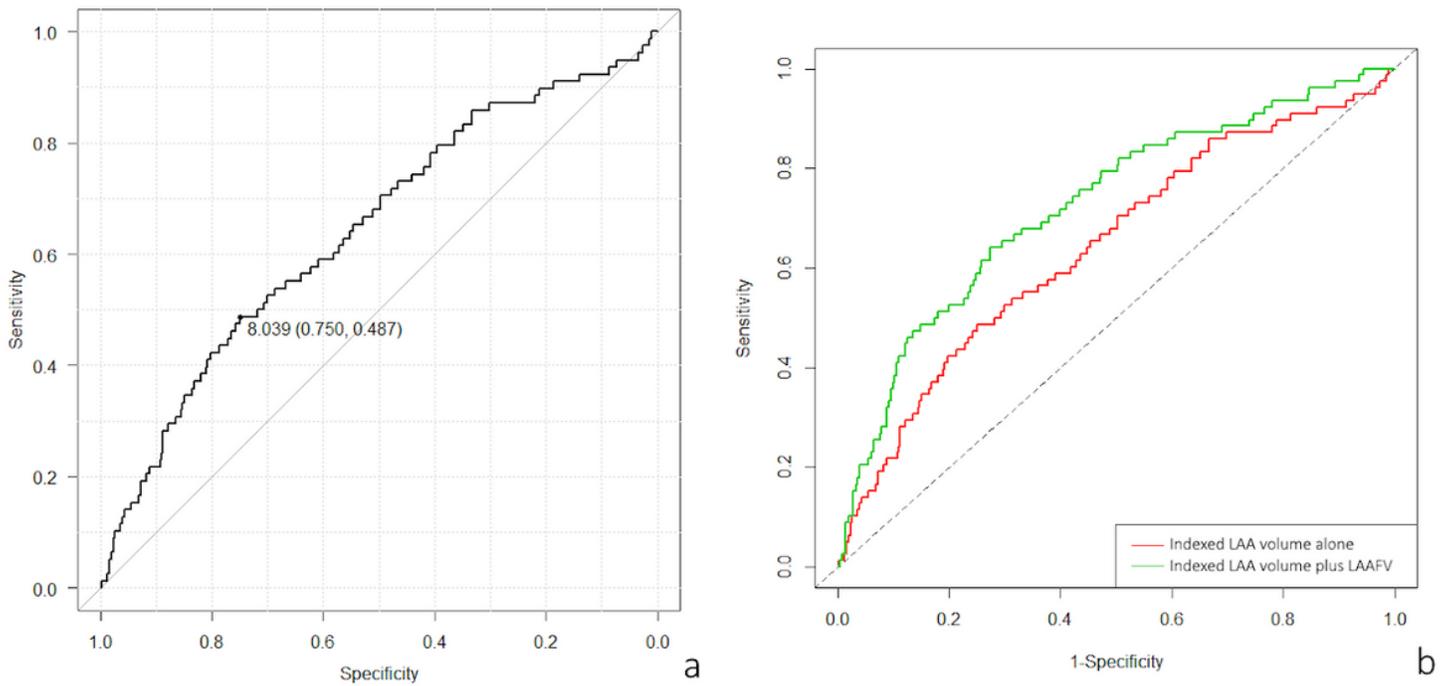
**Figure 3**

Cardiac computed tomography axial image with slice thickness of 0.75 mm of a 57-year-old man with a filling defect of the left atrial appendage (LAA) (arrow). Ao, aorta; PA, pulmonary artery



**Figure 4**

Methods of measuring the volume of the left atrial appendage (LAA) and representative case, a 53-year-old man with an LAA filling defect. LAA volume was quantified by contouring cross-sectional images using 3-dimensional analytical volume software, SYNAPSE VINCENT® (Fujifilm Medical Co., Tokyo, Japan). The operator contoured and filled the LAA at each slice (a–c, green area), and the computer calculated the LAA volume in cubic centimeters (cm<sup>3</sup>).



**Figure 5**

The receiver operating characteristic (ROC) curve for spontaneous echo contrast (SEC) in the left atrial appendage (LAA) shows a risk threshold for indexed LAA volumes above 8.04 cm<sup>3</sup>/m<sup>2</sup> (area under the curve, 0.66; sensitivity, 75%, specificity, 48.7%; 95% confidence interval, 0.575 to 0.711)(a). When LAAFV was added to indexed LAA volumes alone, the area under the curve (AUC) for prediction of SEC increased from 0.642 to 0.724 (P< 0.001) (b).