

Cardiac CT Differentiates Left Atrial Appendage Thrombi from Circulatory Stasis in Acute Stroke Patients

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Abstract. *Background/Aim:* The left atrial appendage (LAA) is the most typical origin for a cardioembolic thrombus stroke etiology. Although transesophageal echocardiography (TEE) is widely used, this technique encounters difficulties in differentiating solid thrombus from circulatory stasis/spontaneous echo contrast (SEC). We assessed whether cardiac computed tomography (cCT) could more accurately detect LAA thrombi. *Materials and Methods:* A total of 102 patients with suspected acute cardioembolic stroke/transient ischemic attack (TIA) without chronic atrial fibrillation underwent arterial and venous phase cCT and TEE. TEE and cCT were consensus read to define LAA thrombus, while TEE alone was used to determine SEC. The LAA/aorta Hounsfield unit (HU) ratio was measured in both phases independently and blinded to prior visual readings. The optimal LAA/aorta HU ratio cut-off value for differentiating thrombi and SEC was estimated. *Results:* TEE indicated 10 SECs and three thrombi. Consensus reading of cCT and TEE indicated that all thrombi detected in TEE were false-positive but revealed three actual thrombi missed in TEE. The LAA/aorta HU ratio correlated significantly with the presence of SEC both in arterial ($p=0.019$) and venous phases ($p=0.024$) and with the presence of thrombi in both phases ($p<0.001$). The best trade-off values for LAA/aorta HU ratio for the detection of thrombi was <0.245 in both phases. SEC was characterized with HU ratios of >0.245 and <0.577 in the arterial phase

and >0.245 and <0.824 in the venous phase. Values of sensitivity, specificity, positive and negative predictive value and accuracy for detection of thrombi were 100% for cCT in both phases. *Conclusion:* cCT is more accurate than TEE in the detection of LAA thrombi, especially when combined with the measurement of LAA/aorta HU ratio.

Cardiogenic emboli are common causes of stroke or transient ischemic attack (TIA) accounting for approximately 20-40% of all ischemic strokes/TIAs (1, 2). It is important when selecting the treatment of patients with acute ischemic stroke/TIA that the potential embolic sources are identified, especially when the underlying cause is suspected to be a cardiac embolism (2). However, brief asymptomatic paroxysmal atrial fibrillation (AF) events may remain undetected by traditional methods of screening. Until now, transesophageal echocardiography (TEE) has been the golden standard for detecting left atrial (LA) and LA appendage (LAA) thrombi (3, 4). TEE using monoplane, biplane or multiplane imaging is known to be able to detect thrombi in both LA and LAA with a high degree of sensitivity and a specificity varying from 93% to 100% (5). TEE has also been used to exclude LA and LAA thrombi before cardiac procedures, e.g. percutaneous balloon valvuloplasty, LAA closure, pulmonary vein isolation and direct current cardioversion are considered to be associated with high-risk for thromboembolism due to the presence of thrombi (5-9). Despite its widespread use, TEE is a semi-invasive test and cannot invariably be conducted in non-co-operative patients or in subjects with swallowing problems. Furthermore, TEE is not available at all times, especially in off-duty hours.

AF leads to an impaired blood flow in LAA due to disorganized contraction of LA (10). This circulatory stasis can often be seen in TEE as a spontaneous echo contrast (SEC) (11, 12). This phenomenon is attributable to an echogenic swirling pattern of blood flow, distinct from

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Key Words: Cardiac computed tomography, transesophageal echocardiography, spontaneous echo contrast, solid thrombus.

white noise artifacts, caused by an increased ultrasonic back-scatter from aggregation of the cellular components of blood in the conditions of low-velocity blood flow (12, 13). The presence of SEC, even without the presence of a solid thrombus, has been associated with a higher risk of thromboembolism and cerebrovascular incidents. The decreased blood flow velocity in TEE may be interpreted as a sign of circulatory stasis and, thus, potentially thrombogenic circumstances in LAA.

SEC is major risk factor for cardioembolic events; however, there are numerous studies claiming that the risk of cardioembolic stroke acutely after cardioversion in a patient with SEC is low, irrespective of whether the patient has received anticoagulation, whereas the presence of an intracardiac thrombus is a contraindication for the procedure (14). Unfortunately, differentiating SEC from a solid intracardiac thrombus is often difficult in TEE (15). It would be beneficial if there was some validated quantitative method that could more accurately distinguish a low blood velocity from a real thrombus (16). There are preliminary reports indicating that multidetector computed tomography (CT) could be used for distinguishing between SEC and LAA thrombi (14-17). The measurement of the Hounsfield unit (HU) ratio between LAA and ascending aorta (LAA/aorta HU ratio) from a single transversal slice in cardiac CT (cCT) might represent one way to differentiate a thrombus from SEC (16). The purpose of this study was to examine whether (i) cCT could be used for quantitative and accurate detection of LAA thrombi and SEC in stroke/TIA patients and (ii) arterial or venous phase cCT should be recommended for this purpose.

Materials and Methods

This prospective EMBODETECT study was approved by the Kuopio University Hospital Research Ethics Board and all clinical investigations have been conducted according to the principles expressed in the Declaration of Helsinki. Written informed consent was obtained from the patients or their legally authorized representative if the patient was unable to provide consent due to impaired mental or physical function caused by stroke.

Study design and population. Patients with acute stroke/TIA of suspected cardioembolic etiology, admitted to Kuopio University Hospital between March 2005 and October 2008, were potential candidates for this study. Altogether, 115 patients with stroke/TIA of suspected cardioembolic etiology other than atrial fibrillation were included. Thirteen patients had to be excluded: TEE was not technically successful in seven patients due to poor patient cooperation; four patients were excluded because of a technical error in CT and two patients refused to undergo TEE. Thus, a total of 102 patients underwent successfully both arterial and venous phase cCT and TEE as a part of acute imaging protocol of stroke/TIA. The time frame between cCT and TEE was 0.92 ± 4.45 (range=-7-27) days although in three patients the interval was more than a week.

Transesophageal echocardiography and cCT imaging. TEE was performed after the standard clinical preparation using the Vivid 7 cardiovascular ultrasound system with its 5- to 7- (6.7-) MHz multiplane TEE probe (GE Medical Systems, Buckinghamshire, UK) as a part of daily routine work of eight consulting cardiologists. TEE images of the LA and LAA were evaluated in the horizontal (0°) plane and in the plane with the rotation of the imaging sector (0° - 180°) during continuous visualization of the LAA.

Contrast-enhanced cCT was performed with a 16-slice scanner (Somatom Sensation 16 and Somatom Definition AS; Siemens Medical Solutions, Forchheim, Germany) without beta-blockers. The aortic arch, as well as cervical and intracranial arteries were scanned first, immediately followed by the scanning of the ascending aorta and heart. First, 100 ml contrast agent was injected through an 18-gauge catheter into the antecubital vein at 5 mL/s, followed by a 50-ml injection at 2 ml/s and a subsequent 20-ml saline chaser. Cardiac imaging was performed during mid-diastole in all study subjects. The collimation was 16×0.75 mm, the rotation time was 0.42 s and the tube potential was 120 kV; the current was set to 500 mAs for the first 80 patients and reduced to 250 mAs thereafter. We calculated the product of the volume CT dose index (CTDIvol) and scanning length (dose-length product in milligrays times centimeters) and estimated the effective dose (in millisieverts (mSv)) using a normalization factor for the adult chest ($0.017 \text{ mSv} \cdot \text{mGy}^{-1} \cdot \text{cm}^{-1}$). The radiation dose per patient was 10.0 ± 3.5 mSv. Mid-diastolic 0.75- to 1.0-mm-thick slices with 20-25% overlaps were reconstructed.

In TEE, the presence of an LAA thrombus was identified by intense echogenicity without swirling patterns in the LAA. SEC was characterized by dynamic clouds of echoes curling slowly into a circular or spiral shape within the LAA cavity. The severity of SEC was not evaluated. In cCT, a thrombus was visually defined as a filling defect that was oval or round in both the arterial and venous phase images. The presence of SEC was not visually interpreted in cCT. Finally, TEE results and confirmatory cCT were evaluated in consensus by an experienced cardiologist (P.S.) and an imaging cardiologist (M.H.) and this was used as the reference standard for the presence of an LAA thrombus.

Blinded to visual assessments made by experts, clinical findings or patient histories, a junior radiology researcher measured the LAA/aorta HU ratio in both the arterial and the venous phases. In this quantitative analysis, regions of interest (ROI) of approximately 50-75 mm² were placed inside the tip of LAA or inside a filling defect seen nearby whether not seen in the LAA tip. Another ROI was placed inside the ascending aorta in the same section to generate the LAA/aorta HU ratio. The venous and arterial phase LAA/aorta HU ratios were calculated from the same section (Figures 1 and 2).

Statistical analyses. Continuous variables with normal distribution are presented as mean \pm standard deviation (SD), whereas categorical variables as absolute values and percentages. Spearman's correlation coefficient was used to investigate the associations between continuous variables, while Chi-square test to investigate nominal variables. Based on the abnormal distribution revealed in the Kolmogorov-Smirnov test, Mann-Whitney U-test was used to compare LAA/aorta HU ratio between patients with and without SEC and thrombus. Statistical significance was set at $p < 0.05$ and high statistical significance at $p < 0.01$. The receiver operating characteristic (ROC) curve analysis was performed to (i)

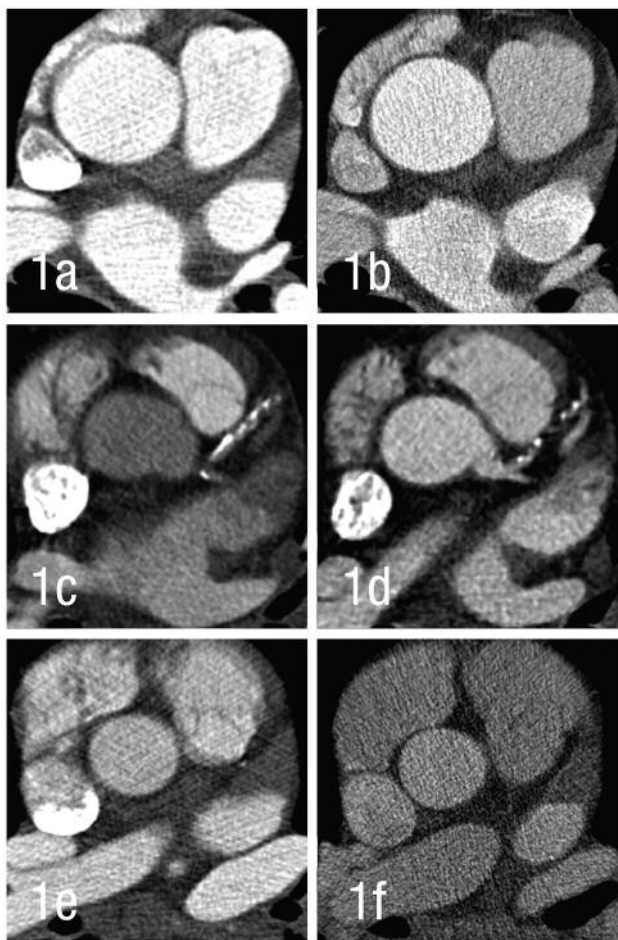


Figure 1. Three patients (1a and b; 1c and d; 1e and f) out of 102 suspected cardioembolic stroke patients without chronic atrial fibrillation had a decreased (<0.245) left atrial appendage (LAA) and ascending aorta Hounsfield unit ratio in cardiac computed tomography indicative of the presence of an LAA thrombus. Figure 1a, c and e are imaged in the arterial phase of contrast agent flow, while Figure 1b, d and f in the venous phase of contrast agent flow. Patients were considered to have spontaneous echocontrast in transesophageal echocardiography (TEE); however, the consensus reading of cardiac computed tomography and TEE revealed real solid thrombi.

determine optimal cut-off points for the diagnosis of LAA thrombi and SEC in both the arterial and venous phases and (ii) test the diagnostic value of the LAA/aorta HU ratio for characterizing LAA filling defects. In order to define the most optimal trade-off between sensitivity and specificity in the ROC curve, the closest coordinates to the point ($x=0, y=1$) were used. With the TEE and cCT being read in consensus by two experts used as the reference standard, the sensitivity, specificity and positive and negative predictive value and accuracy of dichotomized LAA/aorta HU ratio for the detection of LAA thrombi and SEC were calculated. Data were analyzed using SPSS for Windows (version 19, 1989-2010; SPSS Inc., Chicago, IL, USA).

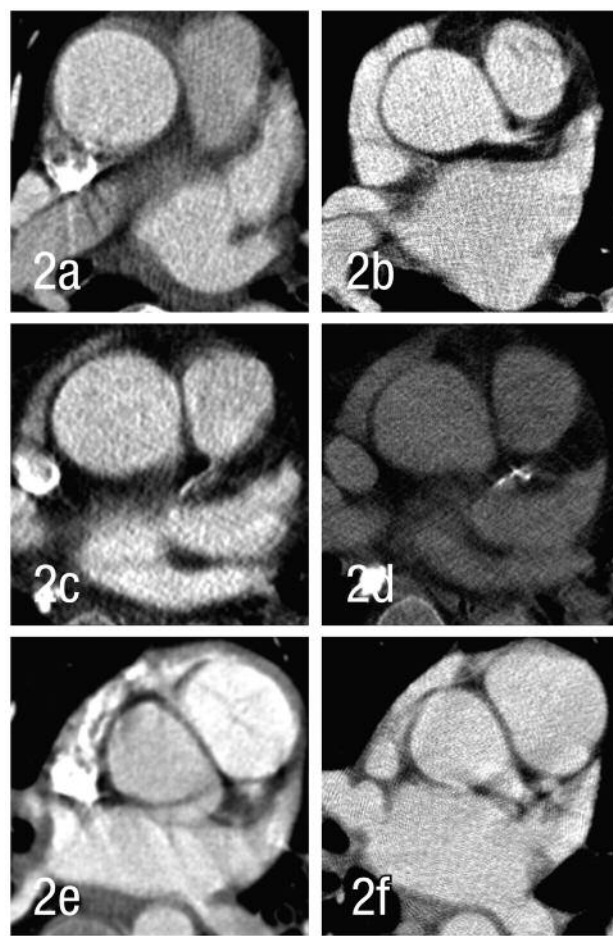


Figure 2. Three patients (2a and b; 2c and d; 2e and f) out of 102 suspected cardioembolic stroke patients without chronic atrial fibrillation had false-negative left atrial appendage (LAA) thrombus in echocardiography (TEE). In the consensus reading of TEE and cardiac computed tomography, all patients were shown to have relatively good blood flow in LAA. Figure 2a, c and e are imaged in arterial phase of contrast agent flow, whereas Figure 2b, d and f in venous phase of contrast agent flow. All patients were having relatively high left atrial appendage and ascending aorta Hounsfield unit ratios in both imaging phases in cardiac computed tomography.

Results

The clinical characteristics of the 102 stroke/TIA patients are summarized in Table I. The results of TEE were interpreted as revealing a total of three LAA thrombi and 10 cases of SEC. After a profound consensus evaluation together with cCT results, all three LAA thrombi in TEE were determined to represent SECs and, in contrast, three SECs were reclassified as solid thrombi. All six patients with a suspected or diagnosed thrombus had undergone cCT prior to TEE. Their arterial and venous phase cCT images are shown in Figures 1 and 2.

Table I. Clinical characteristics of the 102 patients with acute cardioembolic stroke or transient ischemic attack.

Age, years	61.7±10.6
Males, n (%)	70 (68.6)
Body mass index, kg/m ²	27.6±4.4
Body surface area, m ²	2.0±0.2
Caucasian race, n (%)	102 (100.0)
Hypertension, n (%)	65 (63.7)
Hyperlipidemia, n (%)	45 (44.1)
Diabetes, n (%)	15 (14.7)
Smokers, n (%)	31 (30.4)
Current stroke, n (%)	93 (91.2)
Current transient ischemic attack (TIA), n (%)	9 (8.8)
Prior stroke or TIA, n (%)	11 (13.4)
Prior myocardial infarction, n (%)	16 (15.7)

The LAA/aorta HU ratio was measured in a separate session blinded to previous findings in all 102 stroke/TIA patients. The measured LAA/aorta HU ratio statistically correlated significantly with the presence of thrombi confirmed in cCT ($p < 0.001$) in both phases. The HU ratios also correlated with the presence of SEC detected in TEE both in the arterial ($p = 0.019$) and venous phases ($p = 0.024$).

The receiver operating characteristics. ROC-curves for the LAA/aorta HU ratios in both arterial and venous phases are shown in Figure 3 both for thrombi and SEC. The highest value of sensitivity and specificity for detection of LAA thrombus was obtained with the LAA/aorta HU ratio trade-off point of < 0.245 in both arterial and venous phases. The areas under the ROC curve (AUC) for thrombus detection in both phases were 1.0, *i.e.* a perfect predictive value. Subsequently, sensitivity, specificity, positive and negative predictive values and overall accuracy to identify solid thrombus were 100%. The exact values for the LAA/aorta HU ratio were 0.168, 0.196, 0.241 in arterial phase and 0.180, 0.241, 0.245 in the venous phase. Two patients out of three with solid thrombi proved to have paroxysmal AF, whereas, in one patient, 24-h Holter electrocardiogram (ECG) was not capable to identify any arrhythmia.

With respect to the discrimination of SEC from normal blood flow in the arterial phase, the LAA/aorta HU ratio trade-off point with the highest value of sensitivity and specificity was < 0.577 . The AUC for SEC detection in the arterial-phase was < 0.73 indicating an intermediate predictive value.

Discussion

The main finding in the current study was that in stroke/TIA patients cCT, especially when complemented with an LAA/aorta HU ratio measurement, was able to diagnose LAA thrombi more accurately than TEE. TEE missed all

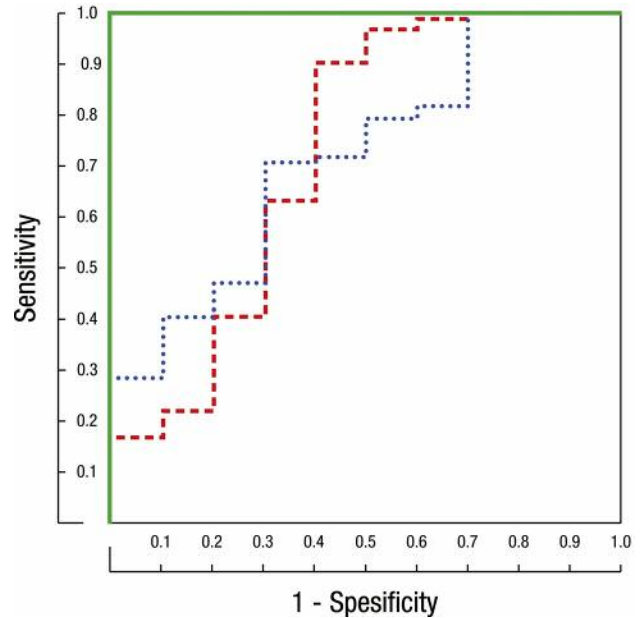


Figure 3. The receiver operating characteristic (ROC) curve for the left atrial appendage (LAA) and ascending aorta Hounsfield unit (HU) ratio as a means of detecting thrombi in both arterial and venous phases is shown as a solid (green) line. Area under ROC-curve for detecting thrombi is 1.0 for both phases. The ROC curve for the LAA/aorta HU ratio, as a means of detecting spontaneous echocontrast (SEC) in the arterial phase, is shown as a dashed (red) line and in the venous phase as a dotted (blue) line. Areas under the ROC-curve for detecting SEC were 0.73 and 0.72, respectively.

three LAA thrombi that were unquestionably present in the cCT in the consensus evaluation performed by an experienced cardiologist and a radiologist. By dichotomizing patients according to an LAA/aorta HU ratio cut-off value of < 0.245 , even a junior radiology researcher was able to correctly detect all three cases of solid LAA thrombi with no false positive findings.

Kim *et al.* have shown that LAA/aorta HU ratio is inversely associated in increasing grades with the presence of SEC and thrombus in TEE in patients with AF (16). They demonstrated that a cut-off value of > 0.25 had a high negative predictive value for LAA thrombi. In the present study, we obtained exactly the same cut-off value for detecting the presence of thrombi in patients with suspected cardioembolic stroke/TIA with no prior diagnosis of AF. Hur *et al.* have previously shown that the LAA/aorta HU ratio displayed a good concordance to the thrombus and SEC seen in TEE also in stroke patients almost all of whom were suffering AF (17). Furthermore, a recent meta-analysis demonstrated that cCT is a reliable, reproducible and accurate method for detecting LAA thrombi and SEC and it was recommended as an alternative method to TEE for the

detection of LAA thrombi (18). In our study, the golden standard of SEC was utilized in the clinical diagnosis of TEE. While the presence of SEC was not based on a consensus reading, the relationship between LAA/aorta HU ratio and visual assessment of SEC in TEE was lower than in previous studies. However, in contrast, we were able to separate SEC from thrombi in all cases.

In the present study, which consisted of patients without known AF, the incidence of LAA thrombi was 3%. This is in line with a previous study conducted in patients both with and without AF (17). The low prevalence introduces limitations in the statistical assessment. However, both the positive and negative predictive value of LAA/aorta HU ratio proved to be excellent even in this challenging study population. Furthermore, our results show that the cut-off value of 0.25 can reliably differentiate real thrombi from SEC seen in TEE. Since SEC is often difficult to differentiate from a solid thrombus in TEE, cCT complemented with LAA/HU ratio measurement can be advocated as both a confirmatory method and the primary imaging tool. The imaging finding of LAA thrombus has a high impact on the treatment, especially in patients with no previous diagnosis of AF, which was the inclusion criterion in the present study.

Percutaneous balloon valvuloplasty, LAA closure, pulmonary vein isolation procedures and direct current cardioversion are contraindicated when TEE reveals the presence of SEC in LAA (7, 8). While the aforementioned procedures frequently require cCT, it is recommended to utilize all the gathered information. cCT, especially when supplemented with HU measurements, is becoming more reliable in its ability to detect SEC, while TEE remains a semi-invasive test that is not always feasible in non-cooperative patients or in patients with swallowing problems. Although TEE does not increase the patient's radiation exposure, it is time-consuming, involves physical discomfort and requires special skills. Previous studies have shown that higher accuracy of cCT can be achieved by using either two-phase or delayed CT imaging technique (15, 17). In the current study, no difference in the accuracy of LAA/aorta HU ratio was detected between the arterial and venous phases of the imaging. Thus, either one of the imaging phases can be used for the measurement of the LAA/aorta HU ratio in a clinical setting.

The clinical examination of acute stroke/TIA patient includes usually not only a brain CT scan but also carotid artery CT combined with imaging of the aortic arch. Current prospectively ECG-gated CT scans involve extremely low radiation doses (19). In further studies, extending the image area of carotid arteries and aortic arch down to the LAA would not significantly increase the radiation dose but would provide a valid and simple method to rule out LAA thrombi in acute stroke/TIA patients (20).

Another important aspect of LAA imaging is the false-positive findings in TEE (6, 18). In this study, there were three LAA thrombi that could not be confirmed by cCT. On the basis of negative cCT findings, the clinical consensus was that anticoagulation treatment should be terminated. All three patients exhibited LAA/aorta HU ratios above the cut-off value of 0.245. In all of these cases, the TEE findings could be explained by anatomical structures of LAA visualized better by cCT. It is well-known that the LAA has multiple anatomical variations (21). Since TEE is still mainly performed by two-dimensional images, the presence of trabeculation and crypts in LAA can lead to a wrong evaluation of thrombus (22). Three-dimensional TEE imaging will potentially provide more accurate appearance of LAA anatomy in the future (23). While it is always recommended that stroke/TIA patients with an evident thromboembolism should receive lifelong anticoagulation therapy, it is important to confirm uncertain TEE findings with other imaging methods, especially in young patients and in patients with a high bleeding risk.

Despite all efforts and an extensive information campaign aimed at the neurologists, a great number of consecutive stroke/TIA patients were not screened and included in the study due to their heavy clinical load. Thus, the main study limitation was that the number of patients in our study was relatively small and that our study included only a small number of positive findings. On the other hand, an inexperienced radiology researcher with the simple LAA/aorta HU ratio measurement was able to correctly detect all thrombi from a clinically relevant patient population. TEE was performed by different clinicians with varying degrees of experience, a fact reflecting clinical reality. Nevertheless, the LAA/aorta HU ratio measurements were performed by a radiology researcher with even less experience.

In conclusion, we herein demonstrated that cCT was more accurate than TEE in the detection of LAA thrombi in patients with suspected cardioembolic stroke without previously diagnosed AF. The LAA thrombi detection using two comprehensive modalities requiring highly specialized readers can be replaced with a straightforward and rapid HU ratio measurement in cCT. The presence of thrombi can be evaluated reliably by using a decreased LAA/aorta HU ratio under 0.245 as a quantitative indicator for the presence of a thrombus.

References

- 1 Bonita R: Epidemiology of stroke. *Lancet* 339: 342-344, 1992.
- 2 Ferro JM: Cardioembolic stroke: An update. *Lancet Neurol* 2: 177-188, 2003.
- 3 Omran H, Jung W, Rabahieh R, Wirtz P, Becher H, Illien S, Schimpf R and Lüderitz B: Imaging of thrombi and assessment of left atrial appendage function: a prospective study comparing transthoracic and transesophageal echocardiography. *Heart* 81: 192-198, 1999.

- 4 Colonna P, Habib G, Ringelstein EB, Sicari R, Zamorano JL, Sitges M, Caso P and European Association of Echocardiography: Recommendations for echocardiography use in the diagnosis and management of cardiac sources of embolism: European Association of echocardiography (EAE) (a registered branch of the ESC). *Eur J Echocardiogr* 11: 461-476, 2010.
- 5 Asher CR and Klein AL: Transesophageal echocardiography in patients with atrial fibrillation. *PACE* 26: 1597-1603, 2003.
- 6 Manning WJ, Weintraub RM, Waksmonski CA, Haering JM, Rooney PS, Maslow AD, Johnson RG and Douglas PS: Accuracy of transesophageal echocardiography for identifying left atrial thrombi. *Ann Intern Med* 123: 817-822, 1995.
- 7 Kronzon I, Tunick PA, Glassman E, Slater J, Schwinger M and Freedberg RS: Transesophageal echocardiography to detect atrial clots in candidates for percutaneous transseptal mitral balloon valvuloplasty. *J Am Coll Cardiol* 16: 1320-1322, 1990.
- 8 Nucifora G, Faletta FF, Regoli F, Pasotti E, Pedrazzini G, Moccetti T and Auricchio A: Evaluation of the left atrial appendage with real-time 3-dimensional transesophageal echocardiography: implications for catheter-based left atrial appendage closure. *Circ Cardiovasc Imaging* 4: 514-523, 2011.
- 9 Orsinelli DA and Pearson AC: Usefulness of transesophageal echocardiography to screen left atrial thrombus before elective cardioversion for atrial fibrillation. *Am J Cardiol* 72: 1337-1339, 1993.
- 10 Shimizu T, Takada T, Shimode A, Fujita Y, usuki N, Kato B, Takaishi S, Hirayama T, Hanzawa K and Hasegawa Y: Association between paroxysmal atrial fibrillation and the left atrial appendage ejection fraction during sinus rhythm in the acute stage of stroke: A transesophageal echocardiographic study. *J Stroke Cerebrovasc Dis* 20: 1052-3057, 2013.
- 11 Wolf PA, Abbott RD and Kannel WB: Atrial fibrillation as an independent risk factor for stroke: the Framingham study. *Stroke* 22: 983-988, 1991.
- 12 Asinger RW, Koehler J, Pearce LA, Zabalgoitia M, Blackshear JL, Fenster PE, Strauss R, Hess D, Pennock GD, Rothbart RM and Halperin JL: Pathophysiologic correlates of thromboembolism in nonvalvular atrial fibrillation: II. Dense spontaneous echocardiographic contrast (The Stroke Prevention in Atrial Fibrillation (SPAF-III) study). *J Am Soc Echocardiogr* 12: 1088-1096, 1999.
- 13 Merino A, Hauptman P, Badimon L, Badimon JJ, Cohen M, Fuster V and Goldman M: Echocardiographic "smoke" is produced by an interaction of erythrocytes and plasma proteins modulated by shear forces. *J Am Coll Cardiol* 20: 1661-1668, 1992.
- 14 Patel SV and Flaker G: Is early cardioversion for atrial fibrillation safe in patients with spontaneous echocardiographic contrast? *Clin Cardiol* 31: 148-152, 2008.
- 15 Sipola P, Hedman M, Onatsu J, Turpeinen A, Halinen M, Jäkälä P and Vanninen R: Computed tomography and echocardiography together reveal more high-risk findings than echocardiography alone in the diagnostics of stroke etiology. *Cerebrovasc Dis* 35: 521-530, 2013.
- 16 Kim YY, Klein AL, Halliburton SS, Popovic ZB, Kuzmiak SA, Sola S, Garcia MJ, Schoenhagen P, Natale A and Desai MY: Left atrial appendage filling defects identified by multidetector computed tomography in patients undergoing radiofrequency pulmonary vein antral isolation: A comparison with transesophageal echocardiography. *Am Heart J* 154: 1199-1205, 2007.
- 17 Hur J, Kim YJ, Lee HJ, Nam JE, Ha JW, Heo JH, Chang HJ, Kim HS, Hong YJ, Kim HY, Choe KO and Choi BW: Dual-enhanced cardiac CT for detection of left atrial appendage thrombus in patients with stroke. A prospective comparison study with transesophageal echocardiography. *Stroke* 42: 2471-2477, 2011.
- 18 Romero J, Husain SA, Kelesidis I, Sanz J, Medina HM and Garcia MJ: Detection of left atrial appendage thrombus by cardiac computed tomography in patients with atrial fibrillation. A meta-analysis. *Circ Cardiovasc Imaging* 6: 185-194, 2013.
- 19 Kondratyev E and Karmazanovsky G: Low radiation dose 256-MDCT angiography of the carotid arteries: effect of hybrid iterative reconstruction technique on noise, artifacts, and image quality. *Eur J Radiol* 82: 2233-2239, 2013.
- 20 Taina M, Vanninen R, Hedman M, Jäkälä P, Kärkkäinen S, Tapiola T and Sipola P: Left atrial appendage volume increased in more than half of patients with cryptogenic stroke. *PLOS One* doi: 10.1371/journal.pone.0079519, 2013.
- 21 Walker DT, Humphries JA and Phillips KP: Anatomical analysis of the left atrial appendage using segmented, three-dimensional cardiac CT: A comparison of patients with paroxysmal and persistent forms of atrial fibrillation. *J Interv Card Electrophysiol* 34: 173-179, 2012.
- 22 Willens HJ, Qin JX, Keith K and Torres S: Diagnosis of a bilobed left atrial appendage and pectinate muscles mimicking thrombi on real-time 3-dimensional transesophageal echocardiography. *J Ultrasound Med* 29: 975-980, 2010.
- 23 Rathi VK, Reddy ST, Anreddy S, Belden W, Yamrozik JA, Williams RB, Doyle M, Thompson DV and Biederman RW: Contrast-enhanced CMR is equally effective as TEE in the evaluation of left atrial appendage thrombus in patients with atrial fibrillation undergoing pulmonary vein isolation procedure. *Heart Rhythm* 10: 1021-1027, 2013.

Received April 24, 2016

Revised May 30, 2016

Accepted May 31, 2016